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ISMP
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Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

CSP accuracy and error prevention should be both a leadership and regulatory mandate

Millions of compounded sterile preparations (CSPs) are produced each year, many in hospital pharmacies. The inherent risks in the sterile compounding process are numerous and include: 1) sterility and contamination concerns, which could lead to possible patient infections; 2) exposure of healthcare personnel, patients, and the environment to potentially hazardous drugs, which could result in adverse health effects; and 3) inaccuracies during preparation (e.g., wrong drug, wrong base solution, wrong diluent, wrong concentration), which could lead to harmful or fatal medication errors.

USP General Chapter <797> provides environmental and personnel standards to promote preparation of CSPs that are free from contaminants and are consistent in intended identity, strength, and potency. USP General Chapter <800> provides standards for safe handling of hazardous drugs to minimize the risk of exposure to healthcare personnel, patients, and the environment. Based on these standards, healthcare leaders are spending millions of dollars to update their facilities' physical environments and pharmacy technology to be in compliance with the sterility standards in USP <797> and the hazardous drugs standards in USP <800>.

These USP standards represent much needed, high-leverage improvements that, when fully implemented, will improve the sterility of CSPs and reduce potential exposures to hazardous drugs. However, healthcare leaders have devoted fewer resources to ensure accuracy (e.g., right drug, right base solution, right diluent, right concentration) during the preparation of CSPs, risking potentially fatal medication errors. Many examples of harmful and fatal CSP preparation errors have been published in the *ISMP Medication Safety Alert!* during the last 25 years.

While some electronic health record (EHR) systems offer their own integrated intravenous (IV) workflow software modules, which utilize barcode scanning technology to verify product selection during the sterile compounding process, they typically lack imaging or gravimetrics to verify volumes of ingredients and completed CSPs. The most reliable way to ensure and achieve accuracy during the preparation of CSPs is through the consistent use of IV workflow management systems interfaced with EHR systems, which use barcode scanning technology to verify ingredients along with imaging and/or gravimetric tools to verify the volumes of ingredients and final preparations.

One health system's experience

A large health system spent several million dollars on pharmacy construction and environmental improvements to achieve facility compliance with USP <797> and <800> standards. In conjunction with this work, the pharmacy director had requested a small fraction of what had been spent for USP <797> and <800> compliance to add an IV workflow management system to help improve and maintain CSP accuracy. Lacking a regulatory mandate for CSP accuracy, this request was not approved. In this health system, pharmacy technicians used the outdated "syringe pull-back"

continued on page 2 — CSP mandate >

Your *Reports* at *Work*

New requirements for manufacturers' expiration date format

Confusion when interpreting expiration dates printed on drug container and carton labels has prompted USP to publish revisions to General Chapter <7> (*Labeling*) that will standardize the format. The revisions will apply to labels on all drug and dietary supplement products that comply with USP standards. The revisions were vetted through the USP Nomenclature and Labeling Expert Committee and approved following USP's routine revision process, with a public comment period from November 1, 2019, to January 31, 2020. USP published the revisions on July 31, 2020. To ensure enough time is available for manufacturers to prepare for the change, the new requirements will go into effect September 1, 2023.

Expiration date-related problems reported to the ISMP National Mediation Errors Reporting Program (ISMP MERP) include confusion with 2-digit year formats, such as 20MAR21, which can be interpreted as March 20, 2021 or March 21, 2020. Also,

continued on page 2 — Your *Reports* >

ECRI and ISMP to create a new joint PSO

ISMP is in the process of giving up our status as a sole-entity patient safety organization (PSO) so we can join with ECRI in a new joint ***ECRI and the Institute for Safe Medication Practices PSO***, a single, unrivaled source for safety. The new joint PSO will combine the global safety voices and skills of ECRI and ISMP to create one of the largest patient safety entities in the world. Watch for more information and details next week when the new joint PSO is officially launched!

> CSP mandate — continued from page 1

method for pharmacists to visually verify the amounts of CSP ingredients used after the preparations had been mixed. When the request for contracting with an IV workflow system was denied, the director independently managed to outfit each workbench/laminar flow hood with a computer tablet, barcode scanner, and camera, to supplement their EHR IV preparation software module. Within a few months, the combined technology was being used for all CSPs prepared in the pharmacy, including premixed IV compounds. The software and hardware combination was also used during the dispensing of certain high-alert medications (e.g., insulin vials) and vaccines, due to ongoing errors despite manual independent double checks.

The pharmacy director worked with information technology staff to receive weekly reports showing when the EHR pharmacy software with the supplemental hardware had detected a possible medication error during product selection when preparing CSPs, high-alert medications, and vaccines. The very first weekly report showed multiple instances of selecting and scanning wrong diluents, drugs, or strengths, particularly with antibiotics. One event caught the director's eye, because it was clear that this particular drug selection error could have resulted in the death of an infant had it not been caught by the newly implemented IV software and hardware and corrected before leaving the pharmacy.

The error

A physician prescribed IV fluconazole 12 mg/kg daily for a premature infant (1.5 kg) with invasive candidiasis in the neonatal intensive care unit (NICU). To prepare each dose, the pharmacy technician typically uses a premixed bag of fluconazole (200 mg in 100 mL of 0.9% sodium chloride) from which the required dose (18 mg [9 mL] in this example) is withdrawn into a syringe. In this case, the technician retrieved a 100 mL premixed bag from the fluconazole bin, but it was actually potassium chloride 40 mEq in 100 mL of fluid. Both the fluconazole and potassium chloride bags were packaged in 100 mL bags, and both bag labels presented the product name and strength in red font while other label text was black. It is presumed that the potassium chloride bag had been incorrectly returned to the fluconazole bin due to confirmation bias when glancing at the red font labeling and bag size (in many pharmacies these bags are typically stored apart from each other).

The potassium chloride bag was then taken into the cleanroom and placed on the workbench to prepare the fluconazole syringe. Fortunately, the bag was scanned before preparation of the syringe, and the error was caught prior to erroneously dispensing the potentially fatal dose of potassium chloride for the infant.

At pharmacy staff meetings, the director shared this error and other errors that were caught using the new technology rather than relying solely on manual independent double checks. Pharmacy staff agreed that events like these had been occurring and reaching patients regularly before utilizing the new software and hardware, and they were thankful that these errors were now being caught. Many pharmacy staff members also agreed that, even if the potassium chloride error had reached the infant and caused a fatality, the infant's death would not have been traced back to the erroneously prepared CSP but instead associated with the infant's medical condition or otherwise deemed an "unexplained death."

Recommendations

Data submitted to the ISMP National Medication Errors Reporting Program (ISMP MERP) have repeatedly shown that the human-based, manual, post-production verification of CSP ingredients by pharmacy technicians and pharmacists is not

continued on page 3 — CSP mandate >

Your *Reports* at *Work*

continued from page 1

2-letter months have been a problem. Does MA indicate March or May? How about JU? June or July?

While USP will allow both all-numeric and alphanumeric formats for expiration dates, the new standard dictates a consistent format for the year, month, and day to prevent confusion. To help healthcare workers, patients, and consumers distinguish between the year and the day, USP will require a 4-digit year format. Also, the use of hyphens or forward slashes is required to separate the year, month, and day to help improve readability. For example, when all-numeric dates are used, they must be formatted using 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). When alphanumeric dates are used, months must be displayed using at least 3 letters (e.g., 2019-JUN-30, 2019/JUN/30, 2019-JUN, 2019/JUN). The USP standard also harmonizes with the International Organization for Standardization (ISO) expiration date standard, with minor modifications. A summary of the changes is available at: www.ismp.org/ext/532.

SAFETY briefs

HIGH-ALERT

Use barcode scanning for inventory replacement. Cartons of bacitracin 50,000 units were accidentally placed in a refrigerator storage bin meant to hold **NOVOLIN** insulins. The cartons of bacitracin and Novo**LIN** insulins are of similar size and have blue and white labeling, although they look dissimilar. The error happened when a pharmacy technician was emptying the totes delivered by the wholesaler. Incidentally, the photograph (**Figure 1**, page 3) is from a previous report where the exact same error was reported.

It is surprising (**Figure 1**, page 3) that both Novo**LIN** N (insulin NPH) and Novo**LIN** R (insulin regular) are stored in the same bin, potentially leading to drug selection errors given the similarity of the insulin cartons. It is also surprising that not all hospitals have separate storage locations that incorporate labels with barcodes that should be scanned

continued on page 3 — SAFETY briefs >

> CSP mandate — continued from page 2

reliable for detecting and correcting CSP preparation and dispensing errors. ISMP strongly believes that the barcode scanning of all base solutions, diluents, medications, and other ingredients is the minimum requirement for pharmacy CSP processes, and that overriding any compounding technology-based alerts requires the review of a pharmacist, not a technician acting alone.

Furthermore, ISMP recommends the acquisition and implementation of IV workflow management system technologies that incorporate barcoding to verify ingredients as well as imaging and/or gravimetrics to verify ingredient and finished CSP volumes. These technologies should undoubtedly be used when preparing chemotherapy and pediatric infusions. We urge healthcare leaders to support the acquisition and implementation of IV workflow management systems as soon as possible in organizations with CSP processes that lack these technologies. The next patient's life could depend upon the decisions healthcare leaders make (or fail to make) today.

To this end, we are in sync with the THR**IV** Coalition, which argues that, just as critical technologies are required to meet sterility standards, IV workflow management systems should be required for achieving CSP accuracy. For guidance, go to the THR**IV** website to view a technology checklist of criteria that an IV workflow management system should meet or exceed (www.ismp.org/ext/530). And while on the THR**IV** website, consider adding your name as a THR**IV** Champion for IV accuracy (www.ismp.org/ext/531), acknowledging that fully efficient IV workflow management systems should be universally implemented and faithfully utilized by pharmacy compounding services to improve CSP accuracy.

In any facility that has yet to install the above technologies, all CSPs should be required to undergo an independent double check of the vials, ampules, prepared syringes, and container labels (drug and diluent) prior to adding them to the final solution, in place of the outdated "syringe pull-back" method or other manual post-production checking procedures.

Additional recommendations can be found in the ***ISMP Guidelines for Safe Preparation of Compounded Sterile Preparations*** (www.ismp.org/node/101). Also, one of the ***2020-2021 ISMP Targeted Medication Safety Best Practices for Hospitals*** (www.ismp.org/node/160, #11) recommends eliminating the use of proxy methods of verification for CSPs (e.g., the "syringe pull-back" method, checking a label rather than the actual ingredients), and instead using technology to assist in the CSP verification process (e.g., barcode scanning verification of ingredients, gravimetric verification, robotics, IV workflow management systems).

ISMP plans to publish more detailed recommendations for pharmacy sterile compounding processes after analyzing the findings from our current ***ISMP Survey on Pharmacy Sterile Compounding*** (www.ismp.org/ext/526). If you are a pharmacist or pharmacy technician who prepares or oversees the production of CSPs, please participate in our survey by **September 18, 2020**. We want to be sure that our future CSP recommendations thoughtfully address the challenges and safety concerns you have related to pharmacy sterile compounding, which we hope you will share with us via the survey.

Conclusion

Although the accuracy of parenteral sterile compounding processes is not as highly regulated as CSP sterility and the reduction of exposure to hazardous medications, it is a critically important component of medication safety and should not be overlooked. Healthcare leaders must direct the same level of resources to CSP error prevention as they do to engineering controls and construction to make the phar-

continued on page 4 — CSP mandate >

> SAFETY briefs cont'd from page 2

when reordering and restocking items. Those that do are in a better position to prevent errors, as each item can be removed from the wholesaler tote, verified with the packing slip against what was ordered, then placed in its storage location after scanning the product and storage container barcodes.

Figure 1. Bacitracin vials accidentally placed in Novo**LIN** bin.

Wakix and Lasix name confusion.

Potential name confusion was reported between **WAKIX** (pitolisant), a drug for adult patients with narcolepsy for excessive daytime sleepiness (EDS), and **LASIX** (furosemide), a diuretic. A medical resident was interacting with a patient via a secure messaging system. The patient asked about a change in his dose of "Wakix" and whether he should get blood tests drawn. The patient had been taking Lasix for some time, and the dose had been changed periodically by his cardiologist. Because the patient had made several spelling errors with other words when writing messages during this interactive session, the resident assumed the patient had made a spelling error when writing "Wakix" and was instead talking about Lasix. Further questioning revealed that the drug the patient was inquiring about was Wakix.

The tablet strengths of these medications do not overlap: Wakix is available in 4.45 mg and 17.8 mg tablet strengths, and Lasix is available in 20 mg, 40 mg, and 80 mg tablets, further decreasing the likelihood of a mix-up. While no error resulted in this case, physicians who treat patients with narcolepsy should be aware of the risk,

continued on page 4 — SAFETY briefs >

> CSP mandate — continued from page 3

macy and other clinical locations compliant with USP <797> and <800>. It is time for CSP accuracy and error prevention to be both a leadership and regulatory mandate. Similar to USP standards for sterility and hazardous drugs, perhaps standards and mandates would advance adherence and leadership prioritization of technologies that facilitate CSP accuracy and error prevention.

New trace element product available soon

Healthcare professionals involved with the provision of parenteral nutrition (PN) need to know that the US Food and Drug Administration (FDA) recently approved a multi-trace element product from American Regent, **TRALEMENT** (trace elements injection 4). This new trace element formulation meets recommendations that the American Society for Parenteral and Enteral Nutrition (ASPEN) made in 2012 (Vanek VW, Borum P, Buchman A, et al. A.S.P.E.N. position paper: recommendations for changes in commercially available parenteral multivitamin and multi–trace element products. *Nutr Clin Pract.* 2012;27[4]:440-91).

Tralement has different amounts of trace elements and dosing instructions than **MULTITRACE–5 CONCENTRATE**, the American Regent adult trace element formulation that is currently available (**Table 1**). Most notably, the product contains less manganese (approximately a 10-fold decrease) and copper. Each mL of the currently available Multitrace–5 Concentrate has zinc 5 mg, copper 1 mg, manganese 500 mcg, selenium 60 mcg, and chromium 10 mcg. The ASPEN position paper recommended decreasing zinc to 3-4 mg per day, decreasing copper to 0.3-0.5 mg per day, decreasing manganese to 55 mcg per day, maintaining selenium in a dose of 60-100 mcg per day, and eliminating chromium (or a maximum of 1 mcg per day). Each mL of Tralement has zinc 3 mg, copper 0.3 mg, manganese 55 mcg, and selenium 60 mcg (provided as selenious acid). No chromium is present. Tralement is expected to become available later this year. American Regent will no longer market Multitrace-5 Concentrate once Tralement is readily available.

Table 1. Difference between Multitrace–5 Concentrate and Tralement, along with ASPEN recommendations for adults

Trace elements	Multitrace–5 Concentrate (trace elements injection 5) per mL	Tralement (trace elements injection 4) per mL	ASPEN recommendation (Vanek VW, et al.) per day
Zinc	5 mg	3 mg	3 - 4 mg
Copper	1 mg	0.3 mg	0.3 - 0.5 mg
Manganese	500 mcg	55 mcg	55 mcg
Selenium	60 mcg	60 mcg	60 - 100 mcg
Chromium	10 mcg	0	0

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> SAFETY briefs cont'd from page 3

educate their patients about the possibility of confusion, and include the indication on all prescriptions for Wakix. In addition, when communicating via secure messaging systems, healthcare providers should always verify all medications discussed with the patient.

While confusion between Wakix and Lasix occurred in this case due to an erroneous presumption that the patient had made a spelling error, these two drug names sound similar. In addition to asking drug applicants to test all new trademarks, the US Food and Drug Administration (FDA) also conducts an extensive review of the risk for drug name mix-ups during the new drug application process. This includes name simulation studies with healthcare professionals, phonetic and orthographic computer analysis (POCA), and expert analysis by FDA staff. Twenty-five drug names were considered for possible confusion with Wakix, including Lasix, but none were assessed as presenting a serious risk of error. The FDA name analysis for Wakix is available at: www.ismp.org/ext/475.

Special Announcements

FREE international ISMP webinars

ISMP is presenting two **FREE** webinars intended for an international audience:

- **August 18:** ***A Look Behind the Scenes: Global Progress in Patient Safety and Prevention of Harmful Medication Errors*** (to register, please visit: www.ismp.org/node/18844)
- **September 15:** ***Enhancing Your Medication Error Reporting Program to Improve Global Medication Safety*** (to register, please visit: www.ismp.org/node/19035)

Accepting Cheers Awards nominations

Nominations for this year's ISMP **CHEERS AWARDS** will be accepted through **September 11, 2020**. These prestigious **AWARDS** celebrate the efforts of individuals, organizations, and groups that have demonstrated an exemplary commitment to medication safety. To submit a nomination, visit: www.ismp.org/node/1036.