A step backward for patient safety? PhRMA seeks repeal of federal regulation that supports safety testing of drug names

If the Pharmaceutical Research and Manufacturers of America (PhRMA) has its way, a federal regulation crucial to medication safety [21 CFR 201.10 (c) (5)] will be repealed. According to this regulation, labeling of a drug may be misleading when a proprietary name is used that, “because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient.” Repeal of this regulation, which gives authority to the FDA to clear proposed drug names, would essentially strip away FDA’s authority to incorporate pre-market safety reviews as part of the drug approval process. It’s unclear how repeal of the regulation would impact post-marketing actions if brand name confusion was known to contribute to harmful medication errors; but even post-marketing actions might be difficult to undertake if the regulation is repealed.

PhRMA requested repeal of the regulation in a formal response to an April 27, 2011, Federal Register notice by FDA requesting suggestions for eliminating any existing rules perceived to be “outmoded, ineffective, insufficient, or excessively burdensome and thus may be good candidates to be modified, streamlined, expanded, or repealed.” PhRMA wants FDA to prove its name review testing program actually prevents medication errors, even though it seems obvious. PhRMA argues that FDA’s name review program is “burdensome and disruptive without showing that it is effective in reducing medication errors.” They also contend there are no validated measures for identifying brand names that are similar enough to be confused. Until such proof can be provided, the group considers the name testing protocol to be “ambiguous and arbitrary” and has, thus, requested its repeal.

As the nation’s only nonprofit organization devoted solely to medication error prevention, ISMP has borne alarming witness to just how easy it is for even

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Misadministration of IV insulin associated with dose measurement and hyperkalemia treatment

**Problem:** We are aware of numerous reports of serious errors associated with the misadministration of insulin. These events have involved various types of practitioners, including physician house officers (HO), nurses, and a pharmacist. Human error (e.g., mental slips, lapses, forgetfulness) associated with insulin dose measurement and hyperkalemia treatment was the predominant proximate cause of these events; most of the human errors were associated with knowledge deficits regarding insulin concentration (specifically that “U-100” means the concentration is 100 units per mL), the differences between insulin syringes and other parenteral syringes, and a perceived urgency with treating hyperkalemia.

In the most recent event, a physician ordered IV dextrose 50% injection (50 mL) along with 4 units of regular insulin IV (U-100) for a patient with renal failure and severe hyperkalemia. However, a nurse drew 4 mL (400 units) of insulin into a 10 mL syringe and administered the dose IV. The patient became severely hypoglycemic and had to be transferred to a critical care unit for treatment and monitoring.

In another case, a nurse accidentally added 50 units of regular insulin to an existing IV infusion instead of 5 units. A physician had asked the nurse to add 5 units to the IV bag. The nurse felt the ½ inch insulin needle on an insulin syringe was not long enough to insert into the IV bag. Thus, the nurse drew the insulin into a 3 mL syringe with a longer needle. However, she accidentally withdrew 0.5 mL (50 units) of insulin instead of the correct volume of 0.05 mL (5 units). She quickly showed the prepared dose to another nurse, who also failed to pick up the error. Later, the nurse recognized her error while preparing a subcutaneous insulin dose for another patient using a U-100 insulin syringe.

A third case involved the incorrect preparation of an insulin infusion. While the pharmacy was closed, a physician ordered an IV insulin infusion for a patient. Near the end of her shift, a new graduate nurse was asked to prepare a “1:1” insulin infusion (1 unit/mL). An experienced nurse who checked the solution failed to notice that the graduate nurse had drawn 10 mL (1,000 units) of insulin into a 10 mL syringe, instead of 1 mL (100 units) in an insulin syringe, and then added that amount to a 100 mL bag of 0.9% sodium chloride. This resulted in a 10 units/mL insulin infusion. Several hours later, both nurses—by then, at home—independently called the hospital because they were worried that “something was not right” with the insulin infusion. When the error was discovered, the patient had already received 160 units of insulin over several hours instead of the prescribed 16 units. The patient’s blood glucose level dropped as low as 13 mg/dL. He was treated and experienced no additional adverse effects.

A similar event was reported, but in this case, a pharmacist prepared an insulin infusion in a 10 units/mL concentration instead of the required 1 unit/mL concentration. It is not unusual to prepare an admixture or dose using half of a vial or more when dealing with other medications that typically come in multiple-use vials. Thus, staff may not find it odd to use half of a vial or more to prepare an insulin infusion, particularly if they are busy, distracted, or preoccupied. But a 10 mL multiple-dose vial of insulin can essentially contain up to 100 doses or more.

We also recently became aware of a case in which a patient with hyperkalemia had continued on page 2 — IVinsulin
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diligent and knowledgeable staff to confuse products with similar names. Confirmation bias often makes it nearly impossible to distinguish between similar drug names, as we have a tendency to see what we believe we should see and unconsciously ignore any disconfirming evidence if we are actually viewing the wrong product name.

Sadly, there is a long history of product mix-ups due to similar drug names that have resulted in patient harm. Without the FDA name review testing program during the drug approval process, there is little doubt that the number of serious errors will be far greater. ISMP firmly believes that patient safety will take a step backward if FDA is stopped from conducting safety reviews. The FDA name testing program provides a crucial safety benefit and should not be repealed simply because there is not a large body of evidence regarding its effectiveness.

Instead, a far better solution would be for FDA, PhRMA leaders, and proprietary name review representatives to meet to discuss and resolve any issues associated with the current FDA name review testing program. All involved parties should find common ground on which to move forward with improved drug name testing, not backward by repealing the basis for such an important safety program.

Full disclosure: Med-ERRS, an ISMP subsidiary, conducts pre-market testing of brand names to promote safety.

SafetyBriefs

High-alert medication

Use of two pumps allows bypass of drug library. Propofol is sometimes prescribed off-label for refractory status epilepticus. Recently, a nurse infused propofol IV for this indication at a rate of 225 mcg/kg/minute. The nurse had been titrating the rate up as directed and confirmed by the patient’s physician. However, due to previous excessive dose adverse events, the smart pump’s drug library was set with a hard stop at 130 mcg/kg/minute. Since the nurse could not make the pump infuse the required dose due to the hard stop, she instead used two infusion pumps to deliver the titrated dose. The nurse had questioned the high propofol dose, but the physician had misconstrued the nurse that the dose was appropriate (even though a 70 kg patient, for example, would go through about 1 bottle of propofol [1,000 mg/100 mL] per hour). The patient’s condition deteriorated. He exhibited symptoms similar to propofol infusion syndrome continued on page 3 – SafetyBriefs

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orders to receive insulin and a 50% dextrose injection, but the patient received only the insulin portion of the treatment and experienced significant hypoglycemia.

In several other recent events reported to us from countries outside the US, physicians were involved in the insulin administration errors. In one case, 10 units of insulin was prescribed, but a medical staff HO inadvertently administered 100 units of insulin using a regular parenteral syringe. In a second case, a HO administered 50 units instead of 5 units of insulin. The HO failed to read the number alongside the first large measurement marking (5 units) on an insulin syringe and assumed the marking on the syringe was for 1 unit of insulin. The patient developed hypoglycemic encephalopathy and later died. In yet another case, 10 units of insulin was prescribed, but the HO inexplicably did not use an insulin syringe and administered 8 mL (800 units) of IV insulin drawn into a 10 mL syringe. In the final case, 8 units of insulin was ordered, but the HO drew the insulin into a 3 mL syringe and administered 300 units IV to the patient. The practitioner who reported these errors could provide no explanation regarding why the Hos confused 10 units with 8 mL (800 units) and 8 units with 3 mL (300 units).

In the events involving physicians outside the US, the hospitals required physicians to administer the first dose of IV medication in case an immediate allergic reaction or other adverse drug reaction occurred. This may have contributed to the errors because many physicians have not received formal education on insulin administration. Requiring physicians to administer the first dose of IV insulin may also cause workflow disruptions and significant delays while waiting for the physician to administer the dose. Although the intention is to have the physician available in the event of an adverse drug reaction, in practice, physicians often administer the IV medication and then immediately leave the patient’s bedside. This can create even greater risk as the nurse may not be available to perform adequate monitoring post drug administration. In fact, requiring physicians to administer the first dose of IV insulin may actually add risk to the process with little or no known benefit.

Safe Practice Recommendations: With insulin, it should not be assumed that all healthcare practitioners are knowledgeable and skilled with measuring doses, preparing insulin infusions, and recognizing doses that exceed safe limits. Consider the following recommendations to enhance safety with this high-alert medication.

Provide education. Education regarding the concentration of insulin products, the differences between insulin syringes and other parenteral syringes, how to measure doses, recognition of safe dosage ranges, and how to administer the drug, should be provided to all who might prescribe, prepare, and/or administer insulin. Restrict insulin preparation and administration to those who have demonstrated competency.

Supply insulin syringes. Insulin syringes should be readily available in all patient care units, and steps should be taken to separate insulin syringes from other parenteral syringes so they cannot be inadvertently mixed-up.

Dispense from pharmacy. To preserve an independent double-check, wherever possible, pharmacy should prepare, label, and dispense insulin doses to treat hyperkalemia. Some organizations dilute the IV insulin dose and dispense it in a minibag. Hyperkalemia is a medical emergency, yet the administration of insulin, in most circumstances, can wait until a pharmacy prepares a stat dose. In general, pharmacy should also prepare all insulin infusions using a standard concentration (e.g., 1 unit/mL). Proportional orders such as “1:1 ratio” should not be accepted, as they can be misinterpreted as 1 mL of drug per 1 mL of IV solution. If the pharmacy does not provide 24-hour services, consider stocking a night cabinet with a pharmacy-mixed insulin infusion and diluted insulin in a syringe (for hyperkalemia treatment) that are discarded and replaced when continued on page 3 – IV insulin
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(www.medscape.com/viewarticle/713867_3), a sometimes fatal disorder seen when the drug is infused at high doses (above 70-80 mcg/kg/minute) for prolonged periods (more than 24-48 hours). The syndrome is characterized by severe metabolic acidosis, rhabdomyolysis, hyperkalemia, renal failure, and cardiovascular collapse. This is not the first time we have heard about this workaround—using two infusion pumps in order to exceed a hard stop on the infusion rate set in a smart pump library. Needing a technology workaround like this or employing other devices in an unintended manner should always prompt an immediate peer review of the conditions that require the workarounds before they are employed. Under most conditions, the need for the workaround is a clear signal of a potentially serious medication error.

**Parenteral Nutrition Safety Survey.** The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) needs data on how you are ordering, compounding, and labeling parenteral nutrition (PN). A.S.P.E.N. will use these findings to develop recommendations and PN safety guidelines at its September 23, 2011, PN Safety Summit, at which ISMP will participate. This survey is open to all clinicians involved with PN. The survey should take about 15 minutes and will close August 29, 2011. To take the survey, please visit: www.surveymonkey.com/s/SWN6WRM.

**ISMP Errata**
**Correction.** In a Safety Brief in our July 28, 2011, newsletter about nuclear medicine products lacking a barcode, we inadvertently referred to DraxImage MDP-25 as one of the products instead of MDP-Bracco. We regret any confusion this might have caused.

**Special Announcement…**
**ISMP webinar.** On September 28, ISMP will present HYDROMorphine: Taking Aim at Events Under the Radar—Regional Initiatives that Show Improvement. HYDROMorphine continues to be associated with patient harm. Some organizations have begun to recognize this risk, while others may not be aware of the number of adverse events associated with this drug. Join us to learn how to uncover these “hidden” events and to hear about safety strategies that several hospitals are implementing to prevent HYDROMorphine-related events. For details, visit: www.ismp.org/educational/webinars.asp.

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necessary (e.g., every 24–48 hours). There are also 3 mL vials of regular insulin available, which can be provided to lessen the risk exposure. Insulin (or any other additive) should never be added to IV solutions that are already hanging or infusing. Pharmacy should dispense a newly mixed infusion if new additives (e.g., insulin) are required after hanging an IV infusion.

**Provide reminders.** In organizations that do not dispense patient-specific insulin doses from the pharmacy, a warning should appear on automated dispensing cabinet (ADC) screens and electronic/computer-generated medication administration records that states the insulin needs to be prepared using an insulin syringe.

**Conduct an independent double-check.** Require an independent double-check of all doses before dispensing and administering IV insulin. Include a double-check of the blood glucose result if the dose of insulin being administered is based on that result. Build the double-check into daily work processes so it can be accomplished without disruption. “Smart” infusion pumps with programmed dose limits can serve as an additional check when administering insulin infusions. Verification of pump settings should also be included in the checking process.

**Consider use of an insulin kit.** Two of the foreign institutions where errors occurred have developed ‘insulin kits’ for use when implementing a hyperkalemia protocol. This kit includes instructions that warn the user to administer insulin using an insulin syringe. Each kit contains an insulin vial, insulin syringes, alcohol swabs, and a photograph that clearly indicates how to measure various volumes and doses of insulin. Although we have not previously recommended such kits, they may make sense in some environments without 24-hour pharmacy services because the kits include all the necessary items, including the insulin, insulin syringes, and 50% dextrose injection. However, in light of the above-cited medication errors, supply only 3 mL vials of regular insulin in these kits instead of 10 mL vials to limit risk exposure.

**Monitor patients.** Gauge the patient’s response to insulin by obtaining blood glucose levels. For hospitalized patients, the nurse who administers the insulin should perform the glucose testing whenever possible to avoid potential communication failures. Pay special attention to patients at risk for hypokalemia and hypoglycemia (e.g., people who are fasting, have autonomic neuropathy, or are taking potassium-lowering drugs). Patients with renal or hepatic impairment may require reduction in total daily doses of all insulin.

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**Deadline extended to September 30 for the ISMP Medication Safety Self Assessment**

**We would like to extend our sincere thanks to all who have already completed the 2011 ISMP Medication Safety Self Assessment for Hospitals.** We have heard from many others who have started the assessment but need more time to complete it. For this reason, and to allow others to join in this important study, we have extended the deadline for submission of the assessment findings via ISMP’s secure web-based portal to September 30, 2011. If you have not yet begun the assessment, please take this extended opportunity to join many other US hospitals in this national medication safety project. To access the project webpage, please visit: www.ismp.org/selfassessments/Hospital/2011/Default.asp.

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