Medication Safety in Compounding Non-Sterile Preparations

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Background

Multiple studies have shown that pharmacy-compounded products are at risk for quality issues resulting in sub-potency, supra-potency, and even contamination. This project aims to identify important considerations for compounding non-sterile preparations in community pharmacy practice by referring to the newly revised *United States Pharmacopeia (USP) Chapter <795> Pharmaceutical Compounding – Nonsterile Preparations (as of May 2011)* and the *National Association of Pharmacy Regulatory Authorities (NAPRA) Guidelines to Pharmacy Compounding (as of October 2006)*.

The USP <795> Chapter defines the specific criteria required to compound preparations of acceptable strength, quality, and purity with appropriate packaging and labelling in accordance with regulatory agencies. In Canada, drug manufacturing is regulated by Health Canada and compounding is an authorized act regulated by provincial authorities.[1] The *NAPRA Guidelines to Pharmacy Compounding*, developed in collaboration with provincial pharmacy regulatory bodies, set the expectations for the quality and safety of compounding practices in Canadian pharmacies.[2]

Before compounding a non-sterile preparation, the need for the compounded product is confirmed by checking for commercially available preparations in the Health Canada's Drug Product Database, and contacting manufacturers. To comply with the Health Canada policy on compounding, this confirmation is required in order to validate the lack of product availability and avoid duplicating an approved drug product.[1]

Methods

An analysis of medication incidents related to non-sterile compounding was performed using reports anonymously submitted to the Institute for Safe Medication Practices Canada (ISMP Canada) Community Pharmacy Incident Reporting (CPhIR) Program from April 2010 to April 2012. Selected medication incidents were used to highlight potential outcomes that may result when non-sterile compounding guidelines are not followed.

Results

4 areas of concern were identified:

(1) PERSONNEL

After confirming the need to compound a preparation, designated managers need to ensure compounders (who are responsible for compounding preparations that are accurate and adhere to provincial standards) have accurate knowledge and expertise.[2] The compounder must use professional judgement when deciding whether they have the expertise to compound a specific product.[2]

(3) PROCEDURES AND RESOURCES

Sample Case[4]: *A pharmacist intended to compound an oral suspension of clonidine (using clonidine powder) for a 15-year-old male. The pharmacist incorrectly compounded the clonidine suspension (due to mixing up during calculations/conversions among grams, milligrams, and micrograms) resulting in a preparation 1,000 times more concentrated than prescribed. Before the error was discovered, the patient was admitted to hospital multiple times.*

This incident emphasizes the importance of independent double checks and following standardized procedures to confirm accuracy and quality of compounded preparations.

Sample Case: *A male patient received a prescription for a 1% hydrocortisone in clotrimazole [cream]. The compounded preparation contained a piece of wax paper. The prescription was prepared from pre-made stock. The pharmacist did not notice the wax paper in the compounded product and the patient used the preparation containing the wax paper.*

In this incident, the pharmacy used pre-made stock to fill the prescription. Unfortunately, the pre-made stock contained wax paper that was included in the dispensed container. Although the wax paper did not cause harm to the patient, compounders are responsible for ensuring the final product appears as expected.[5] If discrepancies are found in the final preparation, compounders need to resolve such discrepancies in preparation and/or appearance before dispensing to the patient.

(2) ENVIRONMENT

Compounders need to prepare non-sterile preparations in designated areas with adequate space, lighting, and storage to prevent cross-contamination and the inadvertent addition of extraneous material to the medication.[2,3] The designated area should have access to potable water (i.e. drinking water) for hand and equipment washing.[2,3] The *NAPRA Guidelines to Pharmacy Compounding* support this practice by including provisions for sanitation.[2]

(4) STABILITY ASSESSMENT

Sample Case: *A patient was prescribed sulfatrim oral suspension to be taken over a period of 90 days. A compounded oral suspension of sulfatrim is only stable for 20 days from its day of preparation.[6] The pharmacist prepared and dispensed a 90 day supply of sulfatrim oral suspension. The medication error was caught during dispensing and the patient was given a 20-day supply with the remaining amount credited as refills.*

In this incident, sulfatrim or co-trimoxazole oral suspension was not commercially available at the time of dispensing due to drug shortages, resulting in the need for the pharmacy to compound or prepare the oral formulation.[6] The pharmacist almost dispensed a compounded preparation intended to be used past the acceptable beyond-use date. This illustrates the need for compounders to understand the concept of beyond-use dates (Table 1).

Table 1. Recommended maximum beyond-use dates for non-sterile compounded preparations:[7]

Type of Non-Sterile Preparation	Beyond-use Date
Non-aqueous Formulations (such as ointments, suppositories, troches, and others where no water is contained)	Not later than the time remaining until the earliest expiration date of any ingredient or 6 months, whichever is earlier
Water-containing Oral Formulations	Not later than 14 days for liquid preparations when stored at controlled cold temperatures (i.e. temperature thermostatically maintained between 2°C and 8°C)
Water-containing Topical/Dermal and Mucosal Liquid and Semisolid Formulations (such as preparations for topical application, like creams, gels, ointments, etc.)	Not later than 30 days

Discussion

Inappropriate compounding practices can put patients at risk for potentially harmful outcomes. Compounding ingredients have defined chemical and physical properties, but the compounding process can change ingredient properties resulting in altered quality, stability, and potency. These changes are highly dependent on the compounding formulation. It is vital for compounders to understand the impact of these alterations on the final product before patients are dispensed the compounded preparations.

ISMP Canada
Institute for Safe Medication Practices Canada
www.ismp-canada.org

CMIRPS
Canadian Medication Incident Reporting and Prevention System
www.ismp-canada.org/cmirps/

CPhIR
Community Pharmacy Incident Reporting Program
www.cphir.ca

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Information on this poster does not represent the entire USP Chapter or the entire NAPRA Guidelines to Pharmacy Compounding. For further information, please consult the complete versions of the USP Chapter <795> and the NAPRA Guidelines to Pharmacy Compounding[2] respectively.