Public consultation on the review of guidance on expiry of compounded parenteral medicines – Pharmacy Board of Australia *Guidelines on compounding of medicines*

1 February 2016

Responses to consultation questions

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

Stakeholder Details

If you wish to include background information about your organisation please provide this as a separate word document (not PDF).

Organisation details
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[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.

Your responses to consultation questions on the draft proposed guidance

1. Has the proposed guidance been expressed clearly?	The proposed guidance is not fully clearly as it appears pharmacist can rely upon various texts / options in assigning an expiry date beyond 24hours. There are concerns also regarding the interpretation of external guidelines that are themselves being revised namely the USP NF guidelines, that being said the USP guidelines deal with the assignment of appropriate safe Beyond-Use Dates-in table 8. HOWEVER There is No reference to appropriate batch sizes other that with regard to sterility testing in USP (71) Sterility Tests and sample sizes, the sterility test needs to be referenced clearly in the guidelines. I propose that the USP ND guidelines in particular table 8 and the USP (71) sterility tests are the SOLE reference for extensions of an expiry beyond 24 hours. This protects the public with regard to aseptic compounding failures both from microbial failure as well as stability and process failures. There must be no potential for interpretations of individual references that do not take into account the whole compounding practice. This is important as the basis of the USP guidelines are concerned with the whole process of compounding as well as acceptable practical expiry date assignment. Considering also that the US has seen the bulk of misadventure with regard to mortality and morbidity due to pharmacy compounding failures. The updated USP guidelines are drafted I believe with a view to improving safety in an unambiguous manner, the same level of care should apply to the Australian guidelines in the very least and these should rely solely on the USP guidelines with no potential of interpretation outside of this control.
2. 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?	Yes I believe the concerns raised by stakeholders in particular with regard to cost, access and distance travel times to supply are addressed by the guidelines referencing the updated USP guideline. In essence the requirements of the USP guidelines will create requirements to sterility testing and culture that will slow the release of Aseptically produced parenteral products once sterility testing is complete- the sterility testing will take two weeks to determine whether contaminants have been cultured this effectively provides a real time expiry of between 14-30 days depending upon storage conditions. These effective expiry times will most certainly meet the concerns raised by Compounding stakeholders. There have been incorrect assumptions and submissions that -TGA registered facilities will cost patients more, will not meet the times to deliver and are a prohibitive alternative, this is wrong and potentially puts patients at risk by lowering the standard of vigilance when considering a pharmacy setting and the level of inspection. An increased volume of production at a TGA facility of compounded products will drive the price down and will result in greater volumes with greater infrastructure for delivery to patients both far and wide. The latest Pharmacy guidelines rely upon USP guidelines the USP guidelines in addition to the Australian guidelines must be clearly used as the SOLE guide for the extension of Sterile compounded Parenteral products beyond an expiry of 24 hours there must be no reference or ambiguity

	with respect to alternative texts as this creates potential non adherence, for the reasons already mentioned.
3. Does the revised guidance support patient safety when supplying compounded parenteral (sterile injectable) medicines?	NO the guidelines should include reference to batch sizes of sterile compounded products. This is very important to protect public safety, the use of the USP standard is considered reasonable provided batch sizes are mandated. Compounding Pharmacies should be restricted to batch sizes and mandated conditions with regard to assigning expiry dates in excess of 24 hours. The revised guidelines should state that in accordance with the **USP NF 797 and USP (71) Sterility Tests** an assignment of an expiry date or Beyond-USE Date (BUD) for sterile compounded parenteral products greater than 24 hours must only occur in the following circumstances. 1. Batches of up to 10 Compounded sterile products are produced from a single Sterile starting component in any 24 hour period the assignment of an expiry date is acceptable in accordance with Table 8 BUDs and the storage characteristics of the Compounded Sterile Product (with / without preservative) for products that are not subjected to sterility testing. 2. Where batches greater than 10 Compounded sterile products (CSPs) but no more than 100 CSPs are compounded from a single Sterile starting component in any 24 hour period, the assignment of an expiry date or Before Use Date in excess of 24 hours is predicated upon **completing mandatory microbial sterility testing prior to dispensing** to a patient. The mandatory sterility testing must be conducted in accordance with USP (71) Sterility Tests in particular Table 3. Minimum number of articles to be tested in Relation to the Number of Articles in a Batch, in the case of 100 CSPs a sample size of 10 is mandated. By including a reference batch size quantity, safety concerns regarding patient protection as a result of excessively large batch size production is restricted and clearly mandated . I recommend a mandatory restriction on batch size of any Compounded Sterile Product to no greater than 100 individual products per 24 hours in order to protect patient safety and restrict the current potential for excessive batch production of sterile parenteral products in Compounding Pharmacies. The sterile production in Compounding Pharmacies must be restricted to prevent uncontrolled large batch production when considering more appropriate TGA licensed facilities in terms of manufacturing safety. The batch restriction together with the USP guidelines fully mitigate any Compounding Pharmacy concerns with regard to individual patient needs. A daily production log should also be mandatory to ensure batches are produced in accordance with daily prescriptions, or prescription volume rates.
4. Do you have any suggestions for questions to be included in the Board's FAQ for pharmacists	Why are restrictions in place regarding daily batch sizes of Sterile Compounded Parenteral Products? Pharmacy Regulations allow the compounding of sterile products in a registered pharmacy upon receipt

on the compounding of medicines, to support pharmacists in their understanding and application of this guidance?	and direction of a valid prescription from an authorized prescriber. The guidelines facilitate the production of sterile products in a maximum batch that would reasonably meet daily prescription requirements. Where batches in excess of 10 CSP's and less than 100 CSP's are compounded, mandatory sterility testing and expiry date assignment regulations as stipulated by USP guidelines apply. Batches up to 100 CSP's facilitate the intention of pharmacy regulations to provide compounded sterile parenteral products on a prescription at hand basis.
5. 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?	The mandating of batch sizes of production in any 24 hour period for a particular compounded sterile product covers potential failures of aseptic environment, and limits potentially unsafe large batch production. A compounding pharmacy is not an environment where the regulations are intended to permit large scale batch production, particularly for sterile parenteral products. Mandatory batch size guidance is essential. The compounding of patient specific sterile compounded products is well covered by the proposed current guidelines **provided** the USP guidelines are the mandatory reference with respect to expiry date assignment and extension beyond 24 hours AND there must be mandatory batch sizes for Compounded Sterile Products for parenteral use. I recommend the deletion of any reference to other reference material for potential use when Compounding Pharmacists assign an expiry date in excess of 24 hours. The USP is clear and unambiguous with regard to expiry assignment and these guidelines take into account the whole Compounding production environment, standards of compliance and enforcement as well as the intrinsic pharmaceutical determinants in assigning an expiry date.
6. Do you have any other comments on the proposed guidance?	I believe the public interest must be paramount, the potential for mortality and morbidity is great in the use of sterile compounded parenteral products. The TGA licensed manufacturing facilities are the most appropriate sources of sterile compounded parenteral products. The Pharmacy regulations allow for the compounding of small scale sterile parenteral products but must not be used to facilitate batches produced in quantities that are excessive as associated risks to patient safety are far too great.

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