

Tragic Error with a Compounded Pediatric Formulation – Shared Learning

ISMP Canada recently received a report of an in-hospital infant death that was related to mislabelling of a compounded liquid formulation prepared in the hospital pharmacy. The case serves to illustrate the complex nature of this type of activity and some of the inherent weaknesses in hospital processes intended to prevent and/or detect such an error.

A 1-month-old infant with a congenital heart defect was admitted to a pediatric intensive care unit (PICU) in the middle of the night. On admission, flecainide suspension 4 mg PO TID was prescribed. Although this was a medication that the infant had been receiving before admission, the medications from home were not available, and a pharmacist was called back to the hospital to prepare a supply.

The on-call pharmacist prepared the flecainide suspension according to directions on a preprinted manufacturing worksheet for the product. The suspension was prepared correctly, with a final flecainide concentration of 5 mg/mL. To administer a dose of 4 mg to the infant, the correct volume per dose would have been 0.8 mL. However, when entering the order in the pharmacy computer system, the pharmacist mistyped the concentration as “5MG/5ML”, and then also typed the dose incorrectly as “4MG (4ML)” This information was displayed on the printed label for the multidose bottle (containing 40 mL of suspension), as well as the electronically generated medication administration record (see Figure 1). (A second printed label was also affixed to the manufacturing worksheet as a record copy of the dispensing label.)

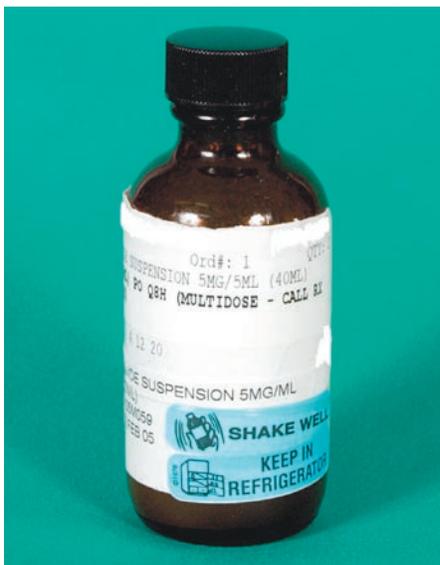


Figure 1. Multidose bottle containing flecainide suspension 5 mg/mL as dispensed. The manufacturing label (lower portion) has the correct concentration of 5 mg/mL (although this information is presented as 5MG/ML), and the dispensing label (upper portion) shows an incorrect “free-form text” entry of the concentration as 5MG/5ML.

The infant received two doses of flecainide 20 mg (instead of the intended 4 mg) during the initial stay in the PICU. After transfer to the general pediatric ward, the infant received an additional four doses of flecainide 20 mg. On the third hospital day, the infant’s condition became unstable, and the baby was transferred back to the PICU. Shortly after readmission to the PICU, the infant suffered cardiac arrest and attempts at resuscitation were unsuccessful.

During a quality-of-care review, the labelling error was discovered. It was concluded that the labelling error, which led to a significant dosing error, was a contributing factor in the development of complete heart block and the infant’s death.

There is evidence suggesting that the prevalence of medication errors is higher in the hospitalized pediatric population (approximately 15% of orders) than in the adult population (5% of orders).¹ Furthermore, the rate of medication errors resulting in harm or death is significantly greater among pediatric patients (31%) than adults (13%).¹ Incorrect dosing, including calculation errors for both dose and dosing interval, is the most commonly reported type of medication error affecting children. Many drugs lack formal approval from Health Canada for pediatric indications and associated dosing guidelines for pediatric administration, which increases the risk of these errors. Several organizations, including the American Academy of Pediatrics¹ and the United States Pharmacopeia (USP)², have published recommendations for the prevention of medication errors in the pediatric inpatient setting. These recommendations describe a broad range of system safeguards intended to decrease the rate of medication errors.

In pediatric therapeutics, the pharmacy plays a vital role in preparing specialized drug formulations that are appropriate for use in children and that are not commercially available. Despite the importance of this role, existing error-avoidance recommendations for pediatrics offer only minimal strategies to prevent errors associated with pharmacy-based extemporaneous compounding. Other than recommendations to standardize compounded products and establish verification processes for product preparation and labelling, this area of pharmacy practice is not specifically addressed by existing published recommendations.

In the incident reported to ISMP Canada, the following factors were identified as possibly contributing to the labelling and dosing errors:

- The pharmacy computer system did not include the compounded flecainide suspension product as a defined item, and the pharmacist was therefore required to “free-form text” (i.e., “key in”) the drug name, concentration, and dosing information for the label.
- The flecainide suspension was prepared after usual pharmacy hours by an on-call pharmacist, and there was no opportunity

for an independent double-check of the compounded product or the dose calculation within the pharmacy.

- Although a standardized manufacturing process, with a preprinted sheet, had been developed for flecainide suspension, the pharmacist was not familiar with either the formulation or the usual dose *volume* for an infant.
- The flecainide suspension was dispensed in a multidose bottle. Unit dose dispensing would have provided opportunity for additional pharmacy checks as subsequent doses were dispensed.

The quality-of-care review that was conducted in response to this case resulted in the following recommendations for pharmacy-based action:

- Implementation of a procedure for an independent double-check of extemporaneously compounded formulations and dose calculations, even when a pharmacist is working alone (e.g., by a second health care professional such as a nurse). Manufacturing sheets would include prompts or checklists to guide the double-check process.
- Enhancement of the functionality of the pharmacy computer system for compounded items, with elimination (as much as possible) of the need for “free-form texting” of label information and dose calculations. This would include standardizing drug concentrations to be compounded and ensuring that the items were included in the computer inventory database. Such enhancements and integrated system safeguards provide support in situations where pharmacists are required to perform unfamiliar activities while on call. (Discussions also supported a requirement to have an independent check by a pharmacist to verify such “inventory build” data entry.)
- Avoidance of the use of multidose bottles for packaging pediatric liquid formulations; instead, standard unit-dose oral syringes are to be used.

References:

1. Stucky ER; American Academy of Pediatrics Committee on Drugs; American Academy of Pediatrics Committee on Hospital Care. Prevention of medication errors in the pediatric inpatient setting. *Pediatrics* 2003;112:431-6.
2. United States Pharmacopeia (USP) – Error-avoidance recommendations for medications used in pediatric populations. Available at: <http://www.usp.org/patientSafety/resources/pedRecommnds2003-01-22.html>. Accessed June 2, 2005.

- Increased educational support and resources for pharmacists to develop clinical expertise in pediatrics.

Discussions with ISMP Canada resulted in the following additional recommendations:

- Expression of concentration as mass per *unit* volume as the standard accepted format for expressing concentration, for example, milligrams per millilitre (mg/mL), instead of milligrams per 5 millilitres (mg/5 mL). Ideally, the pharmacy computer system would be designed and programmed to accept only standard specification of concentration.
- Review of medication labels and manufacturing records to ensure optimal formatting of concentration and dose information and prominence of critical information. Appropriate formatting involves selective use of upper- and lower-case letters, and proper spacing improves legibility. For example, concentration expressed as 5 mg/mL is preferred to “block” lettering with no spaces (5MG/ML).
- Inclusion of a *sample* dispensing label within the manufacturing worksheet to guide appropriate labelling.

Note: Recommendations targeting monitoring parameters and procedures for transfer of care to another unit, which might have identified the adverse drug event sooner, are not covered in this issue of the *ISMP Canada Safety Bulletin*.

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ISMP Canada is a national voluntary medication incident and 'near miss' reporting program founded for the purpose of sharing the learning experiences from medication errors. Implementation of preventative strategies and system safeguards to decrease the risk for error-induced injury and thereby promote medication safety in healthcare is our collaborative goal.

To report a medication error to ISMP Canada: (i) visit our website www.ismp-canada.org, or (ii) e-mail us at info@ismp-canada.org, or (iii) phone us at 416-480-4099. ISMP Canada guarantees confidentiality and security of information received. ISMP Canada respects the wishes of the reporter as to the level of detail to be included in our publications.

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