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ISMP An ECRI Affiliate

Acute Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

Prevent uncontrolled, rapid infusion rates:

Confirm infusions are connected to pumps before opening the clamp!

Problem: Within several weeks, an organization experienced three errors in which patients received uncontrolled intravenous (IV) infusions at rapid rates. As noted in the event descriptions that follow, the infusions were all associated with high-alert medications—heparin, propofol, and phenylephrine—that should have been administered at a controlled rate via a smart infusion pump. However, each infusion was found to be mistakenly administered via gravity at a rapid rate of infusion, rather than connected to a programmed infusion pump with a defined rate of infusion. The patients required treatment after the events, but were not permanently harmed.

Event #1

A patient inadvertently received an entire 500 mL infusion of heparin (25,000 units/500 mL) within 1 hour. The error began when a nurse was to administer an intermittent antibiotic and heparin infusion to the patient. The hospital did not have enough infusion pumps for all infusions and did not require the use of an infusion pump for organization-defined "low risk" medications, including intermittent antibiotics. When starting the antibiotic and heparin infusions, the nurse confused the antibiotic and heparin lines, resulting in slow antibiotic administration through the infusion pump programmed to infuse the heparin, and rapid heparin administration via gravity. The patient received protamine to reduce the risk of bleeding from the rapid heparin infusion and recovered without incident.

Event #2

A patient received a rapid dose of propofol (500 mg/50 mL) that was intended to be administered as a continuous infusion at a much slower rate. A nurse had unclamped the IV administration set for the propofol infusion without noticing that the infusion was never connected to the programmed infusion pump. The entire propofol infusion was administered within minutes. The distracted and hurried nurse who made the error while preparing the patient to leave for a computed tomography (CT) scan had been assisting the patient's primary nurse, who was caring for multiple trauma patients. After the error was discovered, the nurse acknowledged that the required safety steps for setting up the infusion, including tracing the IV tubing from the source infusion, through the pump, and to the patient, had not been followed.

Event #3

A patient accidentally received a bolus dose of phenylephrine (20 mg/250 mL) in the operating room (OR). An anesthesiologist noted a sudden increase in the patient's blood pressure during the procedure, which helped identify the error. The phenylephrine should have been administered more slowly via an infusion pump. However, the pump had been alarming "air in line," and to clear the alarm, the infusion was removed from the pump and the free-flow protection clamp was opened to remove the air in the line and to reprime the line. The infusion was never reconnected to the pump to re-engage the free-flow protection clamp after clearing the alarm, and the phenylephrine infused rapidly via gravity, causing the patient's blood pressure to increase.

While each error has unique root causes, there were several contributing factors identified during investigation of the events:

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SAFETY briefs

HIGH-ALERT

Black port cover added to B. Braun's potassium chloride for injection concentrate bag. In an attempt to distinguish the contents and prevent mix-ups with other parenteral medications, B. Braun has modified its potassium chloride for injection concentrate pharmacy bulk package in a flexible container (www.ismp.org/ext/957) to include a black port set cap (**Figure 1**). This modification aligns with the USP General Chapter <7> *Labeling* requirement that only potassium chloride for injection concentrate can have a black cap and closure. Additional labeling changes to enhance critical information are coming soon.

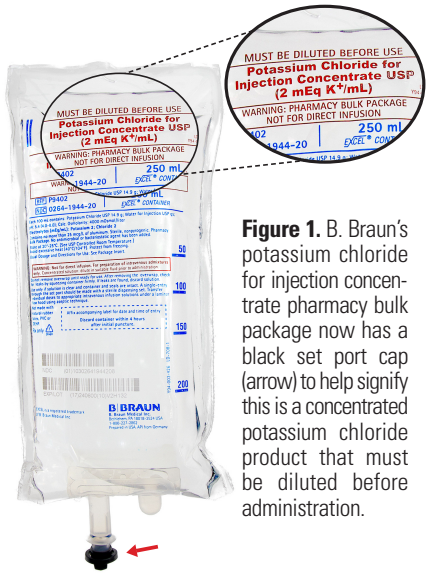

Figure 1. B. Braun's potassium chloride for injection concentrate pharmacy bulk package now has a black set port cap (arrow) to help signify this is a concentrated potassium chloride product that must be diluted before administration.

Observe for possible ExactaMix 2400 valve set port leakage. Baxter has issued an *Urgent Medical Device Correction* communication regarding the potential for leaking valves in the EXACTAMIX 2400 valve sets. Baxter has received an increase in complaints of ports 1 and 2 leaking when in the closed position, resulting in unintended ingredient transfer into the compounded admixture. This leak would be most noticeable when the ExactaMix Compounder is pumping and moving fluid through the

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- Not having an adequate supply of infusion pumps available
- Only using infusion pumps to deliver "high-risk" medications
- Starting infusions without confirming the infusion rate
- Failure to trace infusion lines before opening the clamp on the IV set to start or restart infusions
- Distractions and time constraints during medication administration
- Failure to respond appropriately to infusion pump alarms (e.g., "air in line" alarm)

Safe Practice Recommendations: The following strategies can be implemented to help prevent these types of errors within your organization, many of which can be included in a short, standard safety checklist for practitioners to follow when hanging or changing IV bags, bottles, or syringes.

Establish an expectation. Require practitioners to administer all continuous and intermittent infusions, whether medications or hydrating fluids and regardless of "high-risk" designation, using a smart infusion pump (exception: fluid resuscitation efforts).

Provide an adequate supply of smart infusion pumps. If necessary, purchase additional smart infusion pumps to facilitate utilization of a pump to deliver all medication infusions and hydrating solutions (www.ismp.org/ext/958). Older infusion pumps without free-flow protected tubing should not be purchased or used.

Employ DERS. Maintain a complete drug library in smart infusion pumps, and require practitioners to engage the dose error-reduction system (DERS) when administering all infusions, including those deemed "low risk."

Label lines. Label all infusion lines (and other access lines/catheters) at the point(s) of connection (e.g., above the pump and above the access point into the patient's body).

Trace infusion lines. When infusions are started, reconnected, or changed (i.e., new bag/bottle/syringe), trace the tubing by hand from the solution container to the pump (and channel), to the connection port, and then to the patient to verify the proper infusion, pump/channel, and route of administration. Confirm that the infusion rate has been programmed accurately before starting the infusion.

Confirm before opening the roller clamp. After priming the tubing for infusions (or clearing air from the line), keep the roller clamp below the drip chamber closed until infusion lines have been traced to confirm the connection to the correct infusion pump and channel.

Respond appropriately to pump alarms. After troubleshooting an "air in line" alarm and clearing the line, ensure the tubing is placed back into the smart pump using DERS and then resume the infusion.

Provide handoff reports. Communicate with the care team, especially during handoffs or when someone other than the primary nurse or provider is helping to manage the patient's infusions. Trace all access lines as part of the handoff.

Manage distractions and time constraints. Encourage staff to speak up in situations where they feel that time constraints or distractions are creating an unsafe environment in which an error may be more likely to occur.

Manage the environment. Identify, report, and mitigate environmental factors that impair the ability to practice in a safe and efficient manner. For example, provide proper lighting in patient treatment areas and rooms, and ensure the practitioner's line of sight of both the patient and the pump is not obstructed.

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common fluid pathway. A leaking valve set could result in a patient receiving an incorrect prescribed constituent(s). Baxter said, to date, there have been no reports of serious injury. Until this situation is resolved, to guard against unintended ingredient transfer from a leaking valve set port, practitioners should observe both the pumping process as well as the ingredient vials to ensure their volumes are not being consumed faster than expected. The affected product has been distributed in the United States since September 16, 2021. For more information, please read the entire letter found at: www.ismp.org/ext/955.

Accidental needlestick with Evenity prefilled syringe. A nurse in an outpatient infusion setting experienced an accidental needlestick injury when administering a subcutaneous injection of an **EVENITY** (romosozumab-aqqg) 105 mg/1.17 mL prefilled syringe from Amgen. Evenity is used for the treatment of postmenopausal osteoporosis in patients who are at high risk for fracture, or in patients in whom other available osteoporosis therapy has failed or cannot be taken. Two syringes and two subcutaneous injections are needed to administer the total dose of 210 mg, which should be administered by a healthcare provider. The needles lack a safety guard and are not retractable or removable, so users are not able to change the needle to one that has a safety guard. Other organizations reported the same concern about accidental needlesticks with this product.

Similar concerns have been reported with other subcutaneous prefilled syringes that do not come with a needle safety guard, including **KINERET** (anakinra) and **HUMIRA** (adalimumab). Even with prefilled syringes intended for self-administration, family members, other caregivers, long-term care staff, and hospital inpatient staff often administer these medications. Also, these products could make their way into garbage bins and other forms of common waste, exposing children, animals, and others to unintended needlestick injuries. We have notified the US Food and Drug Administration (FDA) and the manufacturer of this concern and recommended the addition of a needle safety guard for all prefilled syringes with

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Recognize and correct errors. Monitor patients for unanticipated events and investigate pump connections if clinical deterioration or an unexpected adverse effect is detected.

Share good catches. Share impactful stories and recognize staff for good catches, especially when harmful errors were prevented due to tracing the infusion line, catching a programming error, and/or engaging the DERS.

Use data from technology. Utilize data from infusion devices to monitor compliance, establish performance measures, and identify workarounds that impact compliance.

Educate staff. During orientation and ongoing training, educate staff about errors that have occurred when infusions are administered at a much faster rate because they were inadvertently not connected to an infusion pump. During nursing orientation, stress the need to trace infusion lines and practice tracing lines during periodic simulations.

Multi-chamber bag parenteral nutrition is not without risk

Problem: An increase in the number of errors and workarounds related to the shortage of parenteral nutrition (PN) components have been reported to ISMP. To conserve resources, organizations have been forced in some instances to reduce the number of days they provide PN to patients. For example, rather than daily nutrition, an organization reported they had to reduce the administration of PN to three times per week. In other cases, organizations may elect to utilize alternative products, such as multi-chamber bag parenteral nutrition (MCB-PN) for select patients instead of patient-specific compounded PN.

MCB-PN products are commercially available in various standardized compositions. They are available in two- or three-chamber bags. **CLINIMIX** and **CLINIMIX E**, manufactured by Baxter, are available with two chambers. Clinimix comes with one chamber containing amino acids and the other containing dextrose, and Clinimix E comes with one chamber containing dextrose with calcium and the other containing amino acids with electrolytes. **KABIVEN** and **PERIKABIVEN**, both manufactured by Fresenius Kabi, are available with three chambers holding dextrose, amino acids/electrolytes, and lipids. For all MCB-PN products, the seal(s) that separates the chambers must be broken and the chamber contents must be mixed to ensure complete activation prior to administration. While these products require fewer compounding steps, additives may still need to be added to these products in a sterile environment.

Some of the error reports submitted to ISMP involved mix-ups between MCB-PN bags. For example, during a shortage of PN compounding ingredients, one organization purchased Clinimix E 4.25/10 (dextrose with calcium and amino acids **with** electrolytes) as well as Clinimix 4.25/10 (dextrose and amino acids **without** electrolytes). The organization reported multiple errors in which the wrong formulation was dispensed, which was attributed to similar-looking packaging as well as staff unfamiliarity with these products. Other events were related to the failure to activate the MCB-PN bags. This resulted in the omission of certain components of the PN, such as dextrose and calcium. We have previously shared similar errors and actions to take to ensure the proper preparation of MCB-PN bags (www.ismp.org/node/32915, www.ismp.org/node/32885).

Safe Practice Recommendations: If your organization has purchased or is thinking about purchasing MCB-PN, consider the following risk-reduction strategies:

Conduct an FMEA. Conduct a proactive risk evaluation, such as a failure mode and effects analysis (FMEA), prior to use. During the analysis, be sure to review the labeling and packaging of products and how mix-ups will be prevented, how MCB-PN bags will

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an attached needle to prevent accidental needlesticks. The manufacturer has escalated our concern for further follow-up.

Hidden pork content in gelatin capsules. Did you know that some medications, including **COLACE** (docusate sodium), have ingredients sourced from pigs in their gelatin capsules? A nurse reported that a Muslim patient had recently ingested multiple doses of Colace without realizing the gelatin was sourced from pigs. Unfortunately, the container and product labeling do not specify the porcine (pig) content. People with food allergies or intolerances, or who want to avoid animal products for religious, cultural, or dietary reasons, need to know the origin of the ingredients contained in their medications. We contacted Avrio Health, the manufacturer of the brand product Colace (there are several generic formulations as well), and confirmed that the gelatin used in Colace capsules is made from pigskin, but neither the labeling nor the package insert specify this. It appears that, under current regulations, the label is not required to detail the animal source of the gelatin. Alert colleagues and patients to this situation. If practitioners or patients have concerns about the inactive ingredients contained in a medication, the pharmacy should contact the manufacturer for more information.

USP expiration date format. A patient received an expired medication due to confusion with the expiration date format. A vial of **DARZALEX FASPRO** (daratumumab and hyaluronidase-fihj), a monoclonal antibody being used for multiple myeloma, had an expiration of 2022-04-06. With this presentation, staff questioned if the expiration was April 6, 2022, or June 4, 2022. A patient received a dose of medication from this vial at the end of April; however, the expiration date was later determined to be April 6, 2022. We have previously shared errors involving confusion with expiration date formats (e.g., www.ismp.org/node/33236, www.ismp.org/node/33237, www.ismp.org/node/33238).

On September 1, 2023, a revised USP expiration date standard for medication labels in USP General Chapter <7> *Labeling* (www.ismp.org/ext/954) will go into effect. All numeric dates must be formatted using

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be ordered in your electronic health record (EHR) system and displayed on your medication administration records (MARs), and the method that will be used to remind practitioners to activate the bag.

Gather stability data. Require the pharmacy to reach out to product manufacturers to review stability data for any pharmacy additives, and make this information readily available to prescribers, pharmacists, and nurses. Establish a maximum timeframe in which MCB-PN should be administered (hang time).

Store safely. Store MCB-PN separately in the pharmacy, away from similar-looking bags. Avoid storing MCB-PN in an automated dispensing cabinet (ADC), as nurses may not be familiar with the need to activate all chambers.

Require pharmacy activation and compounding. Require the pharmacy to activate all MCB-PN bags (mixing the chambers) and add any prescribed additives, such as multivitamins and trace elements, in a sterile environment. Then dispense the activated PN (with additives, if required) to patient care units.

Apply auxiliary labels. Consider applying auxiliary labels to the overwrap of MCB-PN bags upon procurement in the pharmacy to differentiate the products with and without electrolytes. After pharmacy activation, consider applying auxiliary labels directly on MCB-PN bags for nurses to confirm that the product has been activated prior to administration.

Employ barcode technology. Use barcode scanning technology prior to dispensing, compounding, and administration to ensure the correct MCB-PN product is being used.

Convert PN orders. During transitions of care, work with home infusion pharmacies to determine if orders need to be converted from MCB-PN to patient-specific compounded PN. Require an independent double check of all calculations to verify accuracy.

Educate practitioners. Educate practitioners about how to calculate the amount of macronutrients, electrolytes, and additives patients will be provided from a MCB-PN bag, based on the ordered rate of infusion. Also let pharmacy staff know how to activate the bag, and educate nurses to confirm that the product has been activated prior to administration. Since MCB-PN products are commercially standardized, alert nurses to the likely waste of excess PN volume since each bag may contain more than required for a particular patient (e.g., patient may receive only 1,500 mL from a 2,000 mL bag).

Risk-prone scenarios with multi-trace products

Problem: MULTRYS (trace elements injection 4), manufactured by American Regent, is a combination of four trace elements (zinc sulfate, cupric sulfate, manganese sulfate, and selenious acid) indicated for neonatal and pediatric patients weighing less than 10 kg. Each mL of Multrys contains zinc 1,000 mcg, copper 60 mcg, manganese 3 mcg, and selenium 6 mcg. For patients weighing less than 3 kg, Multrys does not provide the recommended daily dose of zinc; and for patients weighing 0.4 kg to 0.59 kg and 4 kg to 9.9 kg, Multrys also does not provide the recommended daily dose of copper or selenium. This means that, for many pediatric patients, individual supplements of zinc, copper, and selenium will be needed, often every other day, to meet requirements. It can be challenging to ensure patients receive the correct amount of all trace elements and to operationalize a supplementation schedule of **every other day**.

American Regent also manufactures **TRALEMENT**, intended for adult and pediatric patients weighing 10 kg or more. Each mL of Tralement contains zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg. Similar to how Multrys requires

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the year, the month, and, if applicable, the day, separated by hyphens or forward slashes in one of the following formats: YYYY-MM-DD (e.g., 2019-06-30, 2019/06/30) or YYYY-MM (e.g., 2019-06, 2019/06). Alphanumeric dates must be displayed using at least three letters for the month in one of the following formats: YYYY-MMM-DD (e.g., 2019-JUN-30, 2019/JUN/30) or YYYY-MMM (e.g., 2019-JUN, 2019/JUN). Expiration dates stated only using the year and month mean the products expire on the last day of the month. Post this information where medications are dispensed and administered so staff become familiar with the formats. The US Food and Drug Administration (FDA) published similar recommendations in its *Product Identifiers Under the Drug Supply Chain Security Act Questions and Answers* (www.ismp.org/ext/951, page 9-10).

Worth repeating...

Norepinephrine left in a discontinued IV line administered as a bolus

Residual norepinephrine (16 mg/250 mL) remained in a patient's intravenous (IV) line after the infusion was discontinued. The nurse was unable to aspirate the medication out of the line, so it was slowly flushed. The patient quickly experienced a pounding headache, flushing, increased heart rate, and elevated blood pressure. The nurse was prepared to administer an antihypertensive medication, but fortunately, the patient's symptoms subsided in a few minutes.

Since most IV medications are colorless, residual medication left in the IV line may not be apparent to nurses and could be a danger. Similar situations resulting in significant harm due to inadvertent administration of residual high-alert medications, including opioids, oxytocin, and norepinephrine, have been reported (www.ismp.org/node/33232, www.ismp.org/node/25585, www.ismp.org/node/29324).

Discontinued or "held" infusions should be immediately removed from the pump, disconnected from the patient, and discarded. The tubing should be changed to ensure no residual medication is left in the tubing, which could be inadvertently administered as a bolus when the tubing is used to administer other medications and fluids.

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trace element supplementation for certain weight ranges, for adult and pediatric patients weighing 10 kg to 49 kg receiving Tralement, additional zinc, copper, and selenium are required to meet the recommended daily dose.

American Regent previously manufactured **MULTITRACE-4 NEONATAL**, which contained zinc, copper, manganese, and chromium rather than selenium. The product had a clear indication on the label that it was intended for neonates. The current Multrys and Tralement vials do not indicate the intended age group or weight category on the labeling. A mix-up between the two currently available products (Multrys and Tralement) would potentially place neonates at risk for lethal overdoses of trace elements if Tralement was inadvertently used.

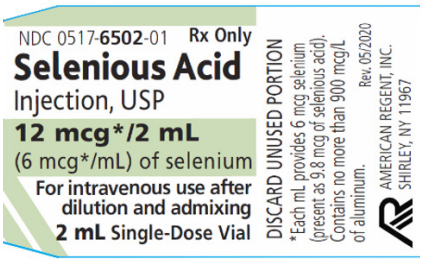

Figure 1. The new single-dose selenious acid vial by American Regent provides 12 mcg/2 mL (6 mcg/mL) of selenium.

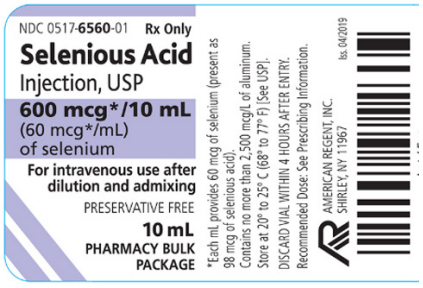

Figure 2. The multidose vial of selenious acid by American Regent provides 600 mcg/10 mL (60 mcg/mL) of selenium.

In addition, American Regent now offers a single-dose vial of selenious acid containing 12 mcg/2 mL (6 mcg/mL) of selenium (**Figure 1**). This new concentration should not be confused with the multidose selenious acid vial that provides 600 mcg/10 mL (60 mcg/mL) of selenium (**Figure 2**). Confusion between the two concentrations of these products could result in 10-fold dosing errors. We have previously reported confusion with selenious acid injection and the amount of active moiety, selenium, in the product (www.ismp.org/node/32853).

Safe Practice Recommendations: If your organization uses Multrys and/or Tralement, be aware of the above limitations and evaluate the various patient weight categories that will require different dosages as well as differing amounts of individual trace elements. Develop a process to accommodate every other day supplementation and standardize your order templates accordingly. Incorporate an independent double check when creating and modifying order templates.

Also, consider selecting predetermined days for when the combination trace products are administered, such as Monday, Wednesday, and Friday, alternating with individual trace supplements on Tuesday, Thursday, Saturday, and Sunday for consistency during the weekend. Alternatively, due to the limitations of the current combination multi-trace products described above, organizations may want to explore purchasing separate trace element ingredients, including selenious acid. If possible, purchase only one concentration of selenious acid and use barcode scanning technology during compounding. Highlight these nuances in your parenteral nutrition (PN) education to generate practitioner awareness.

Special Announcements

FDA offers free on-demand CE webinars

The US Food and Drug Administration (FDA) Division of Drug Information is offering **FREE** on-demand **Home Study CE Webinars**, which provide healthcare professionals with **1 hour of continuing education (CE) credit**. Refer to the individual webinar listing for complete CE information. For a full list of topics, please visit: www.ismp.org/ext/283.

Nominations for Cheers Awards

Nominations for this year's **ISMP Cheers Awards** are being accepted now through **September 9, 2022**. The **Cheers Awards** honor individuals, organizations, and groups from various healthcare disciplines that have demonstrated an exemplary commitment to medication safety. To submit a nomination, please visit: www.ismp.org/node/123.

Virtual MSI workshops

Register for one of our unique 2-day, virtual ***ISMP Medication Safety Intensive (MSI)*** workshops being offered in 2022. Our 2022 workshops are scheduled for **August 4 and 5, October 6 and 7**, and **December 1 and 2**. For more information and to register, please visit: www.ismp.org/node/127.

Resource for specialty pharmacies

ISMP and ECRI have launched a new online membership for specialty pharmacies. Membership provides actionable guidance and practical strategies for safe medication management, including resources that can be used to help meet accreditation standards, stay informed about new technologies and best practices, and create safety improvements to reduce the risk of medication errors. To learn more, please complete and submit the form located at: www.ismp.org/node/31616.

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