

## **Featured Articles (/newsletters/featured-articles)**

# Learning from Errors with the New COVID-19 Vaccines

January 14, 2021

**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 in the last paragraph of this article 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 precaution after experiencing flu-like symptoms from the overdose. According to BioNTech, doses up to 100 mcg (30 mcg is the recommended dose) were administered during a clinical trial of the vaccine, with only mild to moderate, transient local injection site reactions and flu-like symptoms being reported. No serious adverse effects were reported with administration of the higher doses. A **similar error happened in Israel (<https://www.timesofisrael.com/pharmacist-accidentally-injected-with-4-covid-vaccine-doses/>)** because a vaccinator did not know the Pfizer-BioNTech vaccine contained multiple doses.

The Moderna COVID-19 vaccine does NOT require dilution. After thawing, each Moderna multiple-dose vaccine vial contains 10 (perhaps 11) doses of 0.5 mL each. To date, we have not received any reports of unnecessary dilution of the Moderna vaccine.

## Vaccine and Monoclonal Antibody Mix-Up

Instead of receiving the first dose of the Moderna COVID-19 vaccine, 44 adults (77 years and older) at a West Virginia (WV) clinic received IM injections of casirivimab, one of two new Regeneron monoclonal antibodies recently granted EUA in the US to

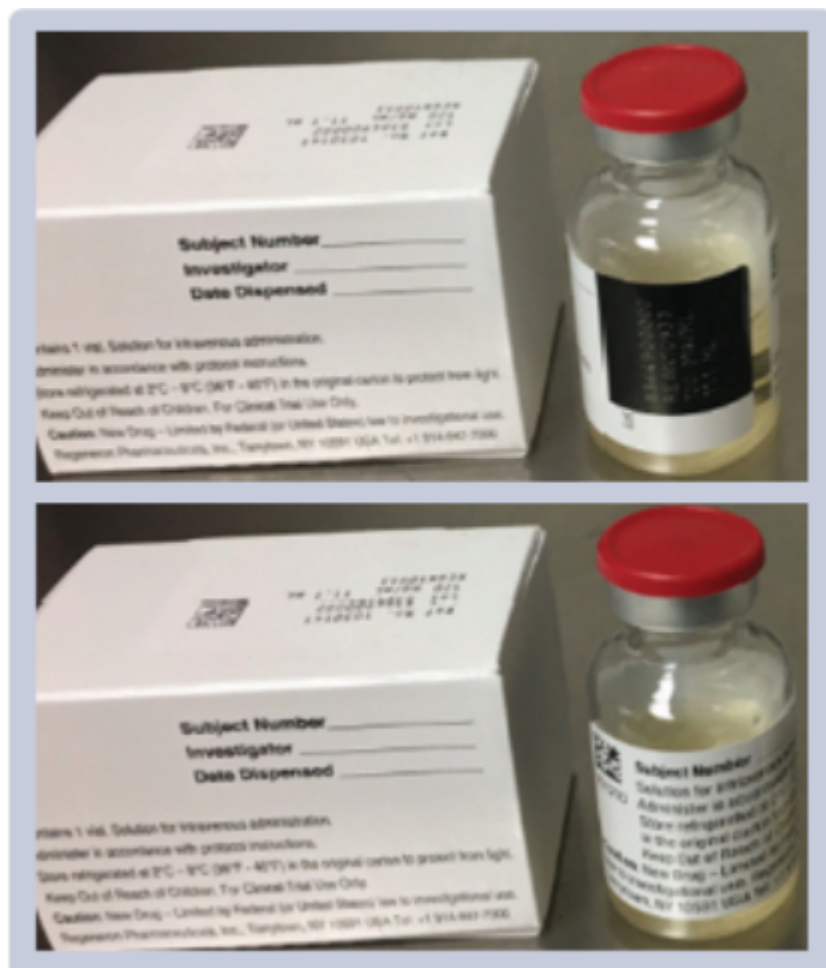
treat adults and children (12 years or older weighing at least 40 kg) with mild to moderate COVID-19 who are at risk for progressing to severe COVID-19 and/or hospitalization. The two monoclonal antibodies, casirivimab and imdevimab, are intended to be administered together as an intravenous (IV) infusion. They are supplied in individual, 2.5 mL or 11.1 mL single-dose vials. To prepare the infusion, 10 mL of casirivimab and 10 mL of imdevimab must be withdrawn into separate syringes and then diluted in the same 250 mL bag of 0.9% sodium chloride injection. Any product remaining in the vials must be discarded.

The mix-up between the Moderna vaccine and casirivimab started during the distribution process. The county health department dispatched two individuals from the National Guard to retrieve COVID-19 vaccine supplies from an area medical center for the WV clinic. When the individuals arrived at the medical center, they signed a chain-of-custody form stating that the product they were picking up was the “Moderna COVID-19 vaccine.” The small white case they were given mentioned REGN10933 (**Figure 1**), which the individuals did not recognize as a monoclonal antibody. According to media reports

([https://www.coalvalleynews.com/news/vaccine-mix-up-causes-confusion-in-boone-co/article\\_dd97f36e-4b8b-11eb-ae31-079b9036a788.html](https://www.coalvalleynews.com/news/vaccine-mix-up-causes-confusion-in-boone-co/article_dd97f36e-4b8b-11eb-ae31-079b9036a788.html)), nothing on the white case led the individuals to believe it was not the vaccine listed on the chain-of-custody form. Instead, they thought it must be special labeling for the new vaccine. The case was then transported to the clinic. Inside the case, the vial cartons and vials were, again, only labeled with REGN10933, not the product name (**Figure 2**). Unfortunately, the error was not recognized, and casirivimab was administered IM to the patients instead of the vaccine. No serious adverse reactions were reported, and patients were offered the vaccine as soon as possible.



**Figure 1.** Front (top) and back (bottom) of a case of a Regeneron monoclonal antibody, which is labeled with a product code name (REGN10933), not the established name, casirivimab.



**Figure 2.** Vial carton and front (top photo)/back (bottom photo) of a vial of Regeneron's casirivimab is labeled with a product code name, not the established name.

Although we do not have a detailed description of why the error happened, product packaging and labeling issues were likely involved. Both the Moderna vaccine and the Regeneron monoclonal antibody are available in 5 mL glass vials. The vaccine vial contains 5 mL (10 doses of 0.5 mL each) while the vials of the monoclonal antibodies are partially full and contain 2.5 mL. It should be noted that both of the Regeneron antibodies (casirivimab and imdevimab) are available in larger vials containing 11.1 mL, which may have been used at the time of the error. Vials of both the Regeneron antibodies and the Moderna vaccine have identical red caps (**Figure 3**). If the clinic staff had previously administered the Moderna vaccine, they may have been expecting a vial with a red cap, similar to the monoclonal antibody, casirivimab, packaged in a vial with a red cap.



**Figure 3.** The Moderna COVID-19 vaccine vial has a red cap, similar to the red cap on vials of Regeneron's monoclonal antibodies (see **Figure 2**).

Also, our December 3, 2020, newsletter called attention to the labeling problems with Regeneron's casirivimab and imdevimab, which clearly played a role in the mix-up. Two versions of vial and carton labels for each monoclonal antibody exist, which were used during investigational trials. Neither version includes the name of the specific antibody contained within and instead lists a product code number for casirivimab (REGN10933) and imdevimab (REGN10987). Although a barcode is on the vial label, it is not functional or tied to a National Drug Code (NDC) number. Initially, supplies of these monoclonal antibodies affixed with investigational new drug (IND) labels were used to meet the immediate demands for this COVID-19 treatment option.

**Regeneron confirms that a third version of the carton and vial label** (<https://www.regeneron.com/sites/default/files/treatment-covid19-eua-preventing-medication-errors.pdf>) meant for EUA use is now being applied to the product and hopefully will be in the field in a few weeks. These EUA-specific labels are color differentiated and include a functioning barcode. While the cap color will remain red for now given current stock, we hope the cap colors will eventually match the new label color schemes. ISMP also believes Regeneron should consider packaging a vial of casirivimab with a vial of imdevimab in a single carton, or mixing the two monoclonal antibodies in a single vial if possible, since they must be administered together.

## Waste of Vaccine Doses

ISMP received one report of vaccine contamination and several emails about concerns associated with unnecessary waste of the COVID-19 vaccines. In the reported event, a vaccinator found that one of the pharmacy-prepared syringes of the Pfizer-BioNTech COVID-19 vaccine dispensed that morning did not have a cap over the needle, and that the safety shield was locked over the needle. The vaccine dose was appropriately discarded.

We also learned that Operation Warp Speed, the federal COVID-19 vaccine response, has been shipping out a variety of syringe types since vaccinations began, some of which are **not low dead-volume syringes**

(<https://www.politico.com/news/2021/01/10/hospitals-syringes-vaccine-waste-doses-457017>) and, thus, not efficient enough to extract more than 5 doses from the Pfizer-BioNTech vaccine or more than 10 doses from the Moderna vaccine vials. While the number of doses withdrawn from a vial is influenced by the healthcare worker's technique, using a syringe designed to limit the dead space between the syringe hub and needle reduces the amount of wasted vaccine and increases the ability to extract an extra dose(s) from COVID-19 vaccine vials.

Finally, we learned about concerns regarding the waste of leftover vaccine doses. Some of the wasted vaccines were due to cancellations of scheduled vaccine appointments or “no-shows” exacerbated by leadership miscommunications regarding vaccine scheduling. The rest of the wasted vaccines were due to leftovers at the end of the day. Since both the Pfizer-BioNTech and Moderna vaccines must be used within 6 hours after dilution (Pfizer-BioNTech vaccine) or vial puncture (Moderna) and cannot be refrozen or refrigerated again, facilities with leftover doses in vials or prefilled syringes at the end of the day are sometimes scrambling to find unvaccinated people or are wasting the unused doses. One vaccinator thought that leadership might be less concerned about the waste because the government is paying for every vaccine dose, even wasted doses. But high vaccine waste could lead to extending the pandemic unnecessarily.

## Administration to the Wrong Age Group

A 17-year-old at one clinic received the Moderna vaccine instead of the Pfizer-BioNTech vaccine, and a 15-year-old at another clinic inappropriately received the Moderna vaccine. According to the EUAs, the Pfizer-BioNTech vaccine is intended for

individuals 16 years and older, and the Moderna vaccine is intended for individuals 18 years and older.

## Error with Scheduling the Second Dose

An elderly patient who had received his initial Moderna COVID-19 vaccination reported that he had misspelled his email address on a registration form, which was needed for registration and confirmation of his appointment for his second dose 1 month later. The patient had been told he would receive an email providing instructions to register for his second vaccination and then to confirm his next appointment. Because of the misspelled email address, the patient never received directions for registering for his second vaccination. Although he contacted the facility where he received his first dose, as well as the state health department, he was unable to register for his second vaccination.

## Allergic Reactions

ISMP received two reports of serious but not life-threatening allergic responses to the Pfizer-BioNTech vaccine that required immediate treatment and overnight hospitalization. Recently, the **Centers for Disease Control and Prevention (CDC)** (<https://www.msn.com/en-us/health/medical/cdc-says-severe-allergic-reactions-to-coronavirus-vaccine-are-rare/ar-BB1cxavp?ocid=uxbndlbing>) confirmed that, so far, 29 individuals have experienced a serious allergic response, mostly within minutes of receiving the vaccine. **According to the CDC** (<https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7002e1-H.pdf>), this equates to a rate of 11.1 per million doses, making it a rare outcome. Most individuals who had a severe allergic reaction had a documented history of allergies.

**Safe Practice Recommendations:** While the voluntary reports and emails submitted to ISMP likely represent just the tip of the iceberg given the massive scope of the global COVID-19 vaccination campaign, please expect that mistakes will be made and, importantly, that lessons can be learned from them so steps can be taken to prevent their recurrence. While this is not a comprehensive list of all that can be done to prevent COVID-19 vaccination errors, consider the following targeted recommendations:

**Safely select vaccination sites.** Be sure vaccination sites have enough space to assess patients before vaccination, observe them after vaccination, and treat patients who experience a reaction, while maintaining social distancing and other pandemic

precautions.

**Verify the competency of vaccinators.** Educate vaccination staff regarding the storage, preparation, and administration of the COVID-19 vaccines, as well as the common types of errors that may occur, including those described above. Provide vaccinators with an up-to-date *Fact Sheet for Healthcare Providers* for the vaccine(s) being used, and verify their competency regarding:

- Proper vaccine storage and temperature monitoring
- Patient assessment prior to vaccination
- Age indications for each vaccine (16 years and older for Pfizer-BioNTech, 18 years and older for Moderna)
- Providing patients with a Fact Sheet for Recipients and Caregivers before vaccination
- Proper dilution of only the Pfizer-BioNTech vaccine
- Withdrawal of the correct dose for each vaccine from multiple-dose vials using strict aseptic technique and low dead-volume syringes/needles
- Identification of the **appropriate IM injection site** (<https://www.ismp.org/acute-care/medication-safety-alert-december-17-2020>)
- Administration of the IM vaccine(s)
- Recognition of the signs and symptoms of an allergic reaction
- Emergency treatment of anaphylaxis (e.g., immediate IM injection of **EPINEPH**rine, transport for further medical care)
- Timing and scheduling of a second vaccine dose

**Dispense pharmacy-prepared syringes.** If feasible within the timeframe for vaccine stability at room temperature (6 hours) and patient scheduling, have the pharmacy verify the number of vaccines needed each day (to prevent waste) and dispense prefilled, labeled syringes of the vaccine for daily vaccination clinics. Check that the needle cap is secure on all vaccine syringes before dispensing.

**Implement an independent double check.** When preparing the Pfizer-BioNTech vaccine, require an independent double check of the dilution process (if staffing permits).

**Maximize doses withdrawn from vials.** Whenever possible, use low dead-volume syringes/needles to withdraw as many doses as possible of the COVID-19 vaccine from each vial (6 or 7 from the Pfizer-BioNTech vaccine vial and 10 or 11 from the Moderna vaccine vial) to reduce the amount of wasted vaccine.

**Identify/differentiate monoclonal antibodies.** If Regeneron monoclonal antibodies are received in investigational drug packaging without the product name on the case, vial carton, or vial (**Figures 1 and 2**, above), establish a process immediately upon receipt to identify and differentiate each antibody from other medications, including the Moderna COVID-19 vaccine. For example, the pharmacy at Beaumont Hospital in Royal Oak, Michigan, affixes brightly colored labels (pink for casirivimab, green for imdevimab) that include the product name, strength, and a scannable barcode (**Figure 4**) to provide visual distinction and verify product selection prior to preparation. NDCs are available in the Fact Sheets and can be used to prepare the barcodes.



**Figure 4.** Hospital affixes barcoded, brightly colored labels to help differentiate investigational labels on casirivimab (top, pink) from imdevimab (bottom, green).

**Separate vaccine storage.** To avoid mix-ups, do not store the Pfizer-BioNTech and Moderna vaccines together in the refrigerator while or after thawing (e.g., use separate shelves). Do not place the vaccines close to the Regeneron monoclonal antibodies.

**Plan for leftover vaccine.** Ensure the vaccine scheduling process is efficient, accurate, and includes a reliable communication system to remind patients and confirm their appointments. Also establish a standard process (e.g., daily list of readily available alternative recipients) for dealing with any leftover doses at the end of a vaccination clinic (but within 6 hours of storage at room temperature). Consider preparing vaccines in small batches for confirmed appointments only to minimize leftover doses at the end of the day.

**Be prepared for allergic reactions.** At all vaccination sites, be prepared to immediately treat an allergic reaction. Make sure emergency equipment and medications (e.g., **EPINEPH**rine prefilled syringe or autoinjector, H1 antihistamine such as diphenhydramine) are readily available to staff. Monitor patients for at least 15 minutes after vaccination for signs of an adverse reaction, or at least 30 minutes if patients have a history of an immediate allergic reaction of any severity to a vaccine or injectable therapy, or a history of anaphylaxis due to any cause. Avoid administration of the vaccine to patients with a known severe allergic reaction to ingredients in the Pfizer-BioNTech and Moderna vaccines, including polyethylene glycol, or a reaction of any severity to polysorbate (due to potential cross-reactive hypersensitivity to polyethylene glycol). Patients with general allergies should consult a healthcare provider prior to administration. Patients with anaphylaxis after the first vaccine dose should not receive the second vaccine dose.

**Establish scheduling workflow.** Establish a vaccination scheduling system that does not allow patients younger than 16 years to obtain an appointment, and schedules appointments for patients who are 16 and 17 years old only for receipt of the Pfizer-BioNTech vaccine. Establish a communication system for confirming all vaccine appointments, including for patients scheduled to receive their second vaccine dose. If relying on email, respond to all unconfirmed deliveries with phone calls or other means of rapid communication. Consider establishing a “hotline” for vaccine scheduling questions.

**Report vaccine errors and adverse reactions.** Report all COVID-19 vaccine errors and adverse reactions to the Vaccine Adverse Event Reporting System (**VAERS** (<https://vaers.hhs.gov>)), which is mandatory for healthcare providers. ISMP also asks providers to report vaccine errors to the **ISMP VERP** (<https://www.ismp.org/report-medication-error>). Vaccinated patients should receive a **“v-safe” information sheet and be encouraged to enroll in the program** (<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html>). V-safe is a smartphone-based monitoring tool from CDC that provides a personalized “check in” after vaccination so patients can easily report any adverse vaccine reactions.

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