Public consultation

1 February 2016

You are invited to provide feedback on this public consultation

Review of guidance on expiry of compounded parenteral medicines – Pharmacy Board of Australia *Guidelines on compounding of medicines*

Please provide feedback in a word document (or equivalent)[1] to pharmacyconsultation@ahpra.gov.au by close of business on Wednesday 30 March 2016.

Public consultation

The Pharmacy Board of Australia (the Board) previously published its *Guidelines on compounding of medicines* (the guidelines) after a period of public consultation. The Board is releasing the attached consultation paper on draft revisions to the guidance in the section titled 'Expiry of compounded parenteral medicines' contained in the guidelines. Given the Board's previous consultation on the complete guidelines, other sections are not part of this public consultation.

You are invited to provide your comments to the questions in the paper, by close of business on Wednesday 30 March 2016. A template document for your response has been provided for your convenience. The feedback from this consultation will be considered by the Board in its further development and finalisation of the guidance.

How your submission will be treated

Submissions will generally be published on the Board's website unless you request otherwise. National Boards retain the right not to publish submissions at their discretion, and will not place on their website, or make available to the public, submissions that contain offensive or defamatory comments or which are outside the scope of the consultation.

Before publication, National Boards remove personally-identifying information from submissions, including contact details. The views expressed in the submissions are those of the individuals or organisations who submit them and their publication does not imply any acceptance of, or agreement with, these views by the National Boards.

National Boards also accept submissions made in confidence. These submissions will not be published on the website or elsewhere. Submissions may be confidential because they include personal experiences or other sensitive information. Any request for access to a confidential submission will be determined in accordance with the *Freedom of Information Act 1982* (Cwlth), which has provisions designed to protect personal information and information given in confidence.

Please let the Board know if you do not want your submission published, or want all or part of it treated as confidential.

[1] You are welcome to supply a PDF file of your feedback in addition to the word (or equivalent) file, however we request that you do supply a text or word file. As part of an effort to meet international website accessibility guidelines, AHPRA and National Boards are striving to publish documents in accessible formats (such as word), in addition to PDFs. More information about this is available at www.ahpra.gov.au/About-AHPRA/Accessibility.aspx.

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Summary

1. The Health Practitioner Regulation National Law, as in force in each state and territory (the National Law), empowers the National Boards to develop and approve codes and guidelines to provide guidance to the profession. It also requires the National Boards to ensure there is wide-ranging consultation on the content on any proposed code or guideline.

2. This consultation paper seeks feedback on draft revised guidance on expiry of compounded parenteral medicines, to replace the currently postponed section "Expiry of compounded parenteral medicines" of the Board's published *Guidelines on compounding of medicines* (the guidelines). The introduction of this section of the guidelines was postponed after the Board received feedback from stakeholders that the guidance was likely to impact access to some compounded medicines.

3. The Board is inviting general comments on the draft revised guidance which seeks to address the concerns raised in feedback to the Board. You may also wish to address in your response the specific questions contained in this consultation paper about the draft revised guidance. A template response form has been provided for your convenience.

4. The Board will consider the consultation feedback in its further development and finalisation of the guidance for publication.

5. Given the Board's previous consultation on the guidelines, other sections are not part of this public consultation.

Please provide feedback in a word document (or equivalent) to pharmacyconsultation@ahpra.gov.au by close of business on Wednesday 30 March 2016.

Background

6. The Board undertook a review of its guideline on compounding of medicines (Guideline 5 *Extemporaneous dispensing (compounding)* of the Board's *Guidelines for dispensing of* medicines) during 2013-2014 in collaboration with keys stakeholders including the Therapeutic Goods Administration (TGA). The TGA had previously consulted on options to regulate the compounding of sterile injectable medicines, as requested by government. This was prompted by the unfortunate case of unsatisfactory compounding of injectable medicines that occurred in the United States where the compounding of a steroid injection resulted in fungal meningitis, which adversely affected more than 700 patients and resulted in the death of more than 60 people.

7. One of the options presented by the TGA in its consultation *Options for reform of the regulatory framework for pharmacy compounding* in June – July 2013, was a regulatory framework requiring pharmacists who compound sterile injectables to obtain a manufacturing licence from the TGA, unless the compounding complied with the guidelines on compounding published by the Board. This proposed "collaborative-regulatory" approach, if approved, would include reference to the Board's guidelines in revised therapeutic goods regulations.

8. The guidance provided in the section *Expiry of compounded parenteral medicines* of the Board's guidelines which specified that compounded parenteral medicines are to be assigned a maximum shelf life (expiry) of 24 hours was consistent with this approach. The specific parenteral medicines that are the subject of this guidance are listed in paragraph 17.

Publication of the *Guidelines on compounding of medicines*

9. After wide-ranging consultation, the Board finalised its *Guidelines on compounding of medicines* based on the feedback it received through consultation. The guidelines were published on the Board's

website at www.pharmacyboard.gov.au/Codes-Guidelines.aspx in March 2015 with an implementation date of 28 April 2015.

Published guidance regarding expiry of compounded parenteral medicines

10. The section of the guidelines *Expiry of compounded parenteral medicines* proposed that pharmacists assign a shelf life of up to 24 hours to compounded parenteral medicines, to avoid the following risks associated with assigning longer shelf lives:

    - enhanced chemical instability of the compounded medicine which may result in reduced therapeutic activity, or enhanced toxicity caused by degradation products
    - increased likelihood of microbial contamination of the compounded product, and
    - increased likelihood of dose administration errors associated with the compounded medicine, for example an infusion bag that was compounded before a dose change, being incorrectly administered to a patient.

11. To align with the TGA consultation on *Options for reform of the regulatory framework for pharmacy compounding* options, the guidance on expiry of compounded parenteral medicines outlined that this did not apply to pharmacists practising in a public hospital who may assign a shelf life of greater than 24 hours if appropriate when specified requirements are met. A copy of this guidance under the section titled 'Expiry of compounded parenteral medicines' can be found on page 8 of the full set of *Guidelines on compounding of medicines*.

12. Following publication and prior to the guidelines' implementation date, the Board received further feedback from pharmacists, prescribers and the public about the guidance in the section *Expiry of compounded parenteral medicines* and the likely impact of the guidance on access to these medicines.

13. Consequently, the Board resolved to postpone the commencement of this section of the guidelines and conduct further consultation to ensure that its guidance strikes the right balance between assuring patient safety, and ensuring ongoing access to compounded parenteral medicines by patients in accordance with prescribers' instructions.

Feedback on the guidance regarding expiry of compounded parenteral medicines

14. Feedback from stakeholders on the Board's guidance on the expiry of compounded parenteral medicines highlighted concerns that it would inhibit or impact access to compounded parenteral medicines, due to:

    - specific difficulties associated with the supply of medicines to patients in rural and remote locations, including the time required for transporting medicines to such locations, in which case a 24 hour product shelf life may be insufficient
    - the need for some patients to receive a daily dose of a compounded injection. This may create problems such as:
        - excessive cost and/or inconvenience for a patient or carer to travel to a compounding pharmacy each day or to pay for a courier to deliver one injection at a time (which is a greater barrier for patients living in rural and remote locations), or
        - the compounding pharmacy not being open seven days of the week to compound and supply the required injection each day.

      In this case, assigning a shelf life of longer than 24 hours would be highly preferable.
    - the need for some patients to have a compounded medicine on hand for 'when required' use, in which case a shelf life of longer than 24 hours is required
    - the high cost associated with sourcing a compounded product from a TGA licensed facility (which can provide products with a longer shelf life), compared to the cost if the product is compounded in a compounding pharmacy if a product with a longer shelf life is required by a patient, and
    - difficulties associated with sourcing a particular product from a TGA licensed facility (e.g. the TGA licensed facility is unable or unwilling to supply the particular product required by a patient).

Development of revised guidance

15. To seek further feedback on the postponed section of the guidelines, the Board in collaboration with the TGA, held two stakeholder meetings with key pharmacy stakeholders, compounding pharmacists and prescribers in Melbourne and Sydney in July 2015.

16. Based on the feedback received at these meetings, as well as the previous feedback received on this section of the published guidelines, revised guidance was developed in consultation with TGA. This was subject to targeted consultation with key stakeholders in September to October 2015, and the feedback received taken into consideration in finalising draft revised guidance on expiry of compounded parenteral medicines for public consultation.

17. The draft revised guidance presented in this paper proposes that longer shelf lives may be assigned to compounded parenteral medicines provided that this is done in accordance with the standard USP-NF (797) Pharmaceutical Compounding – Sterile Preparations. This guidance also defines parenteral medicines for the purpose of the guideline as:

    - injections
    - infusions
    - concentrates for injections or infusions
    - powders for injections or infusions, and
    - gels for injections.

18. A table outlining the differences between the published (postponed) guidance and the proposed revised guidance is provided on page 7 of this consultation paper, to assist stakeholders in their consideration of the revised guidance.

You are invited to provide feedback

The Board is seeking feedback on the draft revised guidance on expiry of compounded partenteral medicines including the following questions:

- Has the proposed guidance been expressed clearly?
- Does the revised guidance adequately address the concerns raised by stakeholders, that the published (postponed) guidance would inhibit or impact patient access to compounded parenteral medicines?
- Does the revised guidance support patient safety when supplying compounded parenteral (sterile injectable) medicines?
- Do you have any suggestions for questions to be included in the Board's FAQ for pharmacists on the compounding of medicines, to support pharmacists in their understanding and application of this guidance?
- Do you have any suggestions on how the proposed guidance could be improved (e.g. any content that should be changed, added or deleted), while still being in accordance with the public interest?
- Do you have any other comments on the proposed guidance?

Estimated impacts of the proposed changes

19. The changes proposed in the draft revised guidance are intended to address the concerns raised about the postponed guidance inhibiting access to compounded parenteral medicines. The draft revised guidance is intended to achieve the right balance between assuring patient safety, and ensuring ongoing access to compounded parenteral medicines by patients in accordance with prescribers' instructions.

20. The revised guidance is intended to provide the following benefits:

    - clarification of the definition of 'parenteral medicines' for the purpose of the guideline
    - enhanced flexibility in assigning a shelf life to a compounded parenteral medicine, through utilisation of published standards recognised as being appropriate for this purpose, in order to facilitate access to these medicines by patients whilst maintaining patient safety
    - advice to pharmacists about the importance of audit of compliance with the published standards on the compounding of parenteral medicines

- advice to pharmacists to confirm that their profession al indemnity insurance (PII) arrangements indemnifies their individual compounding practice, which is consistent with the Board's current PII standard and its revised PII standard which advises pharmacists to make a self assessment based on factors including practice setting and type of services provided, and
- highlights that the Board will periodically review the guidance to ensure alignment with any future changes to the broader regulatory framework for the compounding of medicines.

21. In developing the revised guidance, consideration was given to the objectives and guiding principles of the national registration and accreditation scheme which include:

    - to facilitate access to services provided by health practitioners in accordance with the public interest, and
    - restrictions on the practice of a health profession are to be imposed under the scheme only if it is necessary to ensure health services are provided safely and are of an appropriate quality.

Relevant sections of the National Law

22. Section 35 of the National Law allows the National Boards to develop or approve standards, codes and guidelines for the health profession, including the development and approval of codes and guidelines that provide guidance to health practitioners registered in the profession. Section 39 explicitly states that a National Board may develop and approve codes and guideline to provide guidance to the health practitioners it registers; and about other matters relevant to the exercise of its functions.

Draft revised guidance

(Note: It is proposed that this draft revised guidance replace the section titled 'Expiry of compounded parenteral medicines' on page 8 of the Board's published Guidelines on compounding of medicines*.)*

Compounding of parenteral medicines

Compounding of parenteral medicines poses significant risks to the public if the requirements of relevant legislation, guidelines and practice standards are not strictly adhered to throughout the compounding and supply process. The Board provides guidance to address the compounding of parenteral medicines acknowledging that at any time, relevant authorities may amend existing requirements or introduce new requirements regarding such compounding. The Board will periodically review this guidance to ensure alignment with the broader regulatory framework for compounding of medicines.

The parenteral medicines to which this guidance applies are:

- injections
- infusions
- concentrates for injections or infusions
- powders for injections or infusions, and
- gels for injections.

Compliance with legislation, guidelines and practice standards

When compounding parenteral medicines (as described above), pharmacists must strictly adhere to all relevant legislation, guidelines and practice standards as outlined in the section *Relevant legislation and practice* standards in these guidelines, and the principles and procedures outlined in at least one of the following guides/standards, as applicable to the practice setting:

- the PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments (PE 010-4), or
- the PIC/S Guide to Good Manufacturing Practice for Medicinal Products, as is required by TGA licensed manufacturers (PE 009-8), or
- the USP–NF ⟨797⟩ Pharmaceutical Compounding—Sterile Preparations.

In accordance with the relevant provisions in the National Law, the Board may investigate a notification received about a pharmacist including alleged noncompliance with relevant legislation, guidelines and practice standards and the applicable guides/standard listed above.

Self assessment and audit

To ensure compliance with practice standards, pharmacists are expected to audit their practice against the standards.

Pharmacists should conduct a self assessment/audit of their compounding practice against practice standards and guidelines, and legislation. A third party assessor with expertise may be contracted to assist with auditing of compliance. An authorised entity (state, territory or Commonwealth) may also conduct independent audits of compliance with legislation, guidelines and practice standards. Deficiencies identified during audit must be remedied.

Evidence of ongoing compliance that assures the provision of safe and quality compounded parenteral medicines to the public should be maintained.

Pharmacists must make available to any person authorised to the extent of their lawful jurisdiction, evidence that the compounding of parenteral medicines has been carried out in accordance with all legal requirements, guidelines and practice standards and the applicable guide/standard listed above.

Expiry of compounded parenteral medicines

Pharmacists who compound parenteral medicines for administration to a specific patient must assign expiry dates of appropriate duration given that longer expiries may result in:

- enhanced chemical instability of the compounded medicine which may result in reduced therapeutic activity, or enhanced toxicity caused by degradation products
- increased likelihood of microbial contamination of the compounded product, and

- increased likelihood of dose administration errors associated with the compounded medicine, for example an infusion bag that was compounded before a dose change, being incorrectly administered to a patient.

In this context, expiry date refers to the end of the shelf-life period after which the product should not be used.

Assigning expiry dates to compounded parenteral medicines

To address the risks associated with compounded parenteral medicines that are outlined above, the Board recommends that pharmacists who compound parenteral medicines that are to be administered to a specific patient, should routinely assign an expiry date of up to 24 hours to those medicines.

A longer expiry date may be assigned to a compounded parenteral medicine provided it is assigned in accordance with the guidance in the *USP–NF ⟨797⟩ Pharmaceutical Compounding—Sterile Preparations*. This guidance requires that the following has taken place:

- assessment of the contamination risk level of the medicine, and
- assignment of a time period for the expiry date that corresponds to the storage conditions of the medicine (controlled room temperature, cold temperature or in solid frozen state) applicable to the contamination risk level assigned to the medicine, and
- documentation of evidence that the compounded medicine will remain physically and chemically stable and maintain sterility when stored under the required storage conditions during its assigned expiry date.

If the compounding pharmacist chooses to follow guidance provided in a standard other than the *USP–NF ⟨797⟩ Pharmaceutical Compounding—Sterile Preparations*, the onus is on the compounding pharmacist to document evidence that an equivalent outcome has been achieved that supports assignment of a longer expiry date.

The compounding pharmacist must confirm with their professional indemnity insurance provider, that their policy indemnifies their practice.

Comparison with postponed guidance

Comparison of key proposed changes to the guidance on the expiry of compounded parenteral medicines

The following table outlines the key differences between the draft revised guidance retitled *Compounding of parenteral medicines* and the currently postponed guidance in the section titled *Expiry of compounded parenteral medicines* in the Board's published *Guidelines on compounding of medicines*.

	Expiry of compounded parenteral medicines guideline (postponed and not commenced)	Proposed revised guidance titled ***Compounding of parenteral medicines***
1.	Refers to 'parenteral medicines' which by definition covers a broad range of dose forms. The Board's guidance was intended to address compounded sterile injectable medicines (to align with TGA's consultation on a proposed regulatory framework for compounding of sterile injectables). This was further clarified in published FAQ. The Board received feedback that further clarification was required about the dose forms to which the guidance applied.	Defines 'parenteral medicines' for the purpose of the guideline by specifying the types of parenteral medicines: • injections • infusions • concentrates for injections or infusions • powders for injections or infusions, and • gels for injections. This aligns with TGA's consultation on a proposed regulatory framework for compounding of sterile injectables.
2.	Pharmacists (who are not practising in a public hospital) should assign a shelf life of up to 24 hours for parenteral medicines. This raised significant concerns amongst stakeholders about access to these medicines, such as: • supply to patients in rural and remote locations, including the time required for transport of these medicines • the need for some patients to have a compounded injection daily, in which case a shelf life of longer than 24 hours would be highly preferable, and • the need for some patients to have a compounded parenteral medicine on hand for 'when required' use • high costs associated with sourcing a product from a TGA licensed facility compared to a compounding pharmacy • difficulties associated with sourcing a particular product from a TGA licensed facility.	Outlines that the 24 hour shelf life applies and includes additional guidance about assigning longer shelf lives (in accordance with USP-NF (797) Pharmaceutical Compounding – Sterile Preparations). The process for determining longer shelf lives, as outlined in the named USP standard, requires: • assessment of the contamination risk level of the medicine • assignment of a time period for the expiry date that corresponds to the storage conditions of the medicine (controlled room temperature, cold temperature or in solid frozen state) applicable to the contamination risk level assigned to the medicine, and • documentation of evidence that the compounded medicine will remain physically and chemically stable and maintain sterility when stored under the required storage conditions during its assigned expiry date. Pharmacists would be required to refer to the named USP standard to make individual assessments about longer shelf lives for individual medicines. If they choose to follow guidance provided in another standard, the

	Expiry of compounded parenteral medicines guideline (postponed and not commenced)	Proposed revised guidance titled ***Compounding of parenteral medicines***
		pharmacist must document evidence that an equivalent outcome has been achieved that supports the longer expiry date.
3.	Proposes that pharmacists practising in public hospitals could extend shelf lives provided: • data on chemical and microbial stability of product with a longer expiry is available • compounding takes place in qualified laminar flow work station, and • there is adherence to the *PIC/S Guide to good manufacturing practice for medicinal products*. Stakeholder feedback indicated that the Board's guidance discriminates against private hospitals and community pharmacies, that practice in these locations may be equivalent to or better than practice in some public hospitals, and that there is no national auditing process that appropriately assesses compliance at premises or accredits premises. The next step available to these pharmacists is to obtain a TGA licence.	The draft guideline does not differentiate based on practice location. Extended shelf lives would be assigned by pharmacists in accordance with the named USP standard under the same circumstances in all practice locations. The Board is not able to audit and accredit pharmacy premises as this is not within its functions under the National Law, but it may investigate notifications about pharmacists' practice. Refer to line 5.
4.	Requiring adherence to the *PIC/S Guide to good manufacturing practice for medicinal products* for extended shelf lives was claimed by stakeholders (pharmacists) to be too onerous and that other standards should be considered.	Proposes that pharmacists comply with one of the following three standards (as applicable to their practice setting): • the PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments (PE 010-4), or • the PIC/S Guide to Good Manufacturing Practice for Medicinal Products, as is required by TGA licensed manufacturers (PE 009-8), or • the USP–NF ⟨797⟩ Pharmaceutical Compounding—Sterile Preparations. These options are based on feedback from stakeholders and consultation with TGA about appropriate standards for compounding of sterile injectable medicines by pharmacists in premises that are not licensed by TGA.
5.	Does not address audit of compliance with any standard.	The Board has included guidance about self assessment and audit that outlines that pharmacists are expected to audit their practice against practice standards and guidelines, and legislation. While this applies broadly to pharmacy practice, given the risks that exist in compounding parenteral medicines, this has been specifically highlighted in the proposed guidance.

	Expiry of compounded parenteral medicines guideline (postponed and not commenced)	Proposed revised guidance titled ***Compounding of parenteral medicines***
		This approach aligns with advice in published professional practice standards about how to use the standards. Additionally, the *National Competency Standards Framework for Pharmacists in Australia, 2010* lists specific competencies relevant to audit of practice. Standard 3.4 'Manage quality service deliver, Element 2 'Maintain and enhance service quality' lists the following performance criteria: 1. Ensures services are provided in accordance with professional standards and statutory requirements. 2. Promotes maintenance of, and improvement in, the quality of pharmacy services and the service environment. 3. Plans and implements activities to maintain or improve the quality of pharmacy services and/or the work environment. 4. Uses data and information gathered about pharmacy services to implement changes required to improve services. This is further demonstrated by the list of evidence examples for these elements. The proposed guidance further outlines: • pharmacists who compound medicines should conduct a self assessment/audit against practice standards and guidelines, and legislation. A third party assessor may be contracted to assist with this. • authorised entities audit compliance in some jurisdictions • deficiencies identified during audit must be remedied • evidence of ongoing compliance that assures the provision of safe and quality compounded parenteral medicines should be maintained and made available to authorised entities.
6.	No reference is made to professional indemnity insurance (PII) requirements in the guideline.	Advises pharmacists to confirm that their PII arrangements cover their practice. This aligns with the obligations of pharmacists in the current and revised PII standard. Pharmacists' practice should only be in accordance with what is covered by their PII policy. (Note: also propose to add PII standard to list of references under *Board references* in the full set of *Guidelines on compounding of medicines*.)
7.	Review of the guidance to ensure alignment with the broader regulatory framework in place,	Outlines that the Board will periodically review the guidance to ensure it aligns with any changes to the broader regulatory framework for

	Expiry of compounded parenteral medicines guideline (postponed and not commenced)	Proposed revised guidance titled ***Compounding of parenteral medicines***
	is not specifically mentioned.	compounding of medicines.