Tuesday, 2 May 2017

Therapeutic Goods Administration
PO Box 100
Woden ACT 2606

To whom it may concern,

Please find enclosed the ASCEPT comments to the Consultation: The scheduling policy framework and advertising of pharmacist-only medicines (Schedule 3 substances).

ASCEPT is grateful for the opportunity to provide input into the Consultation. Please do not hesitate to contact the ASCEPT Secretariat at secretariat@ascept.org.au for any further information.

With best wishes,

Professor Dominic Geraghty
President
Consultation: The scheduling policy framework and advertising of pharmacist-only medicines (Schedule 3 substances)

ASCEPT is grateful to have the opportunity to provide input to this Consultation. Many of our members have participated in committees and discussions relating to this consultation so we have the perspective of experience and interest.

ASCEPT supports the principles behind the SPF and SUSMP and their role in promoting uniformity across Australian States and Territories in the scheduling and handling of medicines and nonmedicines, including availability, advertising and safe use. This submission is structured around the proposed reform options contained in the document “Consultation: The scheduling policy framework and advertising of pharmacist-only medicines (Schedule 3 substances)”, Version 1.0, March 2017.

Policy recommendations
Governance

1. Split the SPF into a policy document and a guidance handbook.
   No objection

2. Establish an informal working group comprising state and territory representatives, industry, healthcare professionals and consumers to meet as required to provide advice on possible amendments to the SUSMP
   We strongly support this recommendation. This group could provide comment on both formal submissions as well as discussing the implications of new data on existing schedule for medicines and nonmedicines. Such new data may be in the form of Australian-based pharmacovigilance data or publications in the peer reviewed literature. The discussion with the group may prompt further research and a delegate-initiated submission for an amendment to the SUSMP.
   This working group may highlight emerging toxicity data, facilitating rescheduling at an earlier stage. Although the TGA has an existing pharmacovigilance program for medicines (currently under review), attention must also be given to nonmedicines for which there are increasing data regarding risks to humans post-marketing which may prompt a scheduling change. For example, this may have been useful in the case of dextropropoxyphene which has been removed from some international markets due to safety concerns, but not in Australia (Buckley NA, Faunce TA. Trials and tribulations in the removal of dextropropoxyphene from the Australian Register of Therapeutic Goods. Med J Aust. 2013 Aug 19;199(4):257-60).

   As a minimum, health professionals should be involved in such a working group and ASCEPT would welcome the opportunity to nominate members to participate.

Interim decision

3. Amend the Therapeutic Goods Regulations to allow general public consultation on the interim decision and where appropriate, enable the time available for submissions to be extended.
   No objection to allowing general public consultation on interim decisions.

Extending the time available for submissions may be useful on a case-by-case basis in selected circumstances, but with consideration of the clear wish of applicants and other stakeholders for a fast and efficient process for review. Circumstances where this may be useful can be conceived, for example when the delegate’s decision is limited by minimal or low quality data. However, the timeline...
required to generate new data that are of sufficient quality to influence a decision is unlikely to be achieved with a short timeline. Instead, these data should have been anticipated and it is preferred that they are provided by the applicant with the submission.

**Timing of decision**

4. Explore options for establishing a chemicals scheduling delegate in APVMA to streamline scheduling and marketing authorisation considerations.

No concerns if this is anticipated to improve efficiency.

**Tools for better management of rescheduled substances**

5. Create a new Appendix in the Poisons Standard (SUSMP) to enable additional controls or requirements for Schedule 3 substances to be specified, in particular for substances that have been down-scheduled from Schedule 4 (prescription only).

We support this proposal, along the lines described in the consultation document under “Tools for better ‘management’ of rescheduled medicinal substances”.

Currently the SUSMP mentions criteria upon which an S3 medicine can be supplied by a pharmacist, for example based on indication (site of use) or duration (inferring treatment of an acute condition of short duration). The pack size is stated for some S3 listings and we are aware that the rationale for this is to limit their use to treatment of acute conditions with the intention that the patient is referred to a doctor for further assessment for conditions that persist for longer than this. However, this is inferred in the SUSMP rather than specifically stated so it may not be apparent to all pharmacists.

A new Appendix such as described will minimise the potential gap between the conditions of supply that were expected by the committee at the time of the scheduling decision with those groups who currently develop guidelines and training for pharmacists to support its integration into practice.

This new Appendix may have other roles too, for example when a supply should be recorded and whether the supply needs to be reported to another body such as a State Health Department for drugs of dependence or abuse, or to the police for drugs which can be diverted for criminal activity such as pseudoephedrine.

**Business improvements to TGA processes**

**Decision-making principles**

1A. A clearer explanation of the cascading principle and how it is applied should be included in the SPF.

No objection if stakeholders believe that the current explanation in the SPF is not sufficient.

1B. The structure and the content of the Committee’s advice, and the delegate’s reasons should be revised to ensure they are meeting the needs of stakeholders.

Under the current structure the ACMS and ACCS are privileged Committees such that their advice to the delegate is not publicly available. We recommend that this process is continued to maximise engagement of the membership.

ASCEPT is aware that ACCS and ACMS use a structured approach to review and consider submissions (principles are detailed in the SPF) and that the appropriateness of this is being reviewed as part of this consultation. We support the use of a structured approach to support a risk-benefit assessment.
such as the publication by Brass et al. (2011) for nonprescription medicines outlined in the consultation document.

We also acknowledge the concerns if such tools are rigidly applied. It is possible that rescheduling decisions will be challenged if the risk:benefit assessment is considered incomplete. Although this places an onus on the applicant to provide complete data which is likely to be useful, this will mostly apply to downscheduling. However, it may compromise delegate-initiated submissions for the purpose of upscheduling, particularly in the case of nonmedicines following emerging safety concerns, even if they are relatively limited in number. An example of the latter is pesticides and other chemicals which are shown to be extremely toxic following acute overdose.

Further exploration of tools for the scheduling of nonmedicines is also recommended. Although the current criteria are quite explicit in some respects (eg. the LD50 criteria), other toxicity criteria are less well defined other than by concept (eg. ascertainment of skin sensitisation, organ toxicity). Further, at the time of scheduling these are all largely based on animal data, and there is no specific mention of data on human toxicity because this is unlikely to be available at the time of the initial application. However, as mentioned above, this information will become available with time, especially for the more toxic substances such as pesticides. This prompts the need for a mechanism by which these data can be incorporated into regulatory decisions and a positive step forward in this regard is the informal meetings mentioned above (policy recommendation 2).

The delegate’s decisions and justification are publicly available so it is reasonable to review the structure of this advice to ensure it contains sufficient content to satisfy the requirements of the applicant and other stakeholders. Indeed, this could be useful in circumstances of an incomplete or inappropriate application to highlight the extent to which such shortcomings influenced the decision. We are not aware of concerns raised with the explanatory content of the delegate’s decision (separate to the decision itself). Instead, much of the criticisms that we are aware of regarding decisions relates to stakeholders either not agreeing with the decision (eg. Codeine) or not understanding that the importance of the specific application on the delegate’s decision (eg. Nicotine).

Transparency
2A A public summary should be provided by the applicant that will be published as part of the public consultation process.
We strongly support this recommendation. This will also assist stakeholders to understand the context of the decision of the delegate.

2B Develop a mechanism to alert stakeholders of items being considered for re-scheduling.
We support processes that alert stakeholders to items being rescheduled. The existing process for alerting stakeholders involves an announcement on the TGA website and an email to subscribing individuals and organisations. Further dissemination of this relies on a stakeholder to be proactive, or following dissemination from an organisation or similar group and word of mouth (including the media) to alert others.

From the perspective of health care professionals and scientists, we are aware that relevant organisations who subscribe to these alerts do consult amongst their membership and other relevant parties.
2C Develop communication milestones and application tracking to improve communication between the scheduling secretariat and applicants.
No objection.

Risk:benefit value tree
3 When updating the SPF guidance, consider how greater emphasis can be placed on potential benefits as well as risks for substances proposed for rescheduling.

We have no objection to this principle and it is consistent with the above-mentioned discussion around the content of the submission, its consideration by the Committee and the structure and content of the delegate’s decision. We feel that public safety must remain a key consideration. However, it is anticipated that sponsors and the ACCS and ACMS will always be interested in the benefits of rescheduling (whether up or down). It is expected that the benefits of rescheduling will be clearly articulated in the submission by the applicant along with the new information about the new risks.

Of note, this principle applies to both upscheduling and downscheduling of medicines and nonmedicines. For example, as mentioned above, new information about the toxicity of a pesticide may warrant upscheduling to ensure that use is carefully controlled, which will have health benefits even if these offset the benefits of easier access to a wider proportion of the population. Recent examples where this appears to have been successfully applied in the case of medicines includes alprazolam and codeine. There are also cases where this has been successfully applied to nonmedicines overseas, including the pesticides endosulfan, dimethoate and paraquat.

Interim Decision
4 Include an explanation in the SPF of the legislative nature of scheduling decisions and why they are not appealable.
No objection, we agree that this would be useful.

Timing of decision
5A Include an explanation in the SPF of the jurisdictional requirements for decisions to enhance stakeholder understanding.
No objection.

5B Identify an early alert mechanism to ensure the initial applicant, the jurisdictions, and stakeholder groups have the maximum time available for activities associated with a decision.
In principle, no objection to the concept that stakeholders are notified of a decision at the earliest opportunity. Presumably, the content of this early alert would be the same as that of other alerts and notifications. In which case, if the decision-making process is working efficiently and stakeholders are notified is made soon after this decision is finalised (which is both posted on the website and emailed to interested parties which includes the applicant and those who made a submission) then it is not clear what would be achieved by an “early alert mechanism” compared to the usual alert mechanism.

5C Develop a mechanism to allow early information sharing between the APVMA and the Secretariat to screen and manage chemicals applications.
No objection

Improving the clarity of the SPF
6. **Incorporate a number of changes to the SPF identified during collaboration with jurisdictions to improve the clarity and usability of the SPF.**

No concerns with those listed in the consultation document (Business Improvement Measures 6).

**Ongoing improvements and development of guidance materials**

**Decision-making principles**

1. **Undertake a trial to assess the value of applicants presenting to the advisory committees**

No objection, but an overarching principle is that new information must not be submitted, the presentations are limited in time and conflicts/declarations of interest are defined. It may provide an opportunity for questions to be answered at a relevant time and also to reassure the applicant that their perspective has been heard and considered by the advisory committees.

**Risk:benefit value tree**

2. **Prepare worked examples of the risk:benefit tree for recent scheduling considerations and determine if there is utility for using as part of scheduling applications.**

This would first require ascertainment of an appropriate risk:benefit decision tool, which has not yet been confirmed to our knowledge. Indeed, different approaches for conducting a risk:benefit assessment could be tested using recent decisions with medicines and nonmedicines, and this would be useful for self-reflection by the committees and Departments.

**Proactive consideration of candidate substances for rescheduling**

3. **Implement a system for proactively identifying substances for rescheduling.**

ASCEPT fully supports this principle. Here, substances for which there may be a potential benefit from rescheduling would be referred to the informal group mentioned above (policy recommendation 2) for further consideration and review to determine whether it should be formally considered by an advisory committee. The current system for minimising risk of medicines that have been found to be more toxic than initially thought largely depends on the company voluntarily withdrawing it. This has largely occurred with medicines, but appears to be uncommon with nonmedicines.

Consideration of post-marketing human toxicology data which provide new information on the potential risk to humans and may prompt additional controls, for example an upscheduling. This is necessary due to limitations in pre-clinical (animal) models for risk assessment in human toxicology, in particular following deliberate self-poisoning. Differences between humans and animals may relate to the mechanism of action, or coformulants which have synergistic toxicity that was not identified as toxic by pre-clinical models. This has been discussed above in part with Business Improvements 3. ASCEPT would welcome the opportunity to nominate members to participate.

**Parallel processes**

4A. **Develop a possible mechanism for aligning prescription to OTC medicine rescheduling applications with applications to TGA for market authorisation of products containing the potentially rescheduled substances at OTC medicines.**

No objection so long as public health and safety remain a priority in the decision-making.

4B. **Consider options for market incentives for down-scheduling.**

No objection so long as public health and safety remain a priority in the decision-making.

**Advertising of pharmacist only (Schedule 3) medicines**

Advertising Schedule 3 medicines

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ASCEPT is the professional and independent society in Australia and New Zealand with expertise in the use and toxicity of medicines and chemicals

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1 Develop and consult on options for reforming pharmacist-only medicines (Schedule 3 substance) advertising requirements.
No concerns with reviewing the current approach. We note that further consultation is planned regarding the preferred approach from the various options listed in the consultation document. The implications for the moving from a ‘positive’ to ‘negative’ list in Appendix H is not immediately apparent, if the ability to advertise each S3 entry is already considered by the committee. A non-rigid structured approach to support the committee making this decision is likely to be useful.