

# ISMP Canada Safety Bulletin

Volume 17 • Issue 5 • May 25, 2017

## Death Due to Pharmacy Compounding Error Reinforces Need for Safety Focus

- *Before a compounded product is prepared, each ingredient and its measured amount should be verified through an independent check.*
- *Each ingredient in compounding formulas should have a unique identification number.*
- *Pharmacies should incorporate automated identification of ingredients (e.g., bar code scanning) into the compounding process.*
- *Labelling and packaging of compounding chemicals should be designed to minimize the risk of identification and/or selection errors.*
- *Pharmacies should have written policies, procedures, and/or checklists, based on professional standards and guidelines, for pharmacy staff to follow when preparing compounded products.*

Some patients may require a medication in a dose or dosage form that is not commercially available. Such medications must be specially prepared for the patient in a pharmacy and are referred to as compounded medications. As part of ongoing collaboration with a provincial death investigation service, ISMP Canada received a report regarding the death of a child who had ingested a prescribed, compounded oral liquid suspension that contained the

wrong medication. This bulletin shares some of the contributing factors identified in the case analysis, and provides recommendations to guide pharmacies and other compounding facilities, as well as standard-setting organizations in their efforts to reduce the likelihood of similar errors in the future.

### Case Description

For about 18 months, a young child had been receiving a 3 gram (20 mL) dose of tryptophan 150 mg/mL suspension by mouth at bedtime to treat a complex sleep disorder. A refill of the tryptophan prescription was ordered and picked up from the compounding pharmacy that had prepared the suspension in the past. That night, the child was given the usual dose of medication; the next morning, the child was found deceased in bed.

A post-mortem toxicology test identified lethal levels of the antispasticity agent baclofen. Baclofen had not been prescribed for the child. Testing of the suspension refill revealed that tryptophan, the intended active ingredient, was not present; however baclofen was detected, at the expected concentration of tryptophan. This finding was consistent with a selection error having been made at the pharmacy, whereby one ingredient was inadvertently substituted for another. It was determined that the child had received a dose of baclofen more than 20 times the maximum recommended pediatric dose.

## Background

Tryptophan (or L-tryptophan) is an essential amino acid converted in the body to serotonin and other proteins. Commercially, it is available without prescription in capsule form. Tryptophan can be used on an off-label basis to treat sleep disorders, such as sleep terrors in children.<sup>1</sup> Tryptophan is not commercially available in an appropriate dosage form for pediatric patients and therefore must be compounded if prescribed for a young child.

Baclofen is a skeletal muscle relaxant used to treat spasticity in conditions such as multiple sclerosis or spinal cord injury.<sup>2</sup> It is taken by mouth or given by intrathecal injection<sup>3</sup> for these indications. It is not officially approved for use by children less than 12 years of age;<sup>2</sup> however pediatric dosing information is available. Baclofen is occasionally prescribed, on an off-label basis, as an ingredient in compounded pain preparations intended for topical application.

Health Canada considers compounding to be “the combining or mixing together of two or more ingredients (of which at least one is a drug or pharmacologically active component) to create a final product in an appropriate form for dosing. It can involve raw materials or the alteration of the form and strength of commercially available products.”<sup>4</sup>

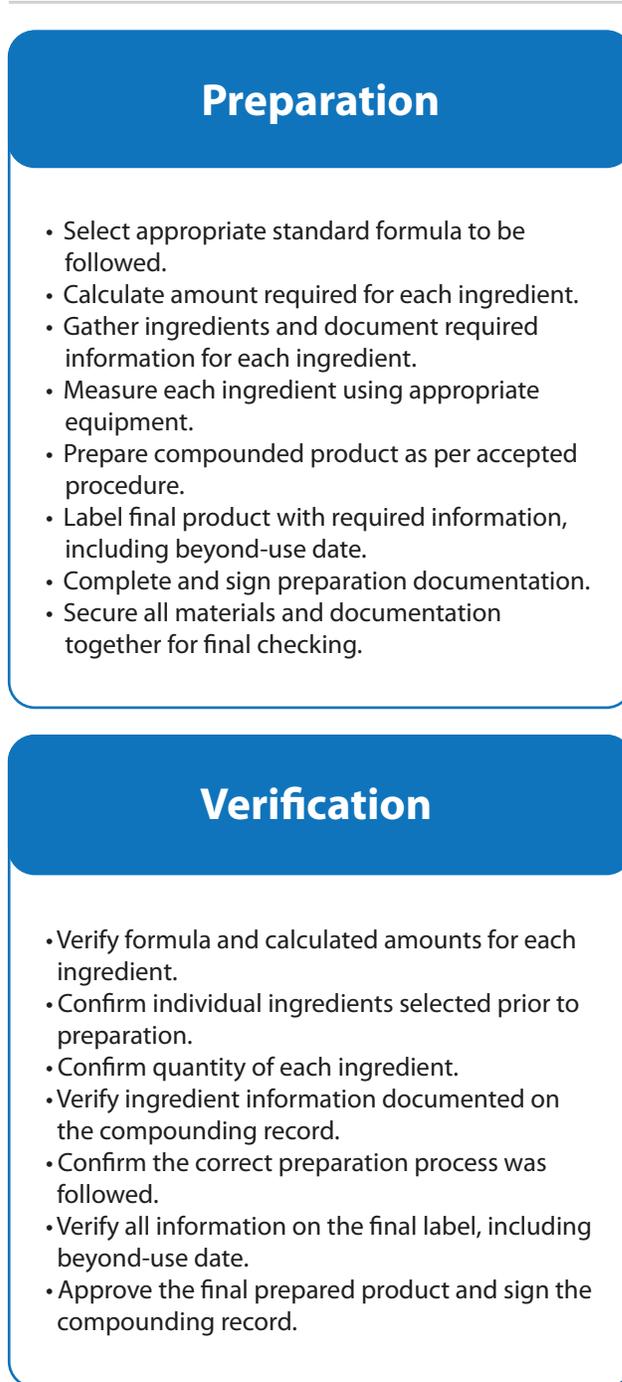
Most pharmacies provide some compounding services. However the scope of such services and the complexity of products compounded are highly variable. Figure 1 outlines some of the key activities in the preparation and verification phases of compounding.

## Discussion

In the described case, it could not be determined how the selection error was missed during the compounding verification process. The incorrect ingredient may have been misidentified during the final check. Alternatively, there may have been a delay in conducting the final check of the completed product. In this latter scenario, the incorrect ingredient used to prepare the product may have been

inadvertently put away before being checked, with the correct ingredient being retrieved later for the final check.

**Figure 1:** Brief overview of the key activities for compounding in a pharmacy



Several factors were identified that might have increased the likelihood of this compounding error.

- **Missing independent verification step:** There was a lack of independent verification of ingredients before mixing, which increased the likelihood that if an incorrect ingredient was inadvertently selected and incorporated into the final compounded product, the error would not be detected.
- **Similar label design:** The 2 compounding chemicals (tryptophan and baclofen) were supplied by the same manufacturer, which uses a similar design for all product labels and packages. The following specific labelling factors were identified at the time of the incident:
  - prominence of the manufacturer's name on the label
  - type size of the drug name (less than half the size of the manufacturer's name)
  - presentation of the drug name in capital letters only. This reduces legibility and readability.<sup>5</sup>
- **Similar physical appearance:** Both tryptophan and baclofen are white powders which, upon visual inspection, show little appreciable difference.
- **Confirmation bias:** This phenomenon, which leads individuals to "see" information that confirms their expectations, rather than information that contradicts their expectations,<sup>6</sup> may have played a role. Similarity of labels and packages can increase the potential for selection and verification errors related to confirmation bias.
- **Lack of use of a unique identifier:** The formula and compounding record did not contain a unique identifier that could be used to verify the ingredients selected and used in the preparation. In contrast, for commercially available medications, pharmacy staff typically uses the drug identification number (DIN) to confirm the product selected and dispensed.
- **Lack of segregated storage of oral and topical compounding chemicals:** Mixed storage of many compounding ingredients intended for either oral or topical use, combined with similar product appearance, increased the likelihood that a product selection error could occur without detection.

## Recommendations

Analysis of this case led to a number of system-based recommendations.

### *Regulatory Agencies*

- Require an independent check for each critical step. These steps include calculations, selection and measurement of ingredients, and mixing technique (if applicable), as well as a final check of the finished product, regardless of the individual(s) preparing the product.
- When conducting routine on-site inspections of pharmacies and drug preparation facilities, review policies and procedures for compounding to ensure compliance with accepted standards of practice, especially the performance of independent checks during the preparation process.

### *Manufacturers of Compounding Chemicals*

- Enhance the labelling of compounding chemicals in accordance with recommendations in Health Canada's Good Label and Package Practices Guide for Prescription Drugs<sup>5</sup> until such time as guidance specific to safe label design for chemical products is available.
- Label compounding chemicals with unique item numbers and bar codes that can be used to verify their identity when selecting and checking ingredients for a compounded product.
- Include a unique chemical identifier for each ingredient in formulas provided to pharmacies.

### *Pharmacy Managers, Pharmacists, and Pharmacy Technicians*

- Designate an area for compounding that is separate from other activities.<sup>7</sup>
- Ensure written policies, procedures, and/or checklists are readily available for pharmacy staff to follow when they prepare a compounded product. Validate newly created procedures and checklists through user testing before full implementation.

- Verify selection of the correct formula, the identity of all ingredients and their measured quantities through an independent check.
  - Ensure ingredients are not returned to stock until verification has occurred.
  - To support verification, include a unique product number, if available, for each chemical ingredient in standard formulas.
- Require documentation for each critical verification step.<sup>8</sup> Document that:
  - calculations, if required, have been checked;
  - the identity of each ingredient has been verified before mixing;
  - lot number and expiry date of each ingredient have been captured;<sup>9</sup>
  - the weight and/or measurement of each ingredient has been verified; and
  - a final check of the finished product has been conducted.
- Incorporate automated identification (e.g., bar code scanning) of ingredients into the compounding process.
- Specialty compounding pharmacies may wish to consider video recording of the compounding process that can be accessed by staff to confirm preparation activities.
- Store products in a way that optimizes label readability (e.g., well-lit and organized storage spaces, ideally at eye-level). Avoiding counter storage of drugs and chemicals will reduce clutter and increase available workspace.
- Segregate oral and topical compounding ingredients on separate, labelled shelves.
- Make use of educational resources, such as training videos. These can be especially helpful for complex compounding processes and/or preparation techniques that are used infrequently.

## Conclusion

Compounding of medications is a high-risk activity that results in a final product for which ingredients cannot be verified through physical examination. Before compounding is undertaken, commercially available alternatives should be considered and there

should be an evidence-based rationale for the use of the compounded product. The selection error described above, with its tragic result, could have occurred in any community or hospital pharmacy or drug preparation facility that compounds medications. ISMP Canada is working with the National Association of Pharmacy Regulatory Authorities (NAPRA) to inform updated standards of practice<sup>10</sup> which will be available in 2017/2018, and will continue its work with other stakeholders to advance compounding safety.

## Acknowledgements

*ISMP Canada extends appreciation to the child's family for allowing details of this medication incident to be shared, with the goal of preventing harm to others in similar situations. ISMP Canada gratefully acknowledges expert review of this bulletin by the following individuals (in alphabetical order):*

Heather Christ BScPharm, Pharmacy Practice Advisor, New Brunswick College of Pharmacists, Moncton, NB; Gregory Cummings RPh CDE, Pharmacist-Owner, Shoppers Drug Mart #669/929, Sault Ste. Marie, ON; Sarah Jennings Acting Manager BSc, BScPhm, RPh, PharmD, Professional and Regulatory Affairs, National Association of Pharmacy Regulatory Authorities, Ottawa, ON; Catherine Lyder BScPharm MHSA, Director, Members and Programs Canadian Society of Hospital Pharmacists, Ottawa, ON; James E G Snowdon RPh BScPhm PharmD FACA, Snowdon Pharmacy, Toronto.

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### **WHO's Third Global Patient Safety Challenge: *Medication Without Harm***

Following on its 2 previous global patient safety challenges, related to infection control and safer surgery, the World Health Organization (WHO) recently announced the launch of its international campaign for safer medication use. Participating countries will be asked to develop interventions targeting 3 priority areas: high-risk situations, polypharmacy, and transitions of care.

Five Working Groups have been established to support implementation of the Challenge: Patients and Public, Health Care Professionals, Medicines, Systems and Practices, and Monitoring and Evaluation. Since April 2016, Canada has been assisting the WHO in the preparation and development phases of the Challenge. ISMP Canada, the Canadian Patient Safety Institute (CPSI), and Patients for Patient Safety Canada are expert contributors to several of the Working Groups. Through these efforts, Canadian organizations continue their work with the WHO to advance medication safety.

More information is available from: <http://www.who.int/patientsafety/medication-safety/en/> and [http://middleeast.thelancet.com/journals/lancet/article/PIIS0140-6736\(17\)31047-4/fulltext](http://middleeast.thelancet.com/journals/lancet/article/PIIS0140-6736(17)31047-4/fulltext)

The Canadian Medication Incident Reporting and Prevention System (CMIRPS) is a collaborative pan-Canadian program of Health Canada, the Canadian Institute for Health Information (CIHI), the Institute for Safe Medication Practices Canada (ISMP Canada) and the Canadian Patient Safety Institute (CPSI). The goal of CMIRPS is to reduce and prevent harmful medication incidents in Canada.



The Healthcare Insurance Reciprocal of Canada (HIROC) provides support for the bulletin and is a member owned expert provider of professional and general liability coverage and risk management support.



The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national not-for-profit organization committed to the advancement of medication safety in all healthcare settings. ISMP Canada's mandate includes analyzing medication incidents, making recommendations for the prevention of harmful medication incidents, and facilitating quality improvement initiatives.

## Report Medication Incidents

(Including near misses)

**Online:** [www.ismp-canada.org/err\\_index.htm](http://www.ismp-canada.org/err_index.htm)

**Phone:** 1-866-544-7672

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## Contact Us

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