

# ISMP Canada Safety Bulletin

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## Death Associated with an IV Compounding Error and Management of Care in a Naturopathic Centre

Patients with a diagnosis of cancer may choose to use complementary and alternative medicine, such as naturopathy, to support conventional medical therapies (e.g., surgery, chemotherapy).<sup>1</sup> The complementary and alternative medicine treatment plan is usually prescribed by a naturopathic doctor and carried out in a complementary care centre (CCC). As part of an ongoing collaboration with a provincial death investigation service, ISMP Canada received a report about the death of an individual who had received, by intravenous (IV) administration at a CCC, a tissue- and wound-healing formulation containing selenium at a much higher concentration than intended. This bulletin highlights some contributing factors identified in the incident analysis, and provides recommendations to prevent similar incidents in the future.

### Case Description

A patient was discharged from hospital after surgical excision of a cancerous tumour and was further treated, in a collaborative arrangement, by a conventional medical team and a naturopathic doctor at a CCC. The naturopathic doctor prescribed a complex tissue- and wound-healing formulation, which included selenium, for twice-weekly IV administration. The selenium solution was prepared by a compounding pharmacy and was added to the formulation on site at the CCC.

The patient had received this healing formula on 12 previous occasions, with no reported reactions.

### Specialty compounding pharmacies:

- Ensure that the formula's units of measure align with the units of measure displayed by the equipment to be used during compounding; additional conversion calculations should not be required in the process.
- Incorporate technology to support patient safety, such as bar coding and scales that print the weight of each item automatically.
- Avoid the use of dangerous abbreviations known to lead to medication errors (e.g., "µg" for "micrograms").

### Complementary care centres:

- Ensure the availability of detailed protocols to be followed if an emergency situation occurs, such as a reaction to an intravenous (IV) infusion.
- Define the limitations of the complementary care centre and its healthcare providers. Clearly describe clinical circumstances in which patients must be transferred to a conventional, higher level of care (e.g., emergency room).
- Use "mcg" to represent "micrograms" in all written documentation.

However, shortly after initiation of the 13th dose infusion, she became nauseous and diaphoretic. The infusion was stopped, and homeopathic remedies were administered, with no clinical improvement. Over the next several hours, the patient's condition

continued to deteriorate. When the patient began to experience hypotension, shortness of breath to the point of cyanosis, and chest pain, she was transferred to the emergency department of a local hospital, where she later died. The timeline of these events is presented in Figure 1. Postmortem investigations showed that the selenium concentration in the infusion was 1000 times greater than intended, which likely contributed to the patient's death.

## Background

The mineral selenium is an essential trace element in the body that is usually consumed through intake of food and water. It has antioxidant properties and has been studied for use in treating many medical conditions. However, high doses of selenium are toxic, leading to gastrointestinal and cardiovascular complications.<sup>2</sup> Selenium is commercially available in many forms, including as a solution for IV administration.

Tissue- and wound-healing formulations are used in the field of naturopathic medicine as postsurgical support. Naturopathic doctors prepare these complex IV admixtures on site at the CCC, usually from commercially available products. Products that are not commercially available (or that cannot be supplied because of shortages) may be outsourced to compounding pharmacies. Most pharmacies offer some compounding services; however, the scope of such services and the expertise of staff are highly

variable. The National Association of Pharmacy Regulatory Authorities (NAPRA) has developed standards for compounding of hazardous and nonhazardous sterile preparations to assist pharmacists and pharmacy technicians in ensuring that the compounding of sterile preparations meets high standards.<sup>3</sup>

## Discussion

This bulletin focuses on 3 key opportunities for improvement (listed in Box 1).

### Box 1. Key opportunities for improvement

#### **At the pharmacy**

- Compounding processes

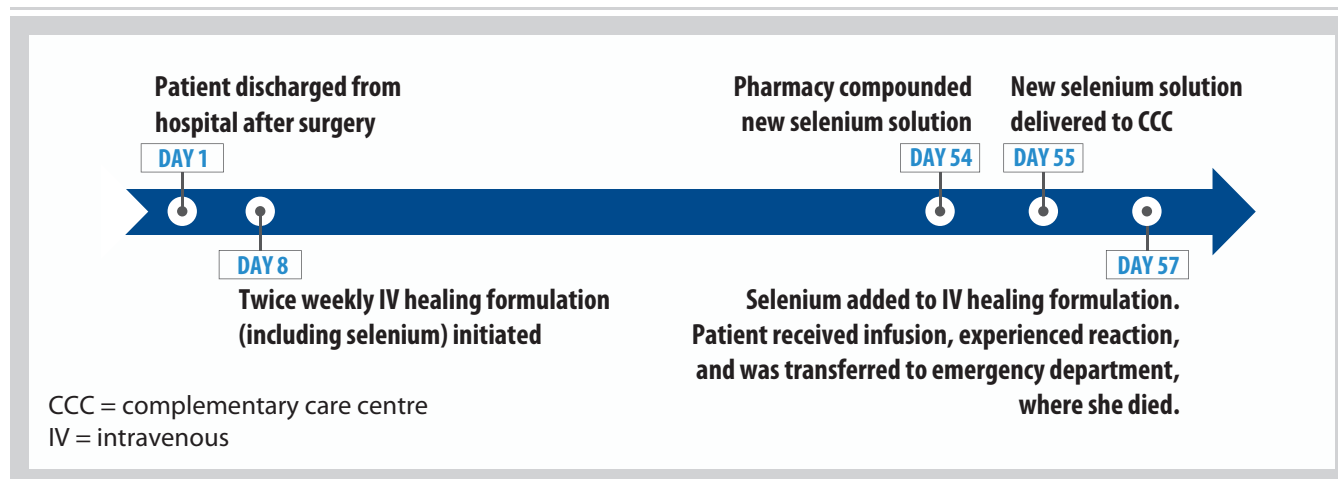
#### **At the complementary care centre**

- Emergency response
- Preparation, storage, and administration of admixtures

### Pharmacy: Compounding Processes

The compounding pharmacy had processes in place to verify calculations and weighing of ingredients, as well as a final product check. Nonetheless, the

**Figure 1.** Timeline of events from the patient's initial hospital discharge until her death



selenium concentration in the prepared solution was 1000 times what was intended, and this error was not detected at any stage before release of the solution to the CCC. The following factors may have contributed to this undetected error:

- Confirmation bias, which leads individuals to “see” information that confirms their expectations rather than correctly interpreting information that contradicts their expectations, may have played a role.<sup>4</sup> When the amount of selenium powder (in milligrams) required for a 40 mcg/mL solution was weighed and checked, the unit of measure displayed by the scale (grams) may have been incorrectly interpreted as milligrams, with the error in interpretation going unrecognized. Such errors can lead to 1000-fold overdoses.
  - The abbreviation “µg” was used for “microgram” in the formula for the selenium solution. This abbreviation is considered dangerous because it is easily confused with “mg” (meaning “milligram”). There have been other medication incident reports where such confusion has led to 1000-fold overdoses.
  - Reliance on a visual check of the weighed amount may have contributed to the error. Scales are available that print out the weight of each item to provide a permanent document that can be attached to the compounding record for checking in the final verification step.
- Avoid the use of dangerous abbreviations known to lead to medication errors (e.g., “µg” for “microgram”).
  - Incorporate technology to support patient safety, such as bar coding and scales that print the weight of each item automatically. Alternatively, have pharmacy staff take photographs of the containers used and the weight readings, and attach the photographs to the compounding record.
  - Conduct a review of existing processes, including a cognitive walkthrough (a procedure that involves physically walking through the process or task of interest, examining the mental activities required at each step and the challenges experienced<sup>6</sup>), to ensure that compounding processes comply with professional standards (e.g., NAPRA Model Standards for Compounding of Non-Hazardous Sterile Preparations<sup>7</sup>) and medication safety principles.

### **Complementary Care Centre: Emergency Response**

For any patient receiving IV treatments in a naturopathic setting, vital signs should be monitored and recorded regularly. In this case, there did not seem to be a standardized approach to patient assessment and monitoring.

Naturopathic doctors are required to refer patients to receive conventional medical therapy if their condition requires diagnostic procedures, monitoring, or treatment that is beyond the scope of practice of the naturopathic doctor. In this case, the patient was treated with homeopathic remedies. These remedies did not produce any clinical improvement. Available documentation also indicated that there may have been a lack of appropriate supervision by, and timely help from, the naturopathic doctor on the day of the incident, which may have contributed to the delay in transferring the patient to a higher level of care (e.g., emergency room).

### **Recommendations**

- Ensure the availability of detailed protocols to be followed in emergency situations, such as reaction to an IV infusion. These protocols should meet the standards of a conventional out-of-hospital facility

### **Recommendations**

- Before compounding a sterile product, refer to the Health Canada Drug Product Database to determine whether the product is commercially available.<sup>5</sup>
- Design formulas and worksheets to present information in a logical sequence, with consistent terminology.
- Ensure that the formula’s units of measure align with the units of measure displayed by the equipment to be used during compounding; additional conversion calculations should not be required in the process. For example, if the scale displays weight in grams, the formula should express the amount to be weighed and verified in grams, without necessitating any additional conversion calculations.

providing IV infusion therapy, including the following provisions:

- designated staff trained in Advanced Cardiac Life Support (e.g., nurse, naturopathic doctor) to oversee the emergency care situation;
  - identification of available emergency/rescue medications and devices, their storage locations, and their indications for use; and
  - appropriate patient monitoring and documentation.
- Define the limitations of the CCC and its healthcare providers. Clearly describe the clinical circumstances in which patients must be transferred to a conventional, higher level of care.

### **Complementary Care Centre: Preparation, Storage, and Administration of Admixtures**

The prepared IV tissue- and wound-healing formulation was a complex admixture of 10 ingredients added to sterile water for injection. There is no uniform standard for the preparation of admixtures in a CCC. From the information available in this case, it appears that handwritten changes to the formula may have been made at each session, and that each solution was prepared individually from bulk ingredients. The sources of components of the final product were unknown, except for the selenium solution, which was obtained from a compounding pharmacy.

### **Recommendations**

- Review and adhere to compounding guidelines developed by jurisdictional naturopathic regulatory authorities and NAPRA, to ensure compliance with expected standards of practice.
- Use “mcg” to represent “micrograms” in all written documentation. Avoid the use of the dangerous abbreviation “µg”, which is known to have contributed to 1000-fold dosing errors.
- Develop preprinted order sets collaboratively with end-users and ensure that these order sets meet the following criteria:
  - present critical information in a logical sequence with consistent terminology;
  - avoid the use of dangerous abbreviations, symbols, and dose designations that may be misinterpreted (see ISMP Canada’s Do Not Use

list, available from:

[https://www.ismp-canada.org/download/ISMP\\_CanadaListOfDangerousAbbreviations.pdf](https://www.ismp-canada.org/download/ISMP_CanadaListOfDangerousAbbreviations.pdf));

- contain only essential information; and
- undergo regular review.

### **Additional Recommendations for Regulatory Agencies**

- Consider specific accreditation for facilities that provide specialty compounding services, with criteria to be developed in collaboration with key stakeholders (e.g., NAPRA, Health Canada, and ISMP Canada). The accreditation process should include assessment of compliance with available standards and guidelines.
- Mandate that personnel working in compounding centres have credentials confirming that they have received appropriate training in applicable safe medication preparation and administration practices.

### **Conclusion**

Sterile compounding of pharmaceuticals is a complex process. Without testing, it is difficult to identify errors in the final prepared product. The incident described here involved a complementary health product; however, a similar error could have occurred with any compounded product. Decisions to compound must consider the potential risks associated with the compounding process. Pharmacies and other facilities preparing sterile pharmaceuticals should carefully consider multiple approaches to reduce risk, including use of commercially prepared products when available and implementation of available technologies.

In settings where IV infusions are to be administered, the importance of establishing emergency protocols, as well as ensuring availability of trained personnel, rescue equipment, medication, and supplies, cannot be overstated. Prompt recognition of symptoms necessitating a higher level of care and access to emergency treatment is critical to mitigate harm.

## Acknowledgements

ISMP Canada extends appreciation to the 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): Dana Lyons RPhT, Manager – Technical Practice, Pharmacy Services, Foothills Medical Centre, Calgary, AB; Eric Marsden BSc ND, Clinic Director/Naturopathic Oncology Residency Director, Marsden Centre for Excellence in Integrative Medicine, Concord, ON; Joyce Tsang RPh PharmD BScPhm HBSc, University Health Network – Toronto General Hospital, Toronto, ON.

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## Stakeholder Consultation on Naming of Biologic Drugs

January 18 to February 9, 2018

On January 18, 2018, the Institute for Safe Medication Practices Canada (ISMP Canada) will post an online questionnaire to seek input from healthcare providers, consumers, and other interested and affected stakeholders on different approaches to the naming of biologic drugs, including biosimilars, in Canada. The questionnaire is being developed collaboratively with Health Canada. Administration of the questionnaire and analysis of responses will be performed by ISMP Canada.

The objective of the consultation is to gain insight into stakeholder views on the practical impacts of different approaches to the naming of biologic drugs and biosimilars throughout the medication-use process, including prescribing, dispensing, and adverse drug reaction reporting.

Results of the consultation will be used to:

- understand the impact of different approaches to biologic drug naming and the perspectives of healthcare providers, consumers, and other interested and affected stakeholders, and
- inform Health Canada's policy decision on a naming convention for biologic drugs.

For more details on this initiative, [click here](https://www.ismp-canada.org/biosimilars/Naming-of-Biologic-Drugs-Consultation-NoticeEN.pdf) (<https://www.ismp-canada.org/biosimilars/Naming-of-Biologic-Drugs-Consultation-NoticeEN.pdf>). Additional details will also be available when the questionnaire is launched on January 18, 2018.

We would appreciate your help to distribute this message to your colleagues, members, or stakeholders to inform them of this initiative and the upcoming consultation. If you have any preliminary questions, please contact us via [info@ismp-canada.org](mailto:info@ismp-canada.org)

## Caution: Unlabelled Marking on a Vaccine Syringe Led to Under-dosing of Adult Patients

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ISMP Canada received a report that described misinterpretation of an unlabelled marking on the Influvac influenza vaccine syringe resulting in multiple adult patients being administered half the intended dose.

Influvac is provided in a prefilled syringe that contains 0.5 mL of vaccine and a small amount of air; the syringe has a black marking to denote 0.25 mL (but not labelled as 0.25 mL). When administering the vaccine to several adult patients, the practitioner interpreted the black marking as the 'measured dose', and the plunger was pressed until only that amount of the vaccine remained (i.e., along with the air, half the dose was expelled through the needle).

Practitioners need to refer back to the original packaging and/or the information leaflet for clarification of any unlabelled markings on the syringe. The manufacturer has been contacted to share these incidents and the labelling concern, as well as the potential for similar errors.

Information about these incidents was also shared through social media for timely notice.



## Med Safety Exchange Webinar Series

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**Wednesday, January 10, 2018**

**Wednesday, February 14, 2018**

Join your colleagues across Canada for complimentary monthly 60 minute webinars to share, learn and discuss incident reports, trends and emerging issues in medication safety!

For more information, visit [www.ismp-canada.org/MedSafetyExchange/](http://www.ismp-canada.org/MedSafetyExchange/)

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

ISMP Canada strives to ensure confidentiality and security of information received, and respects the wishes of the reporter as to the level of detail to be included in publications. Medication Safety bulletins contribute to Global Patient Safety Alerts.

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## Contact Us

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