Learning about COVID-19 vaccination errors from the ISMP Vaccination Error Reporting Program (VERP)

Medication Safety Alert! January 14, 2021

https://www.ismp.org/resources/learning-errors-new-covid-19-vaccines

Vaccines available in US include Moderna and Pfizer-BioNTech mRNA vaccines and Johnson and Johnson (Janssen) viral vector vaccine

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Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Learning from errors with the new COVID-19 vaccines

Problem: In mid-December, the US Food and Drug Administration (FDA) granted emergency use authorization (EUA) to both the Pfizer-BioNTech and Moderna coronavirus disease 2019 (COVID-19) vaccines. Since then, ISMP has received numerous voluntary reports of COVID-19 vaccine errors or hazards through the ISMP National Vaccine Errors Reporting Program (VERP), the ISMP National Consumer Medication Errors Reporting Program (C-MERP), and via email correspondence from professional colleagues. (See the last recommendation on **page 5** regarding a mandatory requirement to report all COVID-19 vaccine errors and adverse reactions to the Vaccine Adverse Event Reporting System (https://vaers.hhs.gov). The following highlights a few of the missteps happening across the nation and internationally, from vaccine dilution errors to look-alike product mix-ups. There is much to be gleaned from these reports, as the same types of errors are likely happening globally, and similar risks exist in most settings. We conclude with safe practice recommendations to help prevent these types of errors in your practice setting.

Dilution Errors

Four dilution errors were reported with the Pfizer-BioNTech COVID-19 vaccine, which was granted EUA for immunization to prevent COVID-19 in individuals 16 years and older. After thawing, each Pfizer-BioNTech multiple-dose vaccine vial contains 0.45 mL, which must be diluted using 1.8 mL of preservative-free (not bacteriostatic) 0.9% sodium chloride injection. Once properly diluted, each vial contains 6, perhaps even 7, doses when using low dead-volume syringes/needles to extract each 0.3 mL (30 mcg) dose. The vaccine is administered intramuscularly (IM) as a series of 2 doses 3 weeks apart.

Dilution errors result in administering too much or too little vaccine. If you add too much diluent, doses may be ineffective; if you add too little diluent, doses may invoke stronger adverse effects (if one happens). In one reported case, mixing the vaccine with too little diluent was suspected when only 0.25 mL remained in the multiple-dose vial when attempting to access the fifth dose. As instructed in the *Fact Sheet*, the 0.25 mL of remaining vaccine was discarded (rather than pooled with excess vaccine from other vials). The previous four doses may represent overdoses.

According to a second report, an inadequate volume of diluent (approximately 1 mL) was added to the vaccine vial. Before the error was discovered, a 60-year-old patient received a nearly 2-fold overdose during his first vaccine dose. The patient had no initial reaction to the overdose and was discharged after an hour, with follow-up calls planned for the next 48 hours. Clinic staff called a Pfizer representative to determine if the patient's second vaccine dose should be altered, but no immediate guidance was offered.

The third dilution error was similar to the previous error in that only 1 mL instead of 1.8 mL of 0.9% sodium chloride injection was used to dilute the vaccine. Again, only one clinic patient received the nearly 2-fold overdose before the error was caught. No details were provided regarding the patient's response to the overdose.

In the last case, which happened internationally, eight healthcare workers in a long-term care (LTC) facility received the entire vial contents (0.45 mL), without dilution, for their first dose of the Pfizer-BioNTech vaccine. Four of the eight workers were hospitalized as a

continued on page 2 — Vaccine errors >

SAFETY briefs

Bamlanivimab confused with belimumab. Four residents at a long-term care (LTC) facility received 700 mg of belimumab (BENLYSTA) instead of the intended bamlanivimab intravenously (IV). Belimumab is indicated for patients with active systemic lupus erythematosus or active lupus nephritis who are also taking other lupus medications. Bamlanivimab was granted emergency use authorization (EUA) for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and children 12 years and older (weighing at least 40 kg) who are at high risk for progressing to severe COVID-19 and/or hospitalization. This event began when a nurse at the LTC facility called the offsite pharmacy with orders but either mispronounced or misread bamlanivimab. The pharmacist heard belimumab, which he prepared and dispensed. The preparations were infused over 60 minutes, but no adverse reactions were reported for any of the residents.

There are several elements in common with belimumab and bamlanivimab. Each drug is added to a 250 mL intravenous (IV) bag of 0.9% sodium chloride injection. Other diluents may also be used with belimumab, but 0.9% sodium chloride injection is one of the recommended base solutions. Also, the dosages can overlap. The pharmacist did not question the dose of 700 mg for belimumab because it aligned with the patients' weights and it fell within a safe dosing range. Both are infused IV over 60 minutes. Bamlanivimab is available in 700 mg vials, while belimumab comes in 120 mg and 400 mg vials for IV use, and in a prefilled syringe or autoinjector for subcutaneous injection. In this case, the pharmacist processing the order was not familiar with either drug. Apparently, the preparations, labeled as belimumab, did not raise a red flag at the LTC facility, either. The incident occurred just as bamlanivimab use was increasing for patients with early

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https://www.ismp.org/resources/learning-errors-new-covid-19-vaccines

Issue: COVID-19 vaccine errors

- Dilution errors leading to under- or overdose of vaccine
- Mixing errors with 2-component vaccines (diluent instead of vaccine or wrong diluent such as sterile water).
- Air injected into vial instead of diluent
- Storage issues (unsegregated vaccine brands in refrigerator)
- Wrong vaccine given for dose 2 (not checking/documenting in immunization information system)
- Administration to wrong age group
- Waste of vaccine and not taking advantage of over-fill in vaccine vials
- Errors in scheduling second dose
- Look-alike vials (vaccine-monoclonal antibody mix-up)
- Shoulder injury related to vaccine administration (SIRVA)

Avoiding shoulder injury from intramuscular vaccines

With the roll-out of COVID-19 vaccination programmes to tens of millions of people, some individuals might receive vaccines, which have received rigorous safety checks and approval from regulatory bodies, via intramuscular injection. However, the safety around the technique used and the site of injection, in particular, has received little attention. As recommended by the Joint Committee on Vaccination and Immunisation (JCVI), adults aged 16 years or older will be the main population receiving the intramuscular vaccine. The JCVI recommends the deltoid muscle as the optimal injection site, shown graphically as a triangle with the base starting around 1–3 cm below the acromion (appendix).[1] However, this site is not universally accepted as the most appropriate; other organisations advocate alternative sites, such as a triangular region with the base around 5 cm below the acromion and the apex at the level of the axilla apex (approximating the middle third of the deltoid muscle),[2] or midway between the acromion and the deltoid tubercle.[3,4]

The site closest to the acromion and origin of the deltoid has several anatomical structures within its vicinity, including the posterior circumflex humeral artery, the anterior branch of the axillary nerve (located 5 cm below the acromion lateral border), and the subacromial–subdeltoid bursa.[2] The subdeltoid bursa can extend to 4·0 cm below the acromion and 1·3 cm below the skin.

A range of injuries have been reported to the Vaccine Adverse Event Reporting System database in the USA following vaccination (mostly for influenza). Injuries were predominantly shoulder pain and dysfunction (due to pain, joint-range restriction, bursitis, and stiff shoulder), and patients reported that the vaccines were administered "too high" on the arm.[5] Spanish pharmacovigilance organisations have similarly reported bursitis and other shoulder injuries following intramuscular vaccination administered in the deltoid.

Anthropometric studies of the optimal site of vaccination have identified that the safest anatomical site in adults of both sexes would be approximately (varying by size and sex) 7–13 cm below the mid-acromion, anatomically midway between the acromion and the deltoid tuberosity (appendix). This region avoids the anterior branch of the axillary nerve or the subacromial–subdeltoid bursa.[3,4] The risk of injury can be further reduced by the recipient placing their hand on the ipsilateral hip (ie, abducting the shoulder to 60°) when receiving the injection. This manoeuvre reduces exposure of the subacromial–subdeltoid bursa to injury. An injection administered at 90° to the skin's surface with a 25 mm needle routinely penetrates at least 5 mm of muscle in men and women.

Updating policy and training vaccinators to safely administer the vaccine in the appropriate intramuscular site will be essential for ensuring efficacy of the vaccine, as placement in a bursa or joint will prevent immune system exposure, and for increasing comfort and reducing pain in vaccine recipients.

We declare no competing interests.

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1 Public Health England. Immunisation procedures: the green book. March 20, 2013. In: Immunisation against infectious disease. https://www.gov.uk/government/publications/immunisation-procedures-the-green-book-chapter-4 (accessed Dec 21, 2020).
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4 Nakajima Y, Mukai K, Takaoka K, et al. Establishing a new appropriate intramuscular injection site in the deltoid muscle. *Hum Vaccin Immunother* 2017; **13**: 2123–29.
5 Hibbs BF, Ng CS, Museru O, et al. Reports of atypical shoulder pain and dysfunction following inactivated influenza vaccine, Vaccine Adverse Event Reporting System (VAERS), 2010–2017. *Vaccine* 2020; **38**: 1137–43.

Time to revise the strategy for Gavi funding of rabies vaccine?

For the **Global Burden of Disease cause and risk summary on rabies** see https://www.thelancet.com/pb-assets/Lancet/gbd/summaries/diseases/rabies.pdf

See Online for appendix

The Global Burden of Disease cause and risk summary on rabies shows the 13 700 deaths worldwide in 2019, close to the estimated 12 700 furious rabies cases in India alone.[1] Figure 4 of this summary is misleading, especially the key. As there is no surveillance in many of the poorest countries, the global annual deaths quoted by WHO[2] of 59 000 is derived from extensive extrapolation. Rabies encephalomyelitis is always fatal in Asia and Africa. Although prevention of infection by correct vaccination after dog bites is extremely effective, vaccines are often inaccessible in most African countries.

Gavi, the Vaccine Alliance, has committed to conditional funding of post-exposure rabies vaccine in Asia and Africa starting in 2021.[3] Preparatory surveys in several African countries show a widespread lack of infrastructure and public health provision. For example, in Chad, only 42% of health clinics surveyed had cold facilities for vaccine storage.[4] Effective distribution and use of vaccines would be difficult and take many years to achieve. The realistic costs of implementation in rural areas were not considered in recent evaluations of possible approaches.[5]

The COVID-19 pandemic has dramatically changed the situation. Innovative concepts, plans, and

For more on the **Vaccine Adverse Event Reporting System database** see https://wonder.cdc.gov/vaers.html

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Educating the Healthcare Community About Safe Medication Practices

Prevent shoulder injuries during intramuscular COVID-19 vaccinations

As our nation begins a large-scale coronavirus disease 2019 (COVID-19) immunization campaign barely a year since the deadly virus emerged in the US, it is critically important for healthcare workers who administer the vaccine to understand proper intramuscular (IM) administration technique in order to avoid a preventable and disabling occurrence called *shoulder injury related to vaccine administration* (SIRVA). This is especially important right now, as healthcare workers who may not normally administer vaccines may be called upon to help administer the new COVID-19 vaccines.

Case Report

A patient recently reported to ISMP that she went to her local community pharmacy to receive the 2020-2021 **FLUBLOK QUADRIVALENT** influenza vaccine as well as **SHINGRIX** (zoster vaccine recombinant, adjuvanted). When one of the vaccines was administered in her right arm, the patient experiencing severe pain, more than previous immunizations she had received. She also described feeling as if the needle had passed straight through her muscle. Later that evening, the pain in her right shoulder, where Shingrix had been administered, intensified. It wasn't until she applied ice to her shoulder that she was finally able to fall asleep. The severe pain had mostly resolved by the next morning.

It has been two months since the patient received these two vaccinations, and she states her right shoulder has not returned to normal. For example, she is not able to reach for things or move her shoulder in certain ways without experiencing pain and discomfort. So, what could this be? SIRVA could be one explanation.

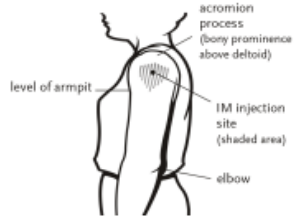

Figure 1. Intramuscular injection site for children and adults. Give vaccine in the central and thickest portion of the deltoid muscle—above the level of the armpit and approximately 2 to 3 finger widths (about 2 inches) below the acromion process. To avoid causing an injury, do not inject too high (near the acromion process) or too low. Adapted from www.ismp.org/ext/622 with thanks to the Immunization Action Coalition.

SIRVA

SIRVA is a shoulder injury triggered by the incorrect injection of a vaccine into the shoulder capsule (joint) rather than the deltoid muscle. It is caused by using an incorrect IM injection technique or improper landmarking of the IM injection site (the deltoid muscle) that results in the unintended injection of the vaccine (and/or trauma from the needle) into and around the underlying bursa of the shoulder. This results in an inflammatory process that causes injury to the musculoskeletal structures of the shoulder (e.g., tendons, ligaments, bursae).[1-3]

Symptoms of SIRVA include persistent shoulder pain, weakness, and limited range of motion that typically develop within hours to a few days after receiving a vaccine; these symptoms do not improve with over-the-counter analgesics. The resulting chronic shoulder pain and the inability to carry out daily activities that were possible prior to vaccination

continued on page 2 — SIRVA >

SAFETY wires

Administer adenosine rapidly for cardioversion. Adenosine injection is often used to restore normal sinus rhythm in patients with paroxysmal supraventricular tachycardia. To be effective, doses must be administered as a rapid intravenous (IV) bolus injection over 1 to 2 seconds. It is typically given via a peripheral venous access site as close to the patient's torso as possible. In addition, adenosine must be immediately followed by a rapid 0.9% sodium chloride flush. Experienced nurses often attach the adenosine syringe and sodium chloride flush syringe to a 3-way stopcock to expedite administration.

Such a rapid sequence of injections is unlike many other medications administered via IV push. This is due to the drug's very short half-life (less than 10 seconds) and the need to carry the drug to the heart as quickly as possible before rapid metabolism inactivates it. Manufacturer syringe and vial labels mention that the drug is intended for rapid IV use; however, some practitioners may be unaware of this fact. We recently received a report in which adenosine injection was administered too slowly during an advanced cardiac life support (ACLS) event, resulting in a failure to convert the patient to normal sinus rhythm.

Retrieval of adenosine from an automated dispensing cabinet (ADC) is often accomplished via override (e.g., during a code), so many safeguards built into orders may not appear on the medication administration record (MAR). Thus, an auxiliary label affixed to adenosine, reminding staff to administer the drug via rapid IV push, may be an important reminder. Prescribers can also remind staff to give adenosine by rapid IV push when giving verbal orders during an emergency. Staff, especially those stationed in the emergency department or

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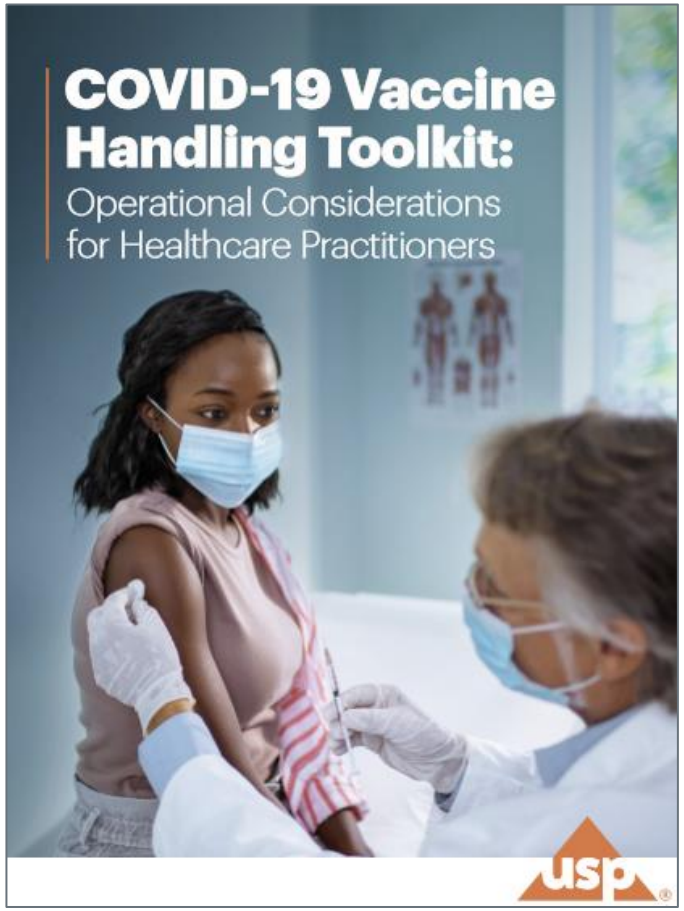
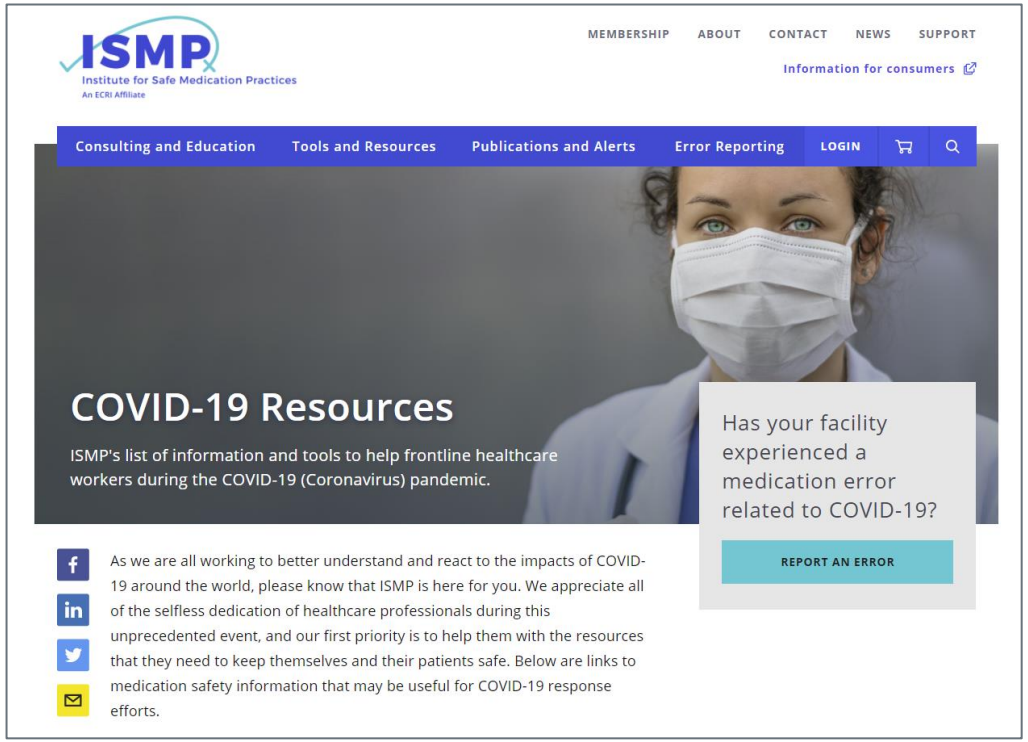
Preventing errors with COVID-19 vaccines

- Verify competency of preparers and vaccinators (many are volunteers)
- Dispense pharmacy prepared and labeled syringes when possible, or one person prepares and administers
- For mass vaccination, utilize a standard, organized process with independent double checks
- Maximize doses withdrawn from vials

- Separate vaccines in storage
- Plan for leftover vaccine
- Be prepared for allergic reactions
- Report vaccine errors and adverse reactions (US requires reporting to VAERS); additional reporting to ISMP is voluntary
- Utilize immunization information systems



https://www.usp.org/covid-19/vaccine-handling-toolkit



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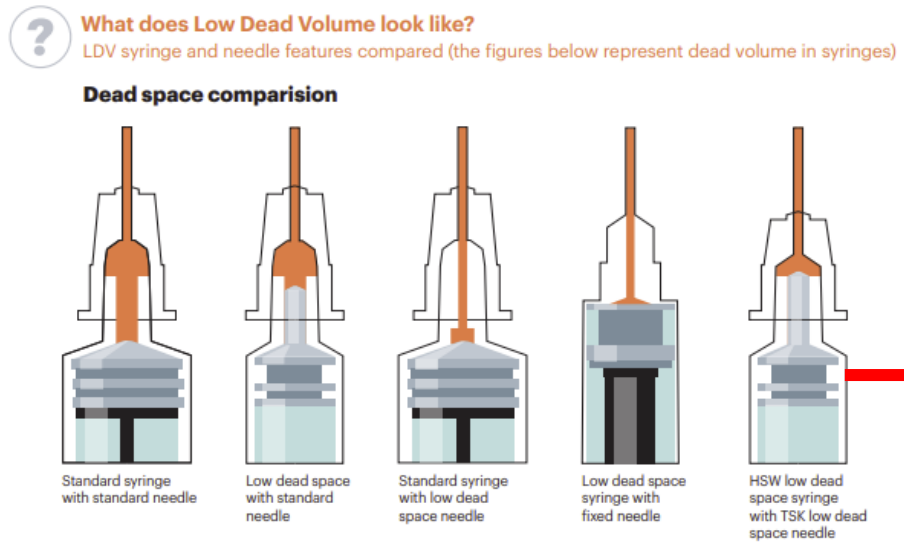

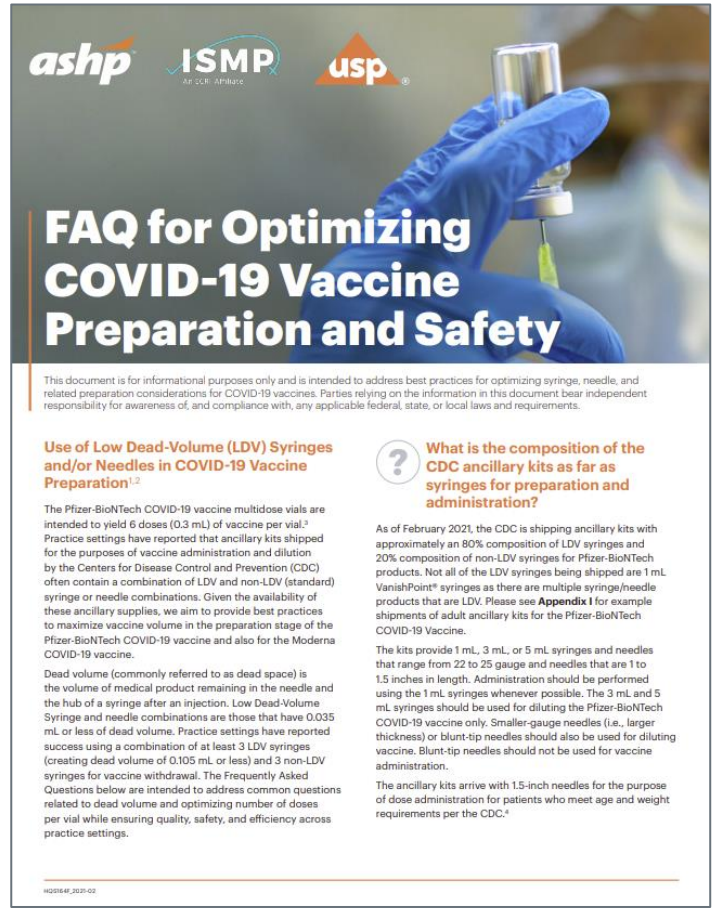

https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/FAQ-optimizing-covid-vaccine-prep-safety.ashx