
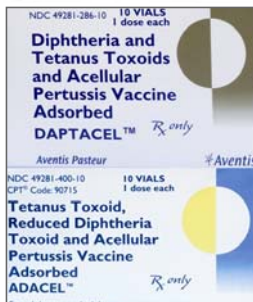


ISMP Medication Safety Alert!®

September 6, 2007 ■ Volume 12 Issue 18

Your Reports at Work

 **Packaging change.** Thanks to your reports about look-alike packaging confusion between **DAPTACEL** (diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed) and **ADACEL** (tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine adsorbed), sanofi pasteur has changed the carton and vial labels for both products (see below). Daptacel is used for active immunization against tetanus, diphtheria, and pertussis in infants and children 6 weeks to 6 years old. Adacel is given as a single dose for active booster immunization in patients 11 to 64 years old; it is the first vaccine approved as a pertussis booster for adults. The component antigens in Adacel and Daptacel are the same, but the relative amounts are much greater in the pediatric vaccination.



New packaging of Daptacel and Adacel (top) with improved color differentiation compared to older labels (left). The new label for Daptacel states "For pediatric use;" the old package did not.

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Fatal 1,000-fold overdoses can occur, particularly to neonates, by transposing mcg and mg

In October 2006, an infant received a lethal dose of zinc stemming from an error that occurred during the order entry and compounding of a TPN solution. While not privy to a full root cause analysis, ISMP has learned details about the event¹⁻³ which are offered below in the sincere hope that the lessons learned from this tragic event will be applied in hospitals across the nation to prevent similar tragedies.

SUMMARY OF THE EVENT

TPN was prescribed for a preterm infant born at 26 weeks gestation. On the day of the event, the physician's TPN order included directions to add zinc in a concentration of 330 mcg/100 mL. Because the automated compounder used for TPN required entry of zinc in a mcg/kg dose, the pharmacist converted the mcg/mL dose to a mcg/kg dose. She performed this calculation correctly, but accidentally entered the zinc dose in the pharmacy computer in mg, not mcg. This resulted in a final concentration of 330 mg/100 mL—a 1,000-fold overdose. Another pharmacist checked the work and product labels that were printed for preparation of the TPN, but she did not notice the mcg to mg error. A pharmacy technician prepared the TPN using a 500 mL bag. The technician had to replenish the compounder syringe that contained zinc 11 times while preparing the solution, which required dozens of vials of zinc sulfate. Several TPN additives had to be added manually, which the technician prepared and brought to a third pharmacist to check before adding them to the solution. The final TPN bag was then dispensed to the neonatal intensive care unit (NICU).

Around 3 a.m., a nurse hung the bag of TPN. Around 6 a.m., the technician who prepared the TPN discussed the previous evening's work with the oncoming lead

technician, noting the unusual preparation of the TPN that required numerous replenishments of the zinc syringe. The oncoming technician checked the order, discovered the error, and alerted a pharmacist, who immediately called the unit to stop the infusion. The pharmacist quickly called Poison Control and searched the Internet for treatment guidelines. The infant received edetate calcium disodium (**CALCIUM DISODIUM VERSENATE**, also referred to as *calcium EDTA*), which had been compounded by an external pharmacy, but the chelation therapy was unsuccessful, and the infant died. The coroner listed cardiac failure caused by zinc intoxication as the cause of death.

SYSTEM-BASED CAUSES OF THE EVENT

The method used to prescribe the zinc additive was different than the method required to enter the order into the automated compounder software program, which contributed to an order entry error. ▼

The automated compounder required entry of the zinc additive in mcg/kg. A preprinted order form was used to prescribe neonatal TPN. The usual TPN ingredients listed on the order form prompted the physician to prescribe their doses by weight (e.g., mEq/kg, mg/kg). However, zinc was not listed on the form, so the physician wrote a free-text order for zinc, 330 mcg/100 mL. The pharmacist had to convert the dose to mcg/kg, after which she mistakenly chose "mg" instead of "mcg" from a pull-down list when entering the dose of zinc. The units of measure were next to each other on the pull-down list.

Dosing alerts did not occur when the TPN order was entered into the pharmacy computer, or when the directions for preparation were scanned into the automated compounder. ▼

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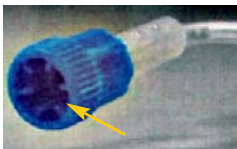


Your Reports at Work continued

With the original packaging, these products were frequently confused, resulting in immunization of adults with the pediatric vaccine and vice versa. Similar brand names, generic designations, and vaccine abbreviations (Tdap, DTaP) also contribute to confusion; thus, mix-ups are still possible even with the new package design. Some drug references, drug information databases, and wholesalers reference Adacel's component antigens as diphtheria, tetanus, and acellular pertussis rather than the way they are listed on the label, with tetanus toxoid first. Another factor that adds to the confusion is a federal regulation that requires listing of nonproprietary names on labels of biologicals *above* the brand name. This is inconsistent with the labeling of other drugs. Also, the font size and typeface of the nonproprietary name must be at least as prominent as that used for the brand name. To prevent mix-ups between these products, separate their storage and build alerts in computer software to warn practitioners about the differences between the adult and pediatric formulations. If possible, configure the order entry system to disallow selection of the wrong product based on the patient's age. Also verify the patient's age prior to dispensing or administering vaccines.



New design. In our October 19, 2006 newsletter, we mentioned a problem with PharMEDium's use of a universal male-female cap to seal the port on IV minibags containing admixtures compounded for the Baxter APII pain management pump. The solid plastic cap had reversible fittings (female on one end, male on the other end), so it was possible to connect it to the Luer end of the pump's tubing if the clinician forgot to remove the cap. Although the cap's design looked like it would allow fluid to flow through it, the cap occluded the fluid pathway, which led to cases in which patients did not receive the intended drug. PharMEDium has now introduced a new cap for use with all pain management admixtures compounded in the Baxter APII containers. The new design features a proximal female Luer for connection to the minibag tubing, and circumferential fins inside the distal end of the cap to prevent connection to the pump's tubing (see photo). We appreciate PharMEDium's efforts to create a safe, sterile product designed to minimize the risk of errors.



New PharMEDium cap has internal "fins" to help avoid accidental connection to pump tubing.

Overdoses continued from page 1

The pharmacy computer order entry system and the automated compounder used to mix the TPN did not alert the pharmacist that a 1,000-fold overdose had been entered into the systems for the zinc additive.

The TPN order was processed during the evening when staffing was limited despite a hospital policy to receive TPN orders and prepare TPN solutions before 5 p.m. ▼

On the day of the error, the physician prescribed the TPN at 4:30 p.m., but the order was not scanned and transmitted to the pharmacy until after 5 p.m. The pharmacist entered the order after 7 p.m. and the TPN solution was compounded later in the evening when less pharmacy staff were available to process complex orders such as TPN. Staffing was further reduced on the evening of the event due to the absence of a technician who typically compounded products.

Limited education and experience, along with ineffective competency validation regarding compounding products, particularly for infants, contributed to the technician's failure to notice the TPN order entry error. ▼

The technician who prepared the TPN did not have sufficient orientation or experience to immediately appreciate the significance of the large volume of zinc required by the automated compounder to prepare the TPN. Her prior training consisted of a week of shadowing another technician, during which she compounded fewer than 20 products using the automated compounder. In that time, she had never replenished a syringe on the compounder. Although she thought it unusual to replenish the zinc syringe 11 times during the course of making the TPN, she did not mention this to a pharmacist. (Zinc was typically added to TPN manually due to the small volume needed, but the compounder was used in this case because the error resulted in directions to add a large volume of the zinc to the bag.) The inexperienced technician also did not think to question the need to use a 500 mL bag to make the TPN, rather than a 250 mL

bag which was typically used for neonatal TPN. Concerns about the technician's level of training had been raised by staff previously, but on the day of the event, the technician had been asked to compound a few products because the usual compounding technician was not available.

The technician reported the unusual circumstance of replenishing the zinc syringe 11 times while compounding the TPN to the lead technician the following morning, but she did not mention her concern to the on-duty pharmacist on the evening of the event. ▼

The inexperienced technician reported feeling intimidated talking to the pharmacist about a condition she found potentially unusual, when she was uncertain whether it signaled an actual error. She believed the pharmacist who entered the order must be correct, and that she should not question the pharmacist.

Ineffective or nonexistent systems for independent double-checks allowed the error to bypass at least six staff members without notice. ▼

At several points during the dispensing and administration process, pharmacists or nurses checked the TPN orders and/or labels, but the error was not recognized. The first check failed, primarily due to human error, when the pharmacist who compared the work and product labels to the original order did not notice that the zinc dose was expressed in mg, not mcg. The next faulty check involved verifying only the additives that had been added manually to the TPN. Hospital policy only required pharmacists to check the vials and syringes of the additives against the label; they were not required to compare the TPN product label to the original order. To verify the additives, the pharmacist in this case looked at the identifying information on the top of the label, and then skipped down to the bottom of the label to identify the additives to be added manually, thus failing to read the middle of the label which noted that 481.8 mL of zinc had been added to a bag that contained 560 mL. Another ineffective check occurred in the

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Worth Repeating...

Preventing mix-ups between various formulations of amphotericin B

The National Patient Safety Agency in the United Kingdom (UK) issued a medication alert on Monday warning healthcare providers of the risk of confusion between different formulations of intravenous amphotericin used to treat serious fungal infections. Alerts issued by ISMP since 1997 and by ISMP Canada since 2002¹⁻⁴ have called attention to mix-ups between the lipid-based and conventional formulations of this drug. Mix-ups have led to overdoses—sometimes fatal—or underdoses resulting in subtherapeutic treatment. Two recent deaths in the UK prompted a call for the country's hospitals to take action, such as the suggestions noted below, which are based on prior ISMP recommendations.

1. Conventional amphotericin B deoxycholate doses should not exceed 1.5 mg/kg daily.
2. Encourage prescribers to communicate orders using both the proprietary name and the complete generic name: **FUNGIZONE** (amphotericin B desoxycholate), **AMBISOME** (amphotericin B liposomal), **ABELCET** (amphotericin B lipid complex), and **AMPHOTEC** (amphotericin B cholesteryl sulfate complex). List both the generic and brand names on protocols, preprinted orders, pharmacy labels, and medication administration records (MARs).
3. Include the patient's weight in kg and dose calculations as part of the prescription.
4. Verify the dose if you are unfamiliar with the drug and/or usual dose prior to prescribing, dispensing, and/or administering the drug.
5. Ensure that detailed, technical drug information is easily and readily accessible in clinical areas that use amphotericin products.
6. Add a warning statement to all IV administration guidelines or drug charts produced by the hospital specifically describing the risks associated with these products.
7. Restrict the preparation and dispensing of amphotericin products to the pharmacy.
8. Differentiate or separate the storage of different formulations of amphotericin within the pharmacy (and in other areas where the drugs might be stored). Use cautionary labels to remind staff about the differences between the products. Add these statements to MARs.
9. Require an independent double-check before administering amphotericin products.

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Overdoses continued from page 2
NICU unit. One nurse read the “numbers” associated with the dose for each ingredient from the TPN label, but not the units of measure (e.g., mg/kg, mg/dL), to another nurse who was reading the original order. While the “numbers” (including “330” for the zinc additive) matched, the accidental entry of mg instead of mcg was, again, not noticed. Sadly, many clues that pointed to the error were overlooked during the verification processes, including the fact that the TPN bag was unusually large—bigger than the infant herself. One final note about check systems: The pharmacist's initial calculation to change the mcg/mL dose to a mcg/kg dose was never verified by another pharmacist. Although the calculation in this case was correct, and the check would not have averted the error, an independent double-check of calculations should always occur.

SAFE PRACTICE RECOMMENDATIONS

- **Standardize the prescribing methods.** Standardize the method of ordering TPN solutions (and other routinely compounded solutions) for neonates, pediatric patients, and adults, so that each prescribed ingredient matches the dosing templates used for entering the orders into the computer system and automated compounder. Use preprinted forms or standard order sets that list typical ingredients and prompt the correct dosing method. On the rare occasions that calculations are necessary, require two clinicians to calculate the dose independently and compare their answers for verification.
- **Prescribe and transmit TPN orders during the day.** Policies that require prescribers to order TPN daily during the day shift should be established and *enforced* to maximize the safety with which these solutions are prepared and dispensed. Pharmacy staff should be aware of patients who are receiving TPN and check if orders have not been received by the established time.
- **Allow manual-only additions of low volume ingredients.** For TPN ingredients that typically require very small volumes, require staff to prepare, check, and inject

those ingredients manually. Do not allow a trace element such as zinc to be loaded on a compounder for automated preparation.

- **Build, test, and heed automated warnings.** Install, test, and maximize automated dose-limit warnings in the pharmacy computer system and automated compounders, particularly for high-alert medications such as TPN and its ingredients. Baxa, an automated compounder vendor with a large share of the hospital market, allows users to add soft warnings and hard stops if a dose limit is breached when entering an order. The company's more recent compounder software has “catastrophic” limits that stop the process completely when 100-fold or 1,000-fold overdoses caused by decimal point errors or mcg to mg selection errors occur. Consider printing all alerts encountered during the order entry process so the person checking the order entry can also view and respond to the alerts. Reinforce the importance of reading and reacting to the alerts with all staff.

- **Heighten the suspicion of an error.** Continually emphasize that the following should trigger a full review of the patient's medications and treatment plan to ensure an error has not occurred:

- ▶ The need to use more than a few dosage containers (whether it be tablets, capsules, vials, ampuls, etc.) to prepare or administer a single dose of any medication
- ▶ Unexpected differences in the appearance of medications or solutions
- ▶ Other unusual circumstances regarding a medication or solution
- ▶ Unexpected patient response to a medication.

Technicians who compound products should be required to **stop the process** if they encounter situations in which they need to add an electrolyte or mineral in large doses or in large volumes in order to complete a single preparation. A full review of the work label and order by a pharmacist should be required before proceeding. Nurses who work in pediatric and neonatal units should question products

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Worth Repeating... continued

10. Include liposomal forms of drugs on your organization's list of high-alert medications; such products are included on ISMP's list (www.ismp.org/Tools/highalertmedications.pdf).

References: 1) Institute for Safe Medication Practices (ISMP). Same old, same old. *ISMP Medication Safety Alert!* Smetzer J, Cohen M. eds. September 8, 1999:3. 2) ISMP. Special alert!! Medication errors with lipid-based drug products. *ISMP Medication Safety Alert!* Cohen M, ed. August 18, 1998. 3) ISMP Canada. Warning: prevent mix-ups between conventional amphotericin B (Fungizone) and lipid based amphotericin B products (Ambisome and Abelcet). *ISMP Canada Safety Bulletin*. June 2002. 4) ISMP. Safety brief. *ISMP Medication Safety Alert!* Wiegman S, Cohen M. eds. November 19, 1997:1.

Look What's New!

■ **Free FDA patient safety videos.** The latest medication safety-related videos, developed by FDA in cooperation with ISMP, are now available free for viewing or downloading on the ISMP website (www.ismp.org/Tools/fdavidoes.asp). See below for the latest 2007 offerings.

September: [Caution on No-Name Drug Patches; Preventing Patient Deaths from Fentanyl Patches](#)

July: [Avoiding Dangerous Mix-ups between Insulin and Heparin](#)

June: [Preventing Drug Mix-Ups: Bumetanide and Norepinephrine](#)

March: [Possible Dose-Counter Errors with the Asmanex Twisthaler](#)

■ **PDUFA IV.** The Pharmaceutical Research and Manufacturers of America (PhRMA) issued a news release last month that acknowledged creation of a "good naming practices" (GNPs) document as noted in our August 9, 2007, newsletter article, *Progress with preventing name confusion errors*. PhRMA noted that the PDUFA IV (Prescription Drug User Fee Act IV) legislation before Congress addresses GNPs but goes even further because it allows FDA to implement other measures to reduce medication errors. For example, it would fund development, in consultation with industry, academia, and others, of guidance statements on proprietary name evaluation and on naming, labeling, and packaging of drugs and biologics. FDA would also initiate a pilot program for industry to submit data in support of drug names. We expect that approval would be based on testing protocols that use healthcare practitioners and safety experts to evaluate names for look-alike and sound-alike similarity, something that ISMP and others have previously suggested.

Overdoses continued from page 3 that are dispensed in larger quantities than typically supplied for children or neonates. Create a culture that encourages all staff, despite their level of experience or education, to speak up about unusual conditions. (See our March 11 and March 25, 2004, issues for suggestions to reduce staff intimidation.)

■ **Carry out effective redundancies.** Conduct independent double-checks during the dispensing and administration processes associated with TPN. At least three verification processes should occur in the pharmacy: after initial order entry of TPN; before manually injecting additives into the TPN; and once the TPN has been compounded. Each verification should require a pharmacist to compare the actual prescriber's order to the printed labels, and the printed labels to the additives and final product, as appropriate. Verification of manual additives should include inspection of the actual vials and syringes that contain the additives. The final verification of the compounded TPN should include a comprehensive review of the TPN order, the label on the product, and the work label. As appropriate, quality control checks and verification of replacement solutions on the compounder either manually or via bar-coding should also be required, as should an independent double-check of any calculations. Before administering TPN, two nurses should also independently compare the label on the solution with the physician's order.

■ **Provide education and validate competency.** Establish a formal training process for pharmacy staff who are required to enter TPN orders into the pharmacy computer, compound the solutions, or check the products after preparation. Designate and train specific staff members to function as preceptors and provide one-

on-one supervision until trainees are comfortable providing the service and have demonstrated the skills and knowledge necessary to function independently. Training should focus on dose and dose concentration, not just the volume of additives, when preparing the solutions. If compounding services are provided for neonatal and pediatric patients, include age-specific training emphasizing weight-based dosing, and validate the competency of all staff who serve the pediatric population. Develop learning modules and competency validation tools to expose trainees to a broad spectrum of responsibilities that they might not encounter during their on-the-job orientation. Plan adequate staffing with trained practitioners to cover vacations, illnesses, and other causes of planned and unplanned absences. Establish guidelines for closer supervision of work if emergency coverage with an inexperienced staff member is necessary.

References: 1) Wells A. Error that led to baby's death slipped through many hands. *Las Vegas Review-Journal*; August 5, 2007. 2) Wells A. Answers bring more tears. *Las Vegas Review-Journal*; July 26, 2007. 3) Nevada State Board of Pharmacy Order of August 9, 2007.

ISMP thanks the Nevada State Board of Pharmacy for its contribution to the above article by sharing many of the details of its investigation of the event with ISMP.

Special Announcement...

ISMP-USP workshops. ISMP and USP are offering workshops on collecting, analyzing, and prioritizing adverse drug event data. The full-day programs, *Using Data Effectively to Manage the Risks to Medication Safety*, will be held in Tampa, Chicago, Rockville, and Las Vegas, between **September and December 2007**. Participants will learn how to select effective risk-reduction strategies and the best way to report findings to demonstrate improvement. Breakout sessions will offer participants an opportunity for hands-on practice working with safety data. For details, visit: www.ismp.org.

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