Pharmacy Compounding Safety

IMSN Conference

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ZERO Preventable Harm From Medications

Institute for Safe Medication Practices Canada

Land Acknowledgement

We acknowledge we are hosted on the lands of the Mississaugas of the Anishinaabe, the Haudenosaunee Confederacy and the Wendat. We also recognize the enduring presence of all First Nations, Métis and the Inuit peoples.[1] We are grateful to live, work and play on this land and we want to contribute to the implementation of the Truth and Reconciliation Commission's eight health-related Calls to Action.

Nous tenons à souligner que nous sommes accueillis sur le territoire traditionel des Mississaugas, des Anichinabés, des Haudenosaunees et des Wendats. Nous voulons également reconnaître la pérennité de la présence des Premières Nations, des Métis et des Inuits. Nous sommes reconnaissants de vivre, de travailler et de jouer sur ce territoire et nous voulons contribuer à la mise en œuvre des huit appels à l'action de la Commission de vérité et de réconciliation en matière de santé.

Find your land acknowledgement at https://native-land.ca/

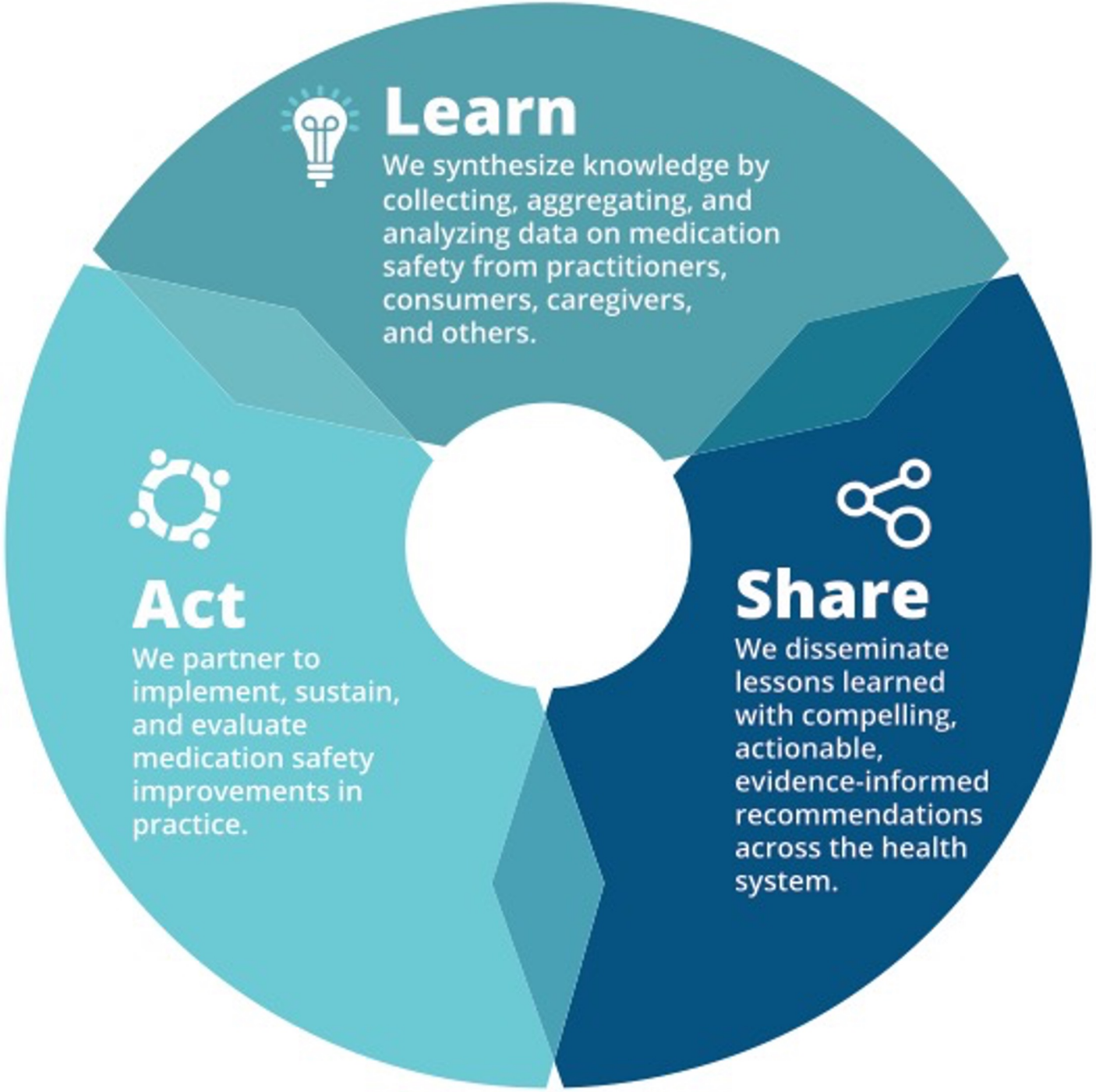
1. https://www.tdsb.on.ca/Community/Indigenous-Education/Resources/Land-Acknowledgement

A Trusted Partner

Strengthening medication safety through timely learning, sharing, and acting to improve health care.

ISMP Canada is a national, independent, not-for-profit organization that purposefully partners with organizations, practitioners, consumers, and caregivers to advance medication safety in all healthcare settings.

ismp CANADA



Andrew Sheldrick

Compounded Medication

Original Prescription
5 tablets daily, before bed

Compounded Liquid
20 mL daily, before bed

Shutterstock Image

Analysis

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REPORT MEDICATION INCIDENTS
Online: www.ismp-canada.org/err_index.htm
Phone: 1-866-544-7672

A KEY PARTNER IN
CMIRPS Canadian Medication Incident Reporting and Prevention System
SCDPIM Système canadien de déclaration et de prévention des incidents médicamenteux

ISMP Canada Safety Bulletin

Volume 17 • Issue 5 • May 25, 2017

Death Due to Pharmacy Compounding Error Reinforces Need for Safety Focus

Scan to access the Bulletin

https://ismpcanada.ca/wp-content/uploads/ISMPCSB2017-05-Tryptophan.pdf

Pharmacy Staff

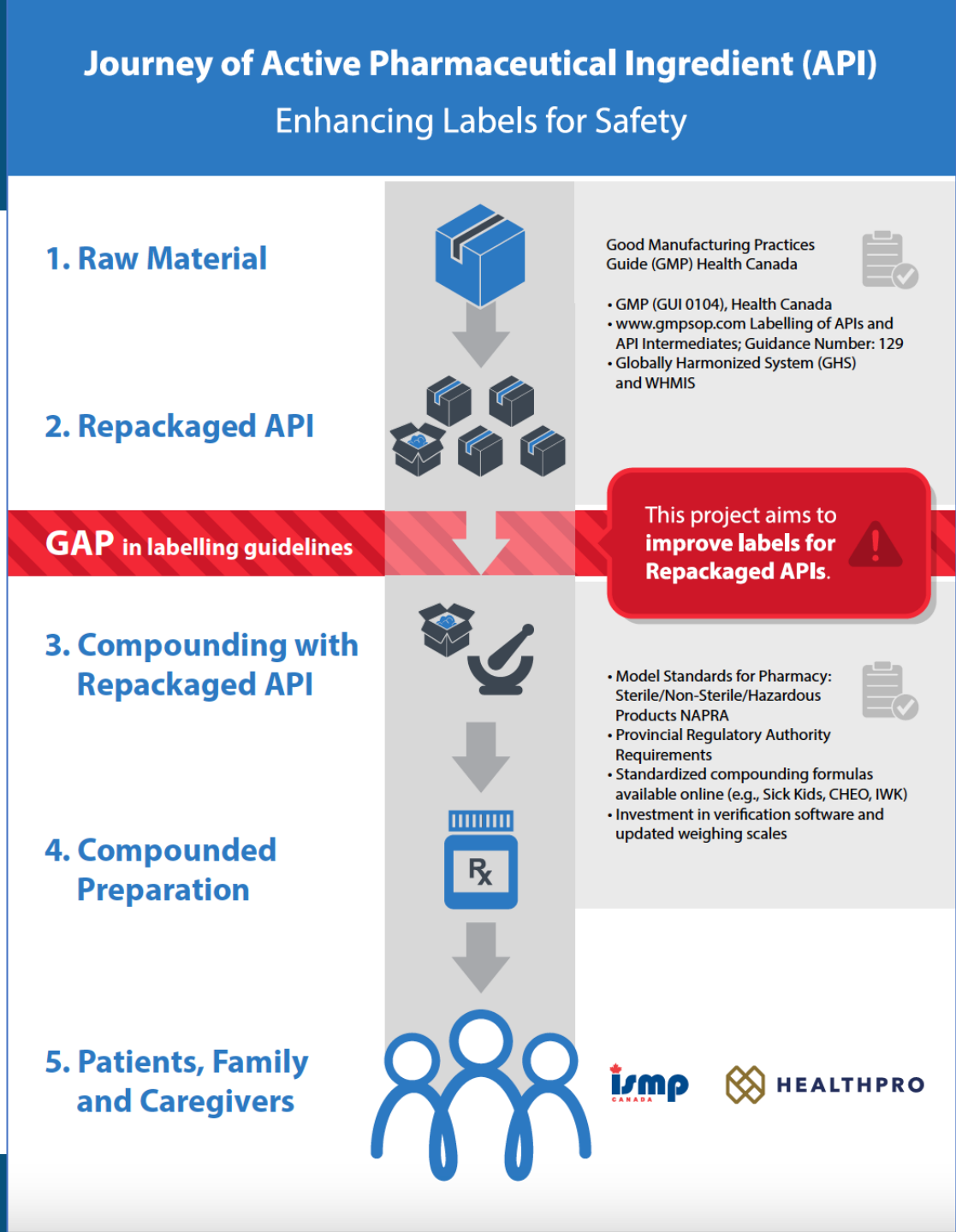
Contributing Factors	Recommendations
Missing independent verification step	Verify selection of the correct formula, the identity of all ingredients and their measured quantities through an independent check.
Confirmation bias	…consider video recording of the compounding process…
Lack of use of a unique identifier	Incorporate automated identification (e.g., bar code scanning) of ingredients into the compounding process.
Lack of segregated storage of oral and topical compounding chemicals	Segregate oral and topical compounding ingredients on separate, labelled shelves.

Label Design

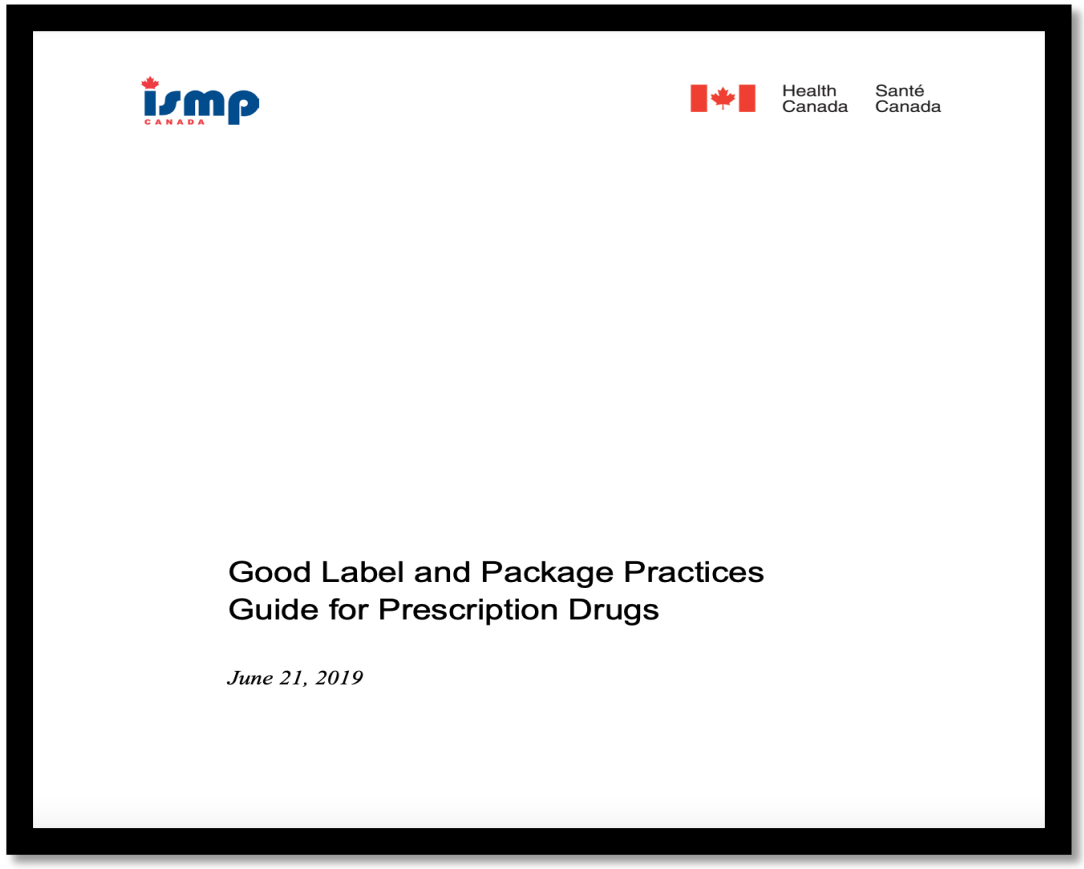
Gaps Identified

- Label design (currently with quality control departments) would benefit from additional guidance

- Limited regulatory guidance for **repackaged** Active Pharmaceutical Ingredients (APIs)
  - Recent update of Good manufacturing practices guidelines for active pharmaceutical ingredients by Health Canada (GUI-0104) does not include the level of detail to address this gap



Good Label and Package Practices Guides



Key Considerations for Safe Label Design

A. Include automated identification (e.g., GS1-compliant barcoding).[4]

B. Use i) the largest possible type size that can be read easily by a variety of users (minimum 6 points for key information), ii) sans serif type style, and iii) mixed-case lettering (i.e., lower-case letters with capitalization for proper nouns).[4]

C. Display the chemical name of the API in larger type size than the name of the manufacturer/ repackager.

D. Stack a long, multiword name, so that the full name can be read without the need to rotate the package.

E. Include the Chemical Abstracts Service (CAS) Registry Number for the API as an additional product identifier. This is analogous to including the Drug Identification Number (DIN) or Natural Product Number (NPN) on drugs and natural health products, respectively.

Key Considerations for Safe Label Design cont.

F. Avoid dangerous abbreviations, symbols, and dose designations (see ISMP Canada's "Do Not Use" list[8]).

G. Use one of the following formats for expiration dating: EXP 2020-JA-11 or EXP 11-JA-2020.[4]

H. Present potency, if applicable (e.g., X mg erythromycin activity per Y grams erythromycin stearate) on the front panel in a manner that simplifies any needed calculations.

I. Consider the use of more than just colour to distinguish between products. Examples of other distinguishing features include the use of frames or keylines (boxes around text).[4]

J. Use colour to draw attention to important label information, such as the API name, or to enhance or bring attention to warning statements.[4]

Closing the Loop

https://bit.ly/3f9zoxk

Consumer Newsletter

https://bit.ly/3DhKacE

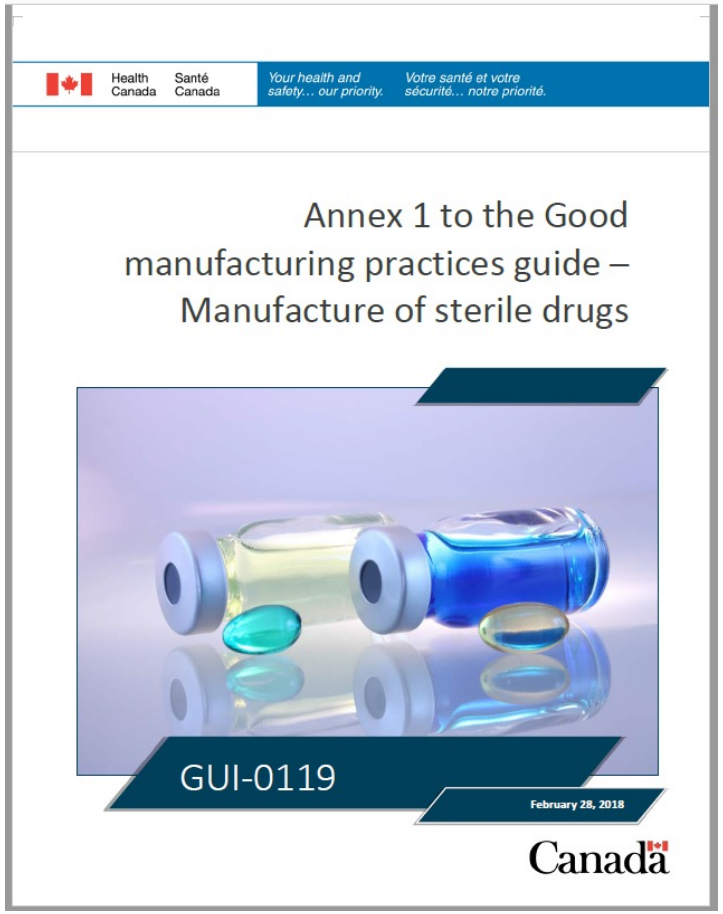
Impact to Date

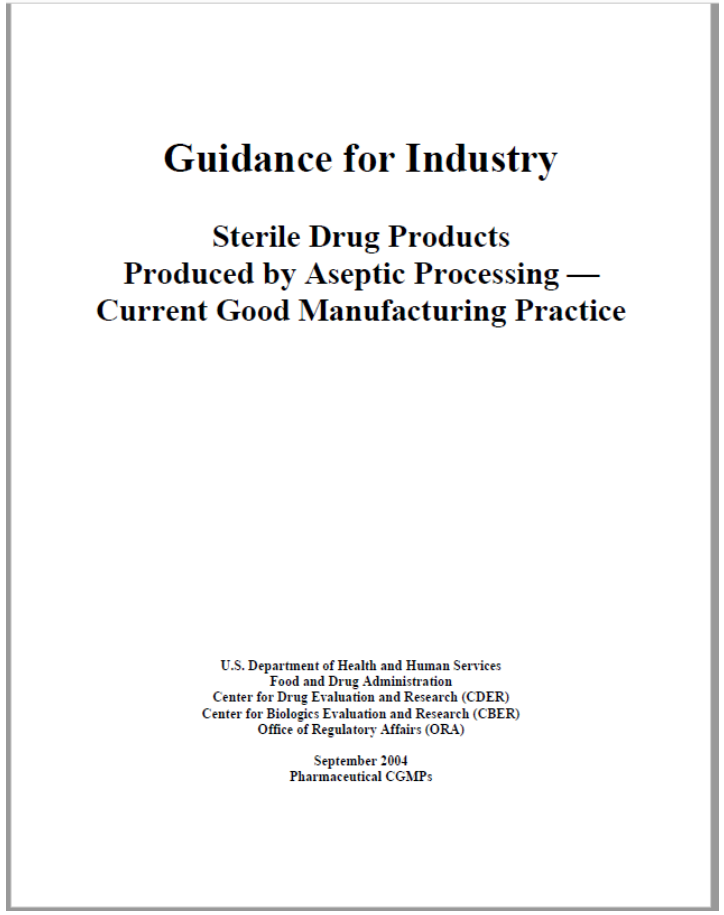
- The Chemical Abstract Services (CAS) number is now included in the Master Formulations Template provided by the National Association of Provincial Regulatory Authorities (NAPRA)
- The CAS number is required (in criteria) for purchasing contract awards by HealthPRO Procurement Services.
- Articles written and disseminated
- CAS number is included in the Epic (electronic health record) system in a provincial health authority (Alberta Health Services).

Next Steps

Pharmacy Compounding
Standards, Competencies, and Guidance

Drug Manufacturing
Guidance for Industry





Commercial Compounding
Amendments to the Food and Drug Regulations are Planned

Health Canada is proposing to develop a new regulatory framework to address commercial compounding to fill a **gap in regulatory oversight.**

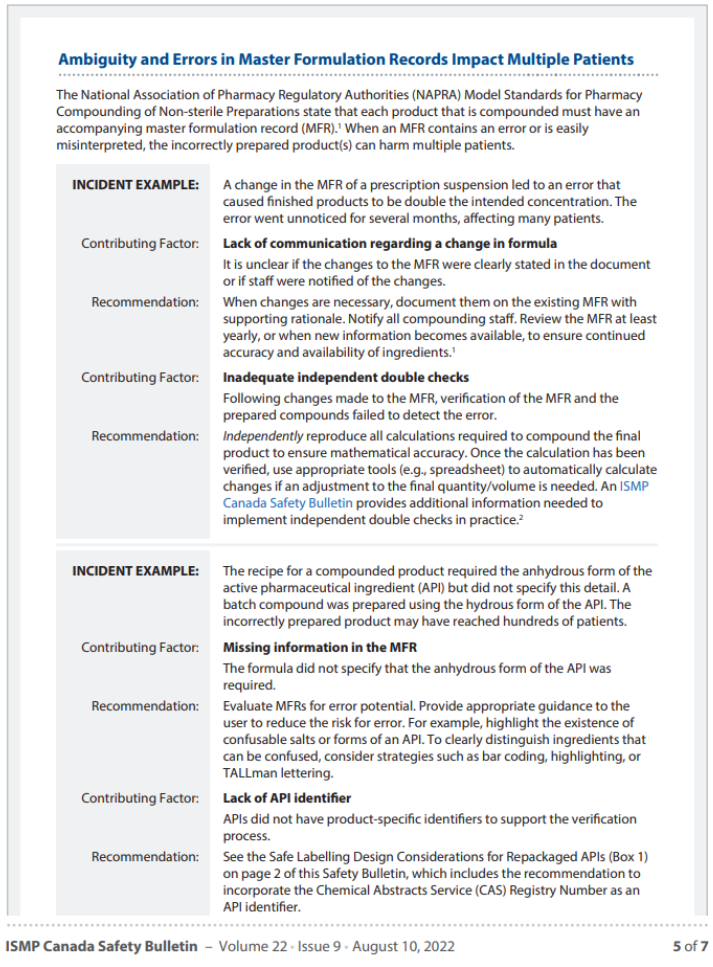
Commercial compounding is a set of activities that combines elements of two well-defined activities that are regulated by different levels of government in Canada:

- drug manufacturing and
- traditional drug compounding performed by pharmacies and hospitals for individual patients.

Health Canada is providing opportunities for stakeholder consultations on the regulatory proposal.

https://www.canada.ca/en/health-canada/corporate/about-health-canada/legislation-guidelines/acts-regulations/forward-regulatory-plan/plan/regulatory-initiative-amendments-food-drug-regulations-commercial-compounding.html

Compounding process - related errors



Ambiguity and Errors in Master Formulation Records Impact Multiple Patients

The National Association of Pharmacy Regulatory Authorities (NAPRA) Model Standards for Pharmacy Compounding of Non-sterile Preparations state that each product that is compounded must have an accompanying master formulation record (MFR).[1] When an MFR contains an error or is easily misinterpreted, the incorrectly prepared product(s) can harm multiple patients.

INCIDENT EXAMPLE:	A change in the MFR of a prescription suspension led to an error that caused finished products to be double the intended concentration. The error went unnoticed for several months, affecting many patients.
Contributing Factor:	**Lack of communication regarding a change in formula** It is unclear if the changes to the MFR were clearly stated in the document or if staff were notified of the changes.
Recommendation:	When changes are necessary, document them on the existing MFR with supporting rationale. Notify all compounding staff. Review the MFR at least yearly, or when new information becomes available, to ensure continued accuracy and availability of ingredients.[1]
Contributing Factor:	**Inadequate independent double checks** Following changes made to the MFR, verification of the MFR and the prepared compounds failed to detect the error.
Recommendation:	*Independently* reproduce all calculations required to compound the final product to ensure mathematical accuracy. Once the calculation has been verified, use appropriate tools (e.g., spreadsheet) to automatically calculate changes if an adjustment to the final quantity/volume is needed. An ISMP Canada Safety Bulletin provides additional information needed to implement independent double checks in practice.[2]

INCIDENT EXAMPLE:	The recipe for a compounded product required the anhydrous form of the active pharmaceutical ingredient (API) but did not specify this detail. A batch compound was prepared using the hydrous form of the API. The incorrectly prepared product may have reached hundreds of patients.
Contributing Factor:	**Missing information in the MFR** The formula did not specify that the anhydrous form of the API was required.
Recommendation:	Evaluate MFRs for error potential. Provide appropriate guidance to the user to reduce the risk for error. For example, highlight the existence of confusable salts or forms of an API. To clearly distinguish ingredients that can be confused, consider strategies such as bar coding, highlighting, or TALLman lettering.
Contributing Factor:	**Lack of API identifier** APIs did not have product-specific identifiers to support the verification process.
Recommendation:	See the Safe Labelling Design Considerations for Repackaged APIs (Box 1) on page 2 of this Safety Bulletin, which includes the recommendation to incorporate the Chemical Abstracts Service (CAS) Registry Number as an API identifier.

Example:

- Reports of incidents related to errors in Master Formulation Records
- Safety bulletin includes recommendations for safeguards

Errors with Compounded Products

Institute for Safe Medication Practices Canada
REPORT MEDICATION INCIDENTS
Online: www.ismp-canada.org/err_index.htm
Phone: 1-866-544-7672

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ISMP Canada Safety Bulletin

Volume 21 • Issue 11 • December 14, 2021

Sharing Matters!

Sentinel Medication Incident Results in Safer Product Labelling

ISMP Canada received a sentinel event report describing inadvertent bolus administration of a HYDROmorphone product that was intended for continuous infusion. A contributing factor was the misinterpretation of critical information on the label (see Figure 1). The practitioner misunderstood the information provided and believed the bag contained 1 mg of HYDROmorphone. As a result, the entire content of the bag (which contained 50 mg of HYDROmorphone) was administered as a bolus. The error was discovered after the patient was found to have an altered level of consciousness; naloxone was given.

The manufacturer, Baxter Corporation, embarked on a collaborative label enhancement initiative that included consultation with nurses, pharmacy representatives, and ISMP Canada. The following changes (see Figure 2), in line with the Good Label and Package Practices Guide for Prescription Drugs *and within the constraints of labelling software,* were introduced earlier this year:

- The primary label statement (in the red box) now states the following critical information: the drug name, total dose, total volume, and final concentration.
- A new secondary label statement has been added, which reads "SLOW INFUSION ONLY. FATAL if not infused slowly".

Figure 1. Previous Label Format

HYDROmorphone 1 mg/mL
in
0.9% SODIUM CHLORIDE INJ USP
TOTAL VOLUME 50 mL
INTRAVENOUS
EACH 50 ML CONTAINS 50 MG HYDROMORPHONE
BRAND: SANDOZ
PROTECT FROM LIGHT DURING STORAGE
BEYOND USE DATE: 15-Oct-2019
Store at Room Temperature 15 to 25°C
BATCH: 19I14CM00039
CODE: PXHYD1N
Date of Manufacture: 14-Sep-2019
Baxter Corporation
Baxter
CIVA003 14 02

Figure 2. New Label Format

HYDROmorphone 50 mg in 50 mL (1 mg/mL)
in
0.9% SODIUM CHLORIDE INJ USP
TOTAL VOLUME 50 mL
INTRAVENOUS
SLOW INFUSION ONLY. FATAL if not infused slowly.
Protect from light during storage.
Brand: Sandoz
BEYOND USE DATE: 21-Nov-2020
Store at Room Temperature 15 to 25°C
BATCH: 20J21CM00001
CODE: HYD1N TEST2
Date of Manufacture: 21-Oct-2020
Baxter Corporation
Baxter
CIVA003 14 02

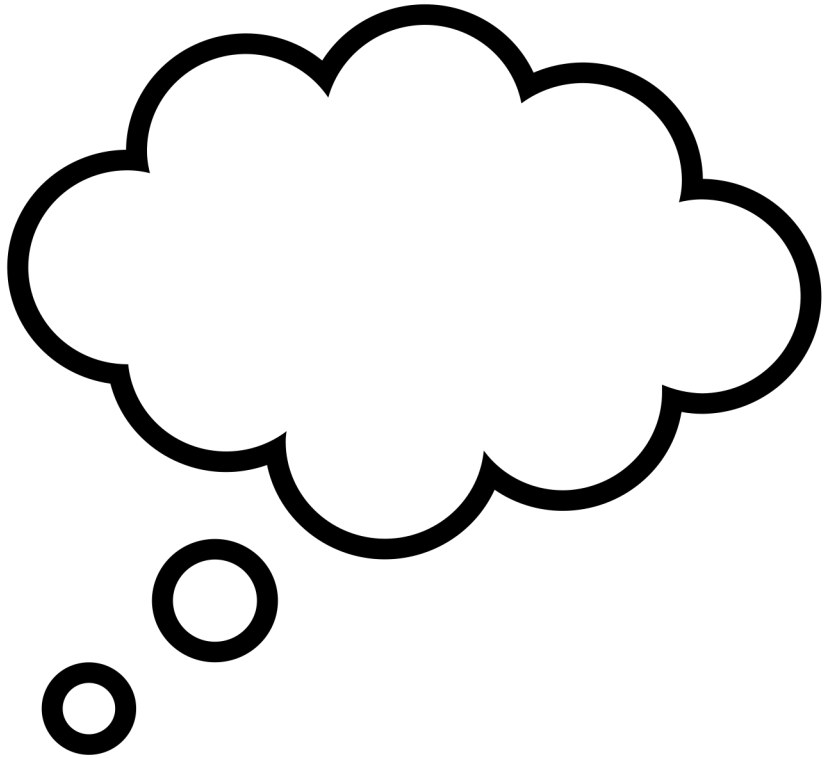
ISMP Canada is grateful to the reporting organization for sharing this incident and thanks Baxter Corporation for prioritizing patient safety.

Example:

- Report of harmful incident shared:
  - 50 mg of HYDROmorphone administered as an IV bolus instead of intended 1 mg dose.
- The Compounding Centre improved the label to:
  - Prominently display the total mg amount in total volume
  - Include a warning statement
- Opportunity: Develop label and package practice guides for compounded products (similar to the guides available for prescription drugs, non-prescription drugs and natural health products).

IMSN Opportunities?

Identify collaborative aims to inform and advance safety in compounding



Please contact us at info@ismpcanada.ca if you have any further ideas.

Thank you for listening.

Any Questions?

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