Medication Safety Alerts

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This column draws on US and Canadian experience and includes, with permission, material from the *ISMP Medication Safety Alert!*, a biweekly bulletin published by the Institute for Safe Medication Practices (ISMP), Huntingdon Valley, Pennsylvania.

INDUSTRY'S DOUBLE STANDARD A RISK FOR CANADIAN PATIENTS

The *Medication Safety Alert Bulletin* dated April 17, 2002, sent out by ISMP Canada, described a preventable sentinel event involving a mix-up of look-alike products. In this case, sterile water for injection was inadvertently infused instead of the intended normal saline solution. The patient suffered harm and required a prolonged stay in the hospital.

Sterile water for injection is intended for pharmacy use only. Although the product label reads, "Pharmacy Bulk Package. Not for Direct Infusion", the warning is not very noticeable. In addition, the 1-L size of sterile water for injection is very similar in appearance to that of the normal saline solution made by the same manufacturer. On checking with our US counterpart, the Institute for Safe Medication Practices (ISMP), we learned that the 1-L packages for sterile water for injection and normal saline marketed by the same manufacturer in the United States are very different looking. The American product has the following clear warning, printed in red block letters on the label:

> Sterile Water
> Sterile Water for Injection USP
> FOR DRUG DILUENT USE ONLY

Although medication errors often have multiple contributing factors, the lack of a distinct warning on the label for the Canadian product and the similarity of the packaging to that of the normal saline product are considered major risk factors for error with sterile water for injection. ISMP Canada is very concerned that a similar error could occur in another Canadian hospital and is now working with the manufacturer to address this issue.

In the interim, we have made some recommendations to prevent a similar adverse drug event.

- Consider having the pharmacy control and purchase the 1-L sterile water for injection product directly.
- Consider affixing, upon receipt of the 1-L sterile water for injection product, a visible, cautionary, auxiliary label. The label might read as follows:

  CAUTION
  STERILE WATER
  For Reconstitution Use ONLY
  DO NOT Infuse
- Consider eliminating the 1-L sterile water for injection product from inventory and replacing it with the 2-L size. The difference in size will reduce the likelihood of confusion with commonly used 1-L IV solutions.
- Review your contingency procedures for back-order situations and ensure that a review of "error potential" is part of the process. Some hospitals use sterile water for injection as a substitute for sterile water for inhalation or sterile water for irrigation. Through such substitutions, sterile water for injection ends up in patient care areas.
- Review the potential risk associated with other sterile water products stocked in the hospital, for example, inhalation solutions and irrigation

solutions. Because these solutions are also available in a variety of sizes, there may be merit in standardizing the irrigation solutions to a 3-L size and the inhalation solutions to a 2-L size. The size differences will help to differentiate these products from IV solutions.

The case outlined above is only one example of a manufactured product with different safety labelling and packaging standards in the United States and Canada. ISMP Canada is working with a number of pharmaceutical companies to make improvements where similar concerns have been identified. So far, the industry has been very supportive and collaborative. There is a need to diligently and vigorously identify labelling and packaging weaknesses proactively to prevent similar adverse drug events.

The pharmaceutical industry in Canada should take note of initiatives implemented by its US counterpart. Most pharmaceutical companies operating in Canada are multinationals. It is important to perform in-depth analyses of drug names, packaging, and labelling in all countries before products are launched and through ongoing market analysis. Failure mode and effects analysis is a process that can be used to determine the error potential of labelling and packaging choices and is recommended to all pharmaceutical manufacturers. The MED-E.R.R.S. division of ISMP (United States) is offering drug product safety testing for the pharmaceutical industry. It has performed hundreds of such tests for most of the manufacturers in that country. The goal is to minimize the potential for errors with new and existing medical products.

Michael Cohen of ISMP expressed similar concerns in the April 18, 2001, *ISMP Medication Safety Alert!* newsletter. We feel that it is appropriate to reprint his comments (see below) to give more examples of how industry should apply the same safety standards in all countries.

SPECIAL FEATURE

The special feature presented below is taken from *ISMP Medication Safety Alert!* volume 6, issue 8, April 18, 2001.

Lessons Lost by the Global Pharmaceutical Industry

Despite many frustrations with the slow resolution of some product-related problems in the US, it is clear that practitioners' efforts to report medication errors to the United States Pharmacopeia (USP), ISMP and FDA [US Food and Drug Administration] have not been in vain. We have learned much from practitioner reports, including evidence that a large percentage of medication errors are attributable, at least in part, to commercial labeling, packaging, and nomenclature issues. As a result, the US pharmaceutical industry, USP, and FDA have been given sufficient information upon which to base improvements in labeling, packaging, and naming of pharmaceuticals aimed at reducing the risk of errors. However, our recent interactions with ISMP Canada demonstrate that, all too often, the pharmaceutical industry has failed to apply many life-saving lessons learned in the US to the same products used in other countries. This leaves patients throughout the world at risk of harm from the very same problems that have already been addressed in the US. Some examples:

- When Losec (omeprazole) was launched in 1989, it was often confused with Lasix (furosemide). Scores of mix-ups and at least two related deaths were reported. As a result, the brand name was changed to Prilosec in the US. Yet Losec remains the brand name in other parts of the world, and in some countries such as Canada, it is still being confused with Lasix.
- After a number of fatalities were reported from inadvertent intrathecal injection of vincristine, USP and FDA issued requirements for US manufacturers to visibly place a warning label on the package. In addition, practitioners are required to place a warning label, "FATAL if given intrathecally. FOR IV USE ONLY," on extemporaneously prepared syringes. The syringe must also be placed into an overwrap with this special warning, which is supplied by the manufacturer. Yet these label and practice changes have not been required or made available to practitioners in other countries, such as Canada or the United Kingdom (UK), and fatalities in children and adults continue to be reported. In one recently published editorial related to a teenager's death in the UK[1] the author notes that 13 identical cases of intrathecal vincristine have occurred in the UK since 1985.
- Recognizing that a 10-fold overdose may occur if the abbreviation "U" (units) is mistakenly read as a zero, or if the decimal point before a trailing zero is not seen, USP specifically bans these designations on US product labels. Yet in Canada, a manufacturer's container of insulin cartridges expresses the concentration as "100U/mL, 3.0 mL cartridges."
- After numerous mix-ups between potassium chloride concentrate and other medications, USP and FDA required US manufacturers to package

only potassium chloride concentrate vials with a black cap, and to list clear warnings, "must be diluted" on the cap, vial ferrule, and in a box on the front label panel. In Canada, a plastic ampule of the concentrate contains only a small black mark on the snap off portion. Labeling requirements similar to those in the US are lacking.

- In Canada, vials of the neuromuscular blocking agent Quelicin (succinylcholine) are devoid of any warning about it being a paralyzing agent that causes respiratory arrest (therefore requiring artificial ventilation when administered). In the US, the vial cap and ferrule state, "Warning: paralyzing agent," and similar warnings appear on the front label panel.

If manufacturers and regulators of products used worldwide fail to translate the lessons we've learned in the US into the wider global market, is there any reason to believe that the US is benefiting from lessons learned in other countries? Are there ways for us to learn about label, package, and nomenclature improvements made in other parts of the world? Are lessons learned in other countries being translated into industry actions here, or are we just waiting for accidents to happen in the US in large enough numbers before taking action? While so much of our improvement efforts have been reactive to date, FDA and pharmaceutical manufacturers in the US are now beginning to routinely analyze proposed brand names, labels, and packages to determine error potential before product approval. Now, it is time for global pharmaceutical industry leaders to understand and give their full support to cooperative improvement efforts, both reactive and proactive, which are implemented everywhere products are used. Both ISMP Canada and ISMP Spain are committed to working with ISMP (US) and facilitating this effort with the pharmaceutical industry and regulatory agencies in their respective countries. Despite language differences, the information contained in a product's name, package, and label is universal and must be clear for all pharmacists, physicians, nurses, and patients worldwide who must make decisions based on the information presented.

Reference

1. Berwick DM. Not again! [editorial]. *BMJ* 2001;322:247-8.

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