November 17, 2016

To: Ontario College of Pharmacists (OCP)

Re: OCP Consultation on Non-Sterile Compounding Standards (NAPRA)

Summit Veterinary Pharmacy Inc. (SVP) welcomes the opportunity to comment regarding the NAPRA proposed Model Standards for Pharmacy Compounding of Non-Sterile Preparations (version 5b), presently found on the OCP website.

BACKGROUND
This is an extensive document, and cannot be summarily addressed in short order. Based on comments to date found on the OCP website, it appears that a large amount of confusion exists within the profession of pharmacy as to how this document will impact upon practices, as well as to whom it will apply. Some comments suggest that because a pharmacy “only does common compounding” (whatever that is), or “do barely any compounding,” that they may be subject to the proposed Standards if implemented. These optics will require clarification in the course of further consideration of this matter, in that the document makes it clear that these minimum standards will be “requirements for all levels of non-sterile compounding activities” (Section 6). The definition of “compounding” (page 54) would encompass any/all “levels” of compounding – whether “common” or “barely done.”

Pharmacy compounding is already held to a high standard to ensure public safety as well as consistency of preparations, through pharmacists adhering to the requirements set out in the United States Pharmacopeia (USP 39-NF 34). Chapters <795> (non-sterile compounding), <797> (sterile compounding), and <800> (Hazardous Drugs -- Handling in Healthcare Settings) specifically apply to compounding, but there are also others that apply in terms of sterility/endotoxin testing, etc. These chapters are used as authoritative references internationally by compounding pharmacists, and are reference standards to which many regulatory bodies hold their members in order to be deemed “in compliance” with “acceptable standards for compounding,” thus protecting both the public and practitioners from harm.

In general, our position is that USP standards should be the “gold standards” for compounding. Adoption of additional standards may create confusion and conflict, may not be as comprehensive/clear as the USP standards, and could increase patient risk. Having said that, we offer the following comments by specific areas of concern, and via table references.

1. Patient-Specific/Office-Use (p8, Regulatory Framework)
A major area of concern to healthcare professionals is the virtual elimination of "office-use" procurement of medications by practitioners as permitted by their licensing authorities, due to use of the term “patient-specific” in the document. The problem is created by the following section on page 8:

“The preparation of medications by compounding has always been an integral part of the practice of pharmacy. It is essential to the delivery of health care and allows for personalized therapeutic solutions to improve patient care. However, compounding must always be carried out within a prescriber–patient–pharmacist relationship, or in the case of a non-prescription drug, within a pharmacist-patient relationship where the drug is prepared for a particular patient. Provincial/territorial pharmacy regulatory authorities are responsible for regulating a pharmacy’s compounding services in these situations.”
In situations involving requests to compound preparations outside of a prescriber–patient–pharmacist relationship, in the absence of a patient-specific prescription, the preparation activities fall under the federal legislative framework. For example, the bulk preparation of non-sterile compounds in the absence of a prescriber–patient–pharmacist relationship would fall under the federal legislative framework, namely the Food and Drugs Act (FDA) and the Controlled Drugs and Substances Act (CDSA).” (emphasis added)

Various PRAs (medicine, dentistry, veterinary medicine) permit their members to legally procure “office-use” medications in order to provide the best care to their patients. This practice is recognized, accepted, and condoned provincially & territorially, as well as by Health Canada on a federal basis. A legitimate prescription could be written by a qualified healthcare practitioner as “for office-use.” It would be recorded as being dispensed to “patient Dr. X” as well as prescribed by “Dr. X” under a prescription (that a drug identified in the prescription be dispensed to the person named in the prescription...being the prescriber in the case of “office-use”). Food & Drug Regulations section C.01.043(1)(b) allows the sale by a person (entitled to possess such drugs) of a prescription drug to a practitioner. No reference to “by a prescription” is made; in fact, the section used to read “A person may sell a Schedule F drug, without having received a prescription therefor, to...” That permits a practitioner to simply buy such drugs from a pharmacist; but the use of a prescription for such orders ensures traceability from source to recipient (including upon a written order of a prescriber for a narcotic, which would then require that its sale be reported in the narcotic sales report using the name of the prescriber as both patient and prescriber).

Concern has previously been voiced to both OCP and NAPRA regarding consultations for the sterile preparation standards, that “healthcare professional-patient-pharmacist” terminology should be used instead of “prescriber-patient-pharmacist” (to remain consistent with what is found in Health Canada’s POL-0051 document “Policy on Manufacturing and Compounding Drug Products in Canada”). It is noted that in the document, Appendix 1 (p58) is an extract from Health Canada POL-0051 and the term used there, repeatedly, is “patient-healthcare professional” – NOT “prescriber-patient-pharmacist,” or “patient-specific,” or any other composition of terms. This further supports why this terminology should be removed from the document, to remain consistent with the federal reference document which was created to differentiate between “manufacturing” and “compounding.”

We also urged the removal of “patient-specific” because it would preclude practitioners who are entitled to procure medications (including compounded preparations), from doing so. It should not be overlooked that "office-use" is considered illegal by the USFDA, which has been trying to eliminate this area of pharmacy practice for years, in part through use of the term “patient-specific prescription.”

There is a significant history of the USFDA ignoring the specific direction of Congress that it (FDA) has no authority to ban office-use, as this is a state jurisdiction. [Ref: http://www.iacprx.org/news/279889/Congressman-Buddy-Carter-Asks-Dept-of-Health--Human-Services-about-Office-Use-Compounding.htm]. In addition, we provide four attachments showing the degree of Congressional concern and history regarding the USFDA overstepping its authority in this area. It is clear why “patient-specific” is not a term conducive to patient best interests, and in fact, will impact adversely upon healthcare professionals being able to fulfill their professional responsibilities in having adequate medications available to treat patients (e.g., veterinary practice where unique species, such as small animals -- parrots, budgies, ferrets, etc. -- require specific doses of medications not commercially available).

Office-use” procurement is acceptable, essential practice recognized by various professions across Canada and is permitted by standards established by individual regulatory authorities of medicine, dentistry, and veterinary medicine in order to properly serve patients’ needs. Even the OCP published an article in its Winter, 2016, edition of "Pharmacy Connection" about the Ontario Narcotic Safety and Awareness Act, identifying to pharmacists how monitored drugs for "office-use" should be captured in the reporting system. It is therefore necessary to define that condition within the standards (it is absent from the Glossary) -- especially when many other Canadian PRAs recognize the practice of "office-use" (i.e., not “patient-specific”) through policies and documents relevant to those professions.

There will be significant impact upon practices should this document be accepted without a clear statement included that permits "office-use." Considerations include:
1) Adverse impacts upon readily-available medications for patient (human) and hospital needs, including emergencies, TPN therapy.

2) Adverse impacts upon emergency room aspects of veterinary clinic requirements (on-hand medications for emergencies such as poisonings, infections, trauma) due to necessary lead times to ensure sterility/endotoxin testing.

3) Nothing should preclude “office-use” preparations when such practice is permitted within various professions (dentistry, veterinary medicine, human) as it is considered essential in terms of good patient care (best practices) that practitioners have adequate stock on hand to dispense in emergency situations, as well as on weekends.

4) Health Canada recognizes "office-use" dispensing; they advise pharmacists on how to report the sale of "straight narcotics/controlled substances" when made in such fashion (i.e., show patient name as being the prescriber, so that the "patient" and "prescriber" fields will bear the same name). This allows auditing/traceability of such substances after drugs leave the pharmacy, keeping the practitioner receiving the drugs accountable for what is done with them afterwards.

5) In Ontario, the Narcotic Safety and Awareness Act has a code for reporting "office-use" sale of monitored drugs through the NMS.

6) There is huge outcry in the USA over the USFDA interpreting the “Drug Quality and Security Act” (DQSA) as not permitting “office-use” dispensing. While the USFDA refuses to recognize any compounding as legitimate, Congress (most recently as June 20, 2016) wrote to the Commissioner of the USFDA and reminded him that on April 19, 2016, the USFDA was directed to “allow for office-use compounding.” That letter further stated:

"Prior to the passage of the Drug Quality and Security Act (DQSA) of 2013, FDA circulated a draft Compliance Policy Guide (CPG) in 2012 to Congress that recognized office-use as legitimate and permissible...The DQSA did not change the statutory language in 503A that was the basis of that CPG. During the consideration of the DQSA, six Members of Congress, on a bipartisan, bicameral basis, made statements in the Congressional record to clarify that the intent of the legislation was to preserve patient access to medications compounded for office-use...Unfortunately, the FDA has to date ignored that congressional intent and substituted the agency's own, incorrect interpretation of the law in implementing and enforcing the DQSA."

The letter was signed by 61 members of Congress, at least one of whom is a pharmacist (attached).

Significantly, the very terms "patient-specific" and “office-use” are not defined in the NAPRA document. These critical terms are used within the document. The terms must be defined in the documents in which they are used, as is done with other important terms found within the documents. If “patient-specific” is to be retained, one such definition suggested is:

"patient-specific" shall include "office-use" prescription orders of a practitioner entitled to prescribe in a province/territory of Canada.

2. Withdrawal Period (p35)
The responsibility for establishing withdrawal periods (aka: withdrawal times) is mandated by veterinary licensing authorities for their members. The pharmacist is not in any position to do so, as this is a practitioner’s professional responsibility. The veterinarian prescribing a drug will know if the animal could end up being “food potential” and as such must discuss withdrawal times with the owner of the animal(s).
The prescription as issued by the veterinarian MAY include this information, with/without a direction to include it on the label (i.e., in Ontario, per the DPRA labelling requirement of “directions for use, as prescribed”). “Withdrawal period” does not convey directions for use of the medication (administration).

This should not be a requirement on a label that is already short of available space, especially when container sizes might not allow for supplementary labels to be affixed to the container in which the drug is dispensed. The words “as determined by the prescriber” should immediately follow the term “withdrawal period” in paragraph 3 of Section 7.11. Similar information is not required to be on the labels of other dispensed drugs where “human harm” could result through direct human ingestion of those drugs.

If it remains as a requirement (if provided by the veterinarian on the prescription), and since the pharmacist realistically may not know that the “patient” will become food, allowance should be made for this information to be conveyed OTHER THAN by inclusion on the dispensing label (such as by handout, leaflet, etc.). In many cases, this information will not be provided on the prescription by the veterinarian due to confidentiality requirements incumbent upon the veterinary profession.

3. APIs (Active Pharmaceutical Ingredients) – Section 7.3.4
Because it is often impossible to obtain ALL ingredients (excipients, etc.) that compose a commercially-available DIN product due to manufacturers protecting their formulations against “piracy”, any use of such products as starting materials for a compounded drug should be a last resort. Starting with a pure API, obtained from a credible facility and supported by a Certificate of Analysis that is also supported by a pharmacopeial reference (such as USP-grade) is, by professional conventional wisdom) the proper route of first choice when compounding a preparation.

This has been expounded upon by experts in the compounding field (e.g., Dr. Loyd V. Allen Jr., who is cited in the Bibliography in the NAPRA document). Allowable ranges of active content in commercial products increases the risk of a final preparation being sub/super potent, whereas using a “pure” (ca. 100%) API to start ensures a final preparation consistent with the prescribed dosage. This should be the practice standard (first choice) when it comes to compounding source material. It is also consistent with Good Compounding Practice to use pure, USP-grade API as starting material for compounds.

4. Tabulated Comments (Other Areas of the Document)
Our observations and comments resulting from our detailed review of the document, further to those already elaborated upon, follow in Table format.

**TABLE of COMMENTS**

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<tr>
<td>3</td>
<td>8</td>
<td>All references to “prescriber-patient-pharmacist” should be replaced with “patient-healthcare practitioner” to reflect the POL-0051 terminology since it is a cross-reference document to the issues contained in this section.</td>
</tr>
<tr>
<td>3</td>
<td>8 (last sentence)</td>
<td>As worded, this will interfere with the acceptable practice of practitioners whose licensing bodies allow them to obtain drugs for “office-use” within their practices. Use of the term “patient-healthcare practitioner” may alleviate this, since as described in more detail in our submission, “office-use” procurements by practitioners for reportable drugs (e.g., narcotics) treat the patient and prescriber as being the prescriber. This is supported by Health Canada narcotic sales report format, and by Ontario’s Narcotic Safety and Awareness Act reporting formats, as re-inforced in OCP’s Winter, 2016, Edition of Pharmacy Connection (p15), re the Narcotic Monitoring System report requirements.</td>
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<td>SECTION</td>
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<td>COMMENTS</td>
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<tr>
<td>3</td>
<td>8 (pg 4)</td>
<td>&quot;commercial compounding manufacturer&quot; is a poor choice of term, given that POL-0051 is designed to distinguish between &quot;manufacturing&quot; and &quot;compounding.&quot; It appears to have originated from the USA, and has no place in Canada as by using two conflicting practice terms as a single category, it creates confusion. Furthermore, it is not defined in the document's Glossary so pharmacists nationally will not be aware of what it refers to; NAPRA should be advised to amend this term to something not incorporating a term which is unique for pharmacy practice (&quot;compounding&quot;).</td>
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<tr>
<td>3</td>
<td>8 (pg 5)</td>
<td>&quot;However, . .&quot; – grammatical error with spacing, etc. &quot;compounding more complex non-sterile preparations...&quot; – &quot;more complex&quot; is vague: why not use the term found in the box on p11 of the document? As is, it's subjective and result in consistency nationally.</td>
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<td>4</td>
<td>10</td>
<td>“GMP” definition should be “Practices” (plural) per Health Canada's regulatory definition.</td>
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<tr>
<td>5.1</td>
<td>11</td>
<td>“products” should be replaced not only here, but by word search throughout the document with the term “preparations” to reflect the compounding aspect and the document’s title, rather than the commercial/manufacturing term.</td>
</tr>
<tr>
<td>5.1</td>
<td>11</td>
<td>The first full pg (&quot;All compounded preparations...&quot;) This statement is consistent with US-terminology in a move to eliminate compounding. It uses archaic “pharmacist/patient/prescriber” terminology and should be addressed in the same way as was discussed in our comments in Section 1. of our submission.</td>
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<tr>
<td>5.2</td>
<td>11</td>
<td>Rather than create “Levels A, B, C” which are confusing and nebulous/unclear, which is evidenced by comments already submitted to the OCP consultation webpage, it would be better to use the USP criteria.</td>
</tr>
<tr>
<td>5.2</td>
<td>11</td>
<td>The last example in the sidebox (&quot;mixing two or more manufactured cream products&quot;) is done, safe to say, in every pharmacy. Therefore, it is further proof that this document has to apply to all pharmacies, especially in such instances, because by mixing two commercial creams you dilute each cream’s content strength by 50% (including the preservatives in the products which may result in lack of potency as well as shelf-life against microbial growth).</td>
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<tr>
<td>5.1</td>
<td>11</td>
<td>The reference to all the pharmacopeia should remain, rather than remove any of them (e.g, CF) as this is consistent with Schedule B of the Food and Drugs Act (Canada). Unless that schedule changes, all should be retained by reference within this document.</td>
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<td>12</td>
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<td>Level A: “separate compounding area” should be defined, because some are confused as to whether it will be a defined room, or “area”. Later in the document, it refers to being able to clean the area, etc. and that would be suggestive of a separate room being necessary – so that should be clearly stated. To have a busy dispensary counter be a preparation area would not appear to suffice, due to high traffic and risk of contamination.</td>
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<td>5.3</td>
<td>14</td>
<td>To prepare a simple preparation that contains a NIOSH hazardous drug could, in fact, contaminate the entire area if it is not within a contained area that is separate from the regular dispensary.</td>
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<td>6.1.1.2</td>
<td>15</td>
<td>Just above “Responsibilities,” the term “provincial/territorial authority” should better define what that authority/category is to be – such as, “regulatory authority” as appears in the last bullet to 6.1.1.2.</td>
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<td>6.1.1.3</td>
<td>16</td>
<td>Top of page: “continuously evaluated” is not possible; rather, use “ongoing” as appears at the bottom of the previous page.</td>
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<td>6.1.1.3</td>
<td>16</td>
<td>“preparing” should be replaced by “dispensing” (below 2nd bullet), consistent with the terminology used in the sterile preparation standard documents (NAPRA).</td>
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<td>6.1.3</td>
<td>16</td>
<td>b) insert “regulatory” in front of “authority”</td>
</tr>
<tr>
<td>6.3.2</td>
<td>20 (pg 3)</td>
<td>It is essential that these requirements be applied and corrected if identified at inspection as being non-compliant. These provisions will essentially make it impossible to have compounding done in the “regular dispensary area” but are 100% necessary in order to guard against contamination of preparations.</td>
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<tr>
<td>7.1</td>
<td>23</td>
<td>All instances in the document of “beyond use” should have a hyphen in the term.</td>
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</tbody>
</table>
7.3.4 27 This is an excellent description of the needs for starting materials and sourcing for compounds. It is noted, however, that the "list of drugs that have been withdrawn from the market" hyperlink is inactive.

7.4 28 Why is a "duplicate label" required to be part of the MFR when such is not required to be in the record for all other prescriptions dispensed? What purpose does this serve, when the label will be part of the patient profile record of dispensing (since these fields are shown as part of the prescription record)?

7.6.1.1 31 "procedure" in the first line should be "policy" for purposes of consistency with other standards.

7.6.1.1 31 The labelling requirement for containers does not take into consideration situations where the physical size of the container may not allow for affixing of a label to the actual container that has the drug content in it. It is also not feasible in many such instances to get all active ingredients and concentrations onto the standard labels available to pharmacies; to date, it has been a standard to put the active ingredient with the highest concentration onto the label and then indicate "cmp" as part of the drug name to denote there are further ingredients (which would be on the prescription record itself, if necessary). There is no need to require "this is a compounded preparation" on the label because the lack of a DIN (as appears for such products via pharmacy computer systems) is evidence; this is a US-based statement that has no place in Canadian practice.

7.6.1.1 31 The last pgh in this section is confusing as to how this would be accomplished in reality practice, and under what scenarios it would even arise to be required. In essence, it would most likely result in "over labelling" of the primary label in order to ensure that the secondary label is attached to the actual container that bears the drug. If it is allowed to be attached to a vial that contains the actual drug container, then should they become separated (a reality with patients) there would be nothing to indicate the identity of the secondary pharmacy that was involved in the dispensing (e.g.: 15g ointment jars).

7.11 35 Pgh 1: "veterinary/client/patient/ pharmacist" – per earlier comments, should be changed but also, this now incorporates a fourth entity rather than what Section 3 references in the PPP term. It is inconsistent with POL-0051's terminology.

9 38 Replace "products" with either "compounds" or "preparations" (also in 10.1).

10.1 38 Last pgh, "cross contamination, well ventilated, close off" should have hyphens between terms.

10.3.2 41 "though" should be "through" in line #1.

10.6 50 Inconsistency in use of "product" vs. "drugs" and then "pharmaceutical products". Better to consistently use "hazardous products" as all-inclusive.

53 The numbering appears to be off, since the previous section was "10"; should the Glossary be "11" (with mods to subsequent sections)?
- "API" definition: "comes" (line 2) should be "becomes"
- "BUD" definition: "use" should be "used"; "sis" should be "is"

55 Incident: "as" at the end of line 2 should be "has"
MFR: This definition does not appear to be complete. Should it not include its additional purpose to "compound a non-sterile preparation and ensure consistent reproducibility from preparation to preparation"?

56 "Pharmacist": This definition for its use within the document is not consistent with all pharmacists in Canada. While all have a degree and may be registered with a PRA, they may not all be able to perform the duties set out in the document (e.g. if in Part B of Ontario's register). To be "registered in good standing" would not allow you perform what is reference by "pharmacist" where it occurs within the document.

56 "Withdrawal Period": The actual regulatory section that defines the term is C.01.001(1), not C.01.001.
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<td>58</td>
<td>Noted re the repeated use of the term “patient-healthcare professional” relationship.</td>
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<td>#7: This definition for “compounding” is not accurate, since it is not an offence to merely indicate through advertising that a pharmacy has a compounding service. That is factual information consistent with advertising regulations for pharmacy practice. The mere advertising of such should not constitute “manufacturing”. If so, the website for the ACPC (<a href="http://www.acpcrx.org">www.acpcrx.org</a>) would automatically put all member pharmacies into violation, simply by listing their services with the intent to assist the public in finding a compounding pharmacy.</td>
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<td>APX 10</td>
<td>79</td>
<td>In the algorithm, the first “NO” response creates difficulty at the pharmacy level because packaging from a supplier may not indicate the contents to be hazardous. By the time the box is opened and discovered to be damaged, it may not have been opened in a Class I BSC. More responsibility is necessary to be upon the suppliers to the pharmacy to properly identify the contents of packages sent to pharmacies, since pharmacies receive many packages over the course of a day.</td>
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<tr>
<td>88</td>
<td></td>
<td>The NIOSH reference (2010) is out of date as a 2014 version is now available.</td>
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Respectfully,

Stephen Organ  
President

Don Organ, R.Ph.  
Chair

Ed Bielawski, R.Ph.  
Designated Manager

Kim Ruthig, R.Ph.  
Chief, Regulatory Compliance

Attach (4):

- Ltr to FDA 20140627
- Ltr to FDA 20151110
- Ltr to FDA 20160620
- IJPC Article Vol 20, #2