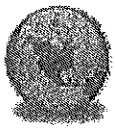
Benzodiazepines



[redacted]

To TGA

The proposal to reschedule of benzodiazepines to S8 medications.

I am accredited pharmacist working in aged aged, and consider the implications for high care facilities particularly would have major consequences on staffing levels as RN required for drug checks and also administration times.
Many low care facilities pack S8 medications in multipacks now and so implications would be minimal. But issues of PRN use becomes an issue and care staff would not be able to administer.

A regular review of benzodiazepines is always followed up with medication reviews performed annually and do consider the use is minimal in my aged care facilities.

I have just completed a short time working in retail pharmacy in local country town for 2 weeks and minimal Temaze was dispensed and occasional Diazepam, usually for associated anxiety. What actual benefit would there be for rescheduling ?
Many pharmacies do not have storage space in safe !

Pharmaceutical Services NSW are unaware of this proposal and consider more consultation required.

Suggest further discussion and explanation and the implications are huge, and feel this has not been publicised for all parties to comment in appropriate time.

Regards

[redacted]

[redacted]

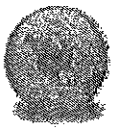
[redacted]

[redacted]

[redacted]

15/05/2013

Benzodiazepines



[redacted]

to whom it may concern

re proposal to change benzodiazepines from schedule 4 to schedule 8 will cause a big headache not only for pharmacy it will cause a big headache for gps and aged care facilities.

this would mean that all benzodiazepines would need to be locked up in a safe so bigger safes will be required in pharmacy and in aged care facilities. in pharmacy it will mean that all benzodiazepines will need to be recorded and every tablet accounted for in the same way as other schedule 8 medications.
this will also mean in aged care facilities that all benzodiazepines will need to be recorded and they will require greater time in administering the medication to the residents and that additional staff would be required over the shift to help with counter signing
the benzodiazepines then cannot be packed in the usual dose administration aids with the regular medications they will have to be packed separately
also for gp's they will have to write prescriptions with limited quantities and there will also be an increase in forged prescriptions to counteract demand and supply.
i dont think that it would be a good idea to change benzodiazepines from schedule 4 to schedule 8
thanks

[redacted]

To the scheduling secretariat, 7th December, 2012

Re. Public Submissions regarding proposed changes to benzodiazepine (BZDP) scheduling from s4 to s8

The increasingly concerning over use of BZDP's, in particular, Alprazolam, has seen a number of BZDP related hospital presentations in recent months. Major complications of acute withdrawal include delirium and seizure, and we've seen numerous post-ictal presentations to our emergency department amongst BZDP abusers. We've seen a number of patients requiring treatment in intensive care for acute symptoms related to BZDP withdrawal, have been involved with in patient management of acute BZDP dependence and there have recently been deaths in patients of which Alprazolam was attributable.

NSW health clinical guidelines recommend out patient management on diazepam for BZDP dependant patients post a period of in patient stabilisation at a specialised withdrawal facility, with titrations then at 2.5-5mg / week; the out pt reduction regimes generally take 3-6 months, and "*the experience of most clinicians is that few patients comply with treatment, and most continue to seek and obtain additional BZDP's*" (NSW drug and alcohol withdrawal clinical practice guidelines, 2008).

There has therefore been a strong push between myself and my colleagues to have the supply of BZDP's, in particular Alprazolam, more heavily restricted, and I fully support the rescheduling of same to s8.

[redacted]

NSW GOVERNMENT Health
South Western Sydney
Local Health District

Webstercare®
webstercare.com.au

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Facsimile: 02 6289 2650

Wednesday, 16 January 2013

Submission:

Benzodiazepines **Proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8.**

Thank you for the opportunity to present the following comments on the proposal to reschedule the benzodiazepine class of medicines from Schedule 4 to Schedule 8.

As an overview, I have concerns about the impact of the proposed changes in a number of key areas.

I have no objection to taking steps to reduce the possibility of diversion. However I do believe that rescheduling to Schedule 8 is not the only solution or even the best solution, and will come at significant cost and inconvenience to legitimate users. I have detailed my reasons below, I have separated out my concerns into categories to represent the potential impact on stakeholders.

1. Community Pharmacist:
   - Our pharmacy services a number of age care facilities in Sydney and currently manages 12 schedule 8 substances. This proposal will add an additional 12, rescheduling benzodiazepines from Schedule 4 to Schedule 8 will double the administrative and management load on our Pharmacists.
   - The proposed changes will increase administration tasks and cost for the community Pharmacist. Changes to the Schedule, does not take into account education of the consumer, Doctor and Pharmacist. Increased education demands will impact on pharmacy workflow. Pharmacists and Doctors will require additional training to counsel consumers appropriately.

MANREX® PTY LTD T/AS WEBSTERCARE® ABN: 63 074 288 088 17-19 Moore St Leichhardt NSW 2040 I Postal: Locked Bag 9, Five Dock NSW 2046
Phone: (02) 9563 4900 I Freecall: 1800 244 358 I Fax: (02) 9563 4955 I Freefax: 1800 626 739 I Email: info@webstercare.com.au

- Increased documentation, recording and monitoring requirements of Schedule 8 medications will significantly impact on the management burden for Pharmacists with significant additional administrative cost.
- The increased storage requirements will impact on dispensary layout and workflow. Existing Schedule 8 storage space will be inadequate. If benzodiazepines are rescheduled as Schedule 8 most Pharmacists will need to double, if not triple, their DD cupboard capacity. In my pharmacy at Leichhardt we will need to triple our investment and storage capacity in high security DD safes. As an example, my pharmacy services 1500 residential aged care clients, temazepam currently takes up 1 square metre of shelf space, these drugs will have to be locked in a DD safe.
- The PBS dispensed quantities for benzodiazepines are typically small, for example temazepam 10mg tablet pack size is 25 which is insufficient to last 1 month. There will be increased pressures for a Pharmacist to have to assist the consumer in obtaining prescriptions from the GP, especially when ensuring continued supply for residential aged care residents.
- I am concerned that when supply is initially restricted the Pharmacists and staff in my pharmacies will have increased vulnerability to criminal activity such as break-ins and hold-ups. Reduced illicit market accessibility of benzodiazepines may increase the street value making pharmacies more attractive targets.

2. Residential Aged Care Facility:
   - Current guidelines such as *Guiding Principles for Medication Management in Aged Care Facilities 2012* identify Schedule 8 medicines as high risk medicines. High risk medications require increased monitoring. Rescheduling of regular benzodiazepines will increase the administration and management burden for RACF nursing staff.
   - Most residential aged care facilities (RACF) mandate a Form 9 register of Schedule 8 Drugs in their policies and procedures in line with best practice guidelines. The Drug register requires two signatures completed as the dose is prepared and signed off when the dose has been administered. This is a time consuming process. Typically medications are administered around meals times with a limited window of opportunity to complete the medication round. Any additional work load will either mean increasing the round time or nurses being forced to rush to complete the round on time.
   - In the majority of RACFs an RN is required to administer S8 medications - especially PRN medications. This generally also means that a co-signature is necessary. Changes to the schedule will mean extra staff will be required to be there when medication is administered. It would impact on their staffing mix, and re-training costs could be

significant. Treatment may be delayed whist a second signatory is found. I have no doubt in some cases where a second person is not available, especially at night time, the medication will not be administered.

- Much like pharmacies, RACFs who store medications in DD cupboards will require additional storage space and staff time to manage DD record books.
- Rescheduling of midazolam and clonazepam may impact on the quality of palliative care.
- In the current Director General's "List of Emergency Medications in RACFs" there is no provision for midazolam and clonazepam, essential at end of life, for stock to be held in a nursing home.

3. Consumer:
   - We must not forget that benzodiazepine therapy does have an evidence based role in the treatment of disease states. Consideration must be given to consumers who have been prescribed these medicines for legitimate purposes such as panic attacks, alcohol withdrawal or epilepsy.
   - Schedule changes may increase the risk of disruption in continuity of supply of benzodiazepines. This may potentially lead to inadvertent withdrawal of medication.
   - Some consumers in rural and regional areas already experience difficulty in obtaining Doctor appointments for ongoing treatment and may find sourcing regular supply of medication challenging.
   - Doctors already face an administrative burden when servicing patients in RACF's. It is difficult enough to get Doctors to visit without adding another burden.
   - The new National Residential Medication Chart that is designed to improve access to PBS medication excludes Schedule 8 medication which must be written on a separate chart and hand written on a separate prescription. Removing the benzodiazepine medication from Schedule 4 will impact on efficiency and effectiveness of this long awaited initiative.
   - The cost of and access to alternative treatment, is often prohibitive especially in rural and regional areas.
   - Consumers who have been prescribed a benzodiazepine may become concerned their medication is addictive and dangerous, and therefore be reluctant to take it. We know some patients feel a stigma when prescribed a pain reliever knowing the drug is considered addictive.

Webstercare®
webstercare.com.au

4. Doctor:
   - There will be additional burdens for GPs when writing prescriptions for regular supply of benzodiazepines as a Schedule 8 medicine prescription has additional requirements.
   - Additional resources will need to be allocated to ensure the availability of non-drug treatments such as psychotherapy or cognitive behavioural therapy. For benzodiazepine restriction to be successful, GPs will need access to additional resources to manage their patients. Currently the accessibility and costs of non-drug therapy is prohibitive or simply unavailable in some areas of Australia.
   - In NSW a Doctor cannot, without authority, prescribe a schedule 8 (type B) medication for continuous therapeutic use by a person for a period exceeding 2 months (*section 28 NSW Poisons and Therapeutic Goods Act 1966 No31*). This will again become an additional burden.
   - Doctors will be tempted to prescribe medication to circumvent the inconvenience of the Schedule 8 prescribing process therefore resorting to less effective and appropriate alternatives.
5. Government and Community:
   - Increased costs to PBS of Schedule 8 payments. There is no monitoring of private prescriptions. The full impact of the changes to supply will not be known. It is reasonable to assume benzodiazepine drugs are prescribed on 'private' prescription in large quantity but not in a RACF. It is possible for Pharmacists to report online benzodiazepine dispensing via their computer software which would soon identify situations of over use.
   - Increased costs for additional and longer prescriber visits. Doctors will require additional resources and training to treat patients who are currently using benzodiazepines.
   - The abrupt withdrawal of a benzodiazepine can have serious consequences and be very traumatic for a patient.
   - Inadequate support and resourcing of alternative therapies. Consumers in rural and regional areas have difficulty accessing psychotherapy and Cognitive Behavioural Therapy (CBT).

Webstercare®
webstercare.com.au

As I have stated, I support measures to address the abuse and misuse of benzodiazepines, I do feel however that rescheduling is neither the right answer, nor the only answer.

To be truly effective the proposed changes would need to be supported by extensively improved access to alternative treatments such as psychotherapy and CBT to support addiction and abuse. Rural and remote access to these services needs to be addressed. Consideration needs to be given to the increased management burdens for Pharmacists, Doctors and RACF staff and the impact on vulnerable residents in RACF's. Additional training and resources will need to be provided.

An alternative solution may be to consider developing a program similar to "Project Stop" which has proven highly successful in reducing pseudoephedrine abuse in the community. Additional funding of alternative programs in aged care such as the use of National Prescriber Service Drug Use Evaluation Kits to promote non-medication solutions for insomnia.

Consideration needs to be given as to how the scheme will be monitored and what outcomes are expected. I feel that before these changes are finalised there needs to be a study of prescribing habits and consumer use. I do believe there are other options before rescheduling is decided upon as the only option. I am sure there are unexpected consequences that cannot be ignored, that will significantly impact on patient care in RACF's.

Again, thank you for the opportunity to provide my view on this proposal and I hope these comments will be taken into account when the TGA committee considers the proposed changes to benzodiazepine rescheduling.

[redacted]

MANREX® PTY LTD T/AS WEBSTERCARE® ABN: 63 074 388 088 17-19 Moore St Leichhardt NSW 2040 I Postal: Locked Bag 9, Five Dock NSW 2046
Phone: (02) 9563 4900 I Freecall: 1800 244 358 I Fax: (02) 9563 4955 I Freefax: 1800 626 739 I Email: info@webstercare.com.au

Benzodiazepines

[redacted]

Thank you for the opportunity to allow me to make a public submission.

As stated in my earlier email, I work as a community pharmacist and can tell from first-hand experience that benzodiazepines (especially alprazolam) are very commonly abused drugs.
That is why I generally welcome the re-scheduling of benzodiazepines, however in my opinion this would only insufficiently reduce the accessibility of benzodiazepines for abuse. Patients that recreationally use benzodiazepines and other prescription drugs are quite creative in obtaining the desired drugs and would still be able to get large quantities of them (e.g. prescriptions from different doctors - 'doctor-shopping').

I personally believe that only a centralized monitoring program for drugs of addiction (benzodiazepines, opioids,...) would be powerful enough to curb the abuse of those medications. Doctors could still readily prescribe benzodiazepines, however the risk of double prescribing would be severely reduced. Patients that do abuse the drugs could be recognized and appropriate help could be offered. Also private prescriptions could then be detected and included in the database.

I am aware that this would be a very cost intensive approach since the whole program would need to be set up from scratch. I do however also believe that the financial benefit from the PBS savings would partly cover the running cost of such a program. And it is needless to say that it would greatly reduce the amount of drugs available on the streets.
These factors might make it worth to at least look into that option. Then it could be decided if a central database would be a viable option.

Again, I appreciate the opportunity to raise my concern and hope that I have given you some insight from a community pharmacist's view.
I am pleased that the Department of Health recognizes the abuse problem of benzodiazepines and acts upon it. Hopefully your decision will help to reduce the abuse of those drugs.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

15/05/2013

Benzodiazepines

[redacted]

[redacted] or Madam,

I am writing to you in regards to the schedule status of alprazolam (Xanax).
Working as a community pharmacist I have realised that most prescriptions for alprazolam are indeed not for therapeutic use but are rather taken for recreational use or sold on the street for that matter.
The pharmacy I work in has a large group of CPOP clients (also known as 'methadone clients') and I can tell you from my personal experiences that alprazolam is by far the most commonly and most preferably abused benzodiazepine amongst drug users.
I have heard rumours that alprazolam is currently considered to be re-scheduled, but so far no official channel could comment on the matter.
This is why I would like to ask if there has ever been any consideration to re-schedule alprazolam to Schedule 8?

I am looking forward to hearing from you and meanwhile wish you a merry Xmas!

[redacted]

Benzodiazepines

[redacted]

2 Attachments

image001.jpg image003.jpg

To Whom It May Concern,

I am submitting our views & concerns in response to the proposal to re-schedule certain medications, including benzodiazepines from Schedule 4 to Schedule 8 as a public notice was issued by DoHA – TGA on 29 Novemeber 2012 inviting for submissions. I work in the aged care industry for around 20 years in management.

Please take our views and concerns (as below) into consideration when you meet in March 2013 to consider the above matter to come to a conclusion.

Potential issues for RACF of the proposed re-scheduling

1. **Storage**

   - If rescheduled to S8, some high care facilities may have inadequate storage space in S8 cupboards.

2. **Workload**

   - Likely increased work hours required for recording receipt and administration in the S 8 register. Requesting recognition of this increased workload by ACFI may be appropriate to ensure resident care is not compromised as RN's will be required to spend significantly more time in the recording process.

   - Likely increase in workload required to assist withdrawal of benzodiazepines in some residents, and to manage non-drug strategies for promoting sleep.

3. **Continuity of supply**

   - Supply of benzodiazepines to residents may be interrupted with potential for withdrawal symptoms if prescriptions are not promptly provided to supplying pharmacies as legally required for S8's to be dispensed. This may increase the workload also for GP's and supplying pharmacies.

4. **Low Care facilities**

   - While low care facilities are not legally required to record S8 drugs, best practice guidelines and we recommend recording of regular non-blister packed S8 drugs and all PRN S8 drugs. As many benzodiazepines are prescribed on a PRN basis, there may be

significant impact on low care facilities in order to continue to follow recommended best practice guidelines.

5. Alternate agents

- Prescribing alternate agents with sedative effects (eg antipsychotics, antidepressants, sedating antihistamines) for residents with insomnia may be inappropriate and also associated with potentially harmful adverse effects. In addition, we note the proposed rescheduling at this stage does not include the non-benzodiazepine hypnotic agents or 'z' drugs, namely Zolpidem (Stilnox) and Zopiclone (Imovane) which may be increasingly prescribed if they remain S4 but have similar risks and adverse effects as the benzodiazepines.

Thank you for your consideration.

Regards,

[redacted]

[redacted] Please consider the environment before printing this email

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra, ACT 2601

17 January 2013

Dear Sir/Madam,

Regulation 42ZCZK of the Therapeutic Goods Regulations 1990 – Proposal to amend benzodiazepines from Schedule 4 to 8

We write as both experienced health professionals with significant research experience in the area of pharmaceutical drugs and related harms. I (A. Rintoul) am a Doctor of Public Health Candidate at Monash University. Over the past three years I have conducted studies on trends in prescription drug supply and detection deaths in Victoria, with a particular focus on populations who use opioids. My colleague (Dr S Nielsen) is a pharmacist and current NHMRC Research Fellow has focused her research for the past 10 years on pharmaceutical drugs including benzodiazepine related harms. It is with this experience that we write to support the proposal to move benzodiazepines from Schedule 4 to Schedule 8.

Firstly, Schedule 8 is reserved for classes of drugs that have potential to cause addiction, there is clear evidence in the medical and scientific literature that demonstrates the addictive potential of benzodiazepines.

Clinical guidelines recommend if a pharmaceutical treatment is indicated, benzodiazepines should only be prescribed for short term use. Current prescription volume data suggests a disconnect between prescribing practices and clinical guidelines, particularly in relation to alprazolam (see **Appendix 2**). Moving benzodiazepines to Schedule 8 would be a relatively simple and effective mechanism to support improved quality in the supply of benzodiazepines due to the additional scrutiny provided to drugs in this schedule. A Schedule 8 classification would encourage clinicians to hesitate before writing a benzodiazepine prescription. This move could also function as a reminder that there is no evidence of the effectiveness of long term use of benzodiazepines in the treatment of anxiety.

Opioid dependent people are a population already at risk of drug toxicity. One study found use of a benzodiazepine within 12 hours of using heroin resulted in a 28 fold increase in risk of overdose when compared with instances where benzodiazepines were not used [1]. Despite this risk, the use of benzodiazepines by opioid-dependent people is known to be widespread. The 2011 Victorian Illicit Drug Reporting System (IDRS), a sentinel survey of people who inject drugs (PWID), reported 92% lifetime and 71% recent use (in the past 6 months) among PWID [2]. PWID use benzodiazepines for a number of reasons; to manage anxiety, manage withdrawal symptoms or to enhance the intoxicating effects of heroin or other opioids [3].

We recently conducted research investigating trends in the detection of benzodiazepines in heroin related deaths (HRD) in Victoria over the period 1990-2010, with a particular focus on alprazolam [4]. Over this 21 year period, at least one benzodiazepine was detected in over half (54%) of all

HRD, however the highest proportion detected was in the most recent year of our study with over three quarters of these deaths (78%) involving at least one benzodiazepine (see **Table 1** and **Figure 1**). Similarly, in a study investigating drug toxicity deaths involving oxycodone in Victoria in the decade to 2010, we found 75% of all oxycodone involved drug toxicity deaths involved at least one benzodiazepine, with an increasing share of these deaths involving alprazolam (*forthcoming, unpublished data relating to this study [5]*).

However, not all benzodiazepines are alike. Alprazolam is increasingly reported to be associated with disproportionate level of harm including poor physical health [6], amnesia, traffic injuries, violent crime, and theft [7, 8]. In Australia, alprazolam is approved for short term treatment of panic disorder, but only as a second line option because of concerns about tolerance, dependence and misuse. Alprazolam has a rapid onset and offset of action and is more potent than other benzodiazepines [9]. In a study examining alprazolam and its relationship with crime, a consistent and concerning theme was the use of alprazolam being associated with serious and often uncharacteristic crime, in addition to its common link with minor crimes and other harms [10] (**see Appendix 4**).

Despite being a second line treatment, alprazolam is increasingly prescribed. In Victoria the base supply of alprazolam increased 1,432% between 1990 and 2010 [4]. Of particular concern, was the increase in supply of the 2mg dose formulation - the strongest dose available (see **Appendix 2, Figure 2**). Reasons for the increase in supply of the 2mg formulation are not clear from our study, but this does indicate potentially inappropriate prescribing.

The increase in base supply of alprazolam is occurring despite evidence that it is not more effective than other benzodiazepines in the treatment of panic disorder [9]. It is also occurring in a context of converging evidence of harms at the population level. For instance, our study that investigated trends in the detection of alprazolam in HRD showed a strong and statistically significant, linear relationship between supply and detection of alprazolam in HRD [4]. While this study does not suggest causation between increasing community supply and increased detection in HRD, it does indicate a concerning trend in alprazolam use amongst a population already vulnerable to drug toxicity. Combining the use of opioids and benzodiazepines increases the risk of overdose, but as alprazolam is known to be relatively more toxic in overdose than other benzodiazepines [11] this is of particular concern.

We did not seek to determine the source of the alprazolam for the deceased in this study, but the IDRS report that a large proportion of PWID obtain alprazolam from diverted sources. However, ultimately the supply chain starts with prescribers, and therefore moving alprazolam and other benzodiazepines to schedule 8 would be a useful way to improve the quality of supply of benzodiazepines in the community.

There are useful precedents that demonstrate the success in restricting supply of benzodiazepines (see **Appendix 3**). In 1993, flunitrazepam was moved to Schedule 8 after concerns including a high detection rate in HRD and the role of flunitrazepam in facilitating rape. **Figure 3** shows the relationship between the reduced supply of flunitrazepam and decreased detection in HRD. Similarly, the popularity of temazepam gel cap injection among PWID in the late 1990s and 2000 resulted in serious injection wounds among this population. As a consequence, temazepam gel caps became authority required in May 2002 and were ultimately withdrawn by the manufacturer, Sigma, in 2004. **Figure 4** shows the decline in temazepam supply at the time of these changes, and a corresponding decrease in HRD.

Rescheduling all benzodiazepines to schedule 8 would better reflect the addictive potential of these drugs, that have no evidence of medical benefit beyond short term use. However, if the committee decides not to reclassify the entire class of benzodiazepines, there is evidence of benefit in selectively rescheduling problematic benzodiazepines as demonstrated by the success of reducing the detection of flunitrazepam and temazepam in HRD.

In conclusion, there would be considerable public health benefits in moving benzodiazepines from Schedule 4 to Schedule 8 and we strongly support the proposal for the rescheduling of these drugs. In the event that rescheduling all benzodiazepines is not supported by the committee, we would at the very least strongly encourage selective rescheduling of alprazolam which has become particularly problematic over the past several years.

Sincerely,

References

1. Dietze, P., et al., *Transient changes in behaviour lead to heroin overdose: results from a case-crossover study of non-fatal overdose.* Addiction, 2005. **100**(5): p. 636-642.
2. Kirwan, A., P. Dietze, and B. Lloyd, *Victorian Drug Trends 2011: Findings from the Illicit Drug Reporting System (IDRS)*, in *Australian Drug Trends Series No. 76*, National Drug and Alcohol Research Centre, Editor 2011, The Macfarlane Burnet Institute for Medical Research and Public Health & Turning Point Alcohol and Drug Centre,: Melbourne
3. Jones, J.D., S. Mogali, and S.D. Comer, *Polydrug abuse: A review of opioid and benzodiazepine combination use.* Drug and Alcohol Dependence, 2012. **125**: p. 8-18.
4. Rintoul, A.C., et al., *Recent increase in detection of alprazolam in Victorian heroin-related deaths* Med J Aust, 2013 **(in press)**.
5. Rintoul, A.C., et al., *Increasing deaths involving oxycodone, Victoria, Australia, 2000–09.* Injury Prevention, 2011. **17**(4): p. 254-259.
6. Horyniak, D., et al., *The use of alprazolam by people who inject drugs in Melbourne, Australia.* Drug Alcohol Rev, 2012. **31**(4): p. 585-90.

7. Drugs and Crime Prevention Committee, *Inquiry into the misuse/abuse of benzodiazepines and other forms of pharmaceutical drugs in Victoria* 2007, Parliament of Victoria Melbourne.
8. Loxley, W., *Benzodiazepine use and harms among police detainees in Australia.* Trends and Issues in Crime and Criminal Justice, 2007(336).
9. Moylan, S., et al., *The efficacy and safety of alprazolam versus other benzodiazepines in the treatment of panic disorder.* J Clin Psychopharmacol, 2011. **31**(5): p. 647-52.
10. Jones, K., et al., *'A Pinch in Every Bottle': Expert Perspectives of Alprazolam Use and its relationship to offending. Poster Presentation, Australasian Professional Society on Alcohol and other Drugs Conference; November 13-16th 2011; Hobart, Australia.* 2011.
11. Isbister, G.K., et al., *Alprazolam is relatively more toxic than other benzodiazepines in overdose.* British Journal of Clinical Pharmacology, 2004. **58**(1): p. 88-95.

Appendix 1

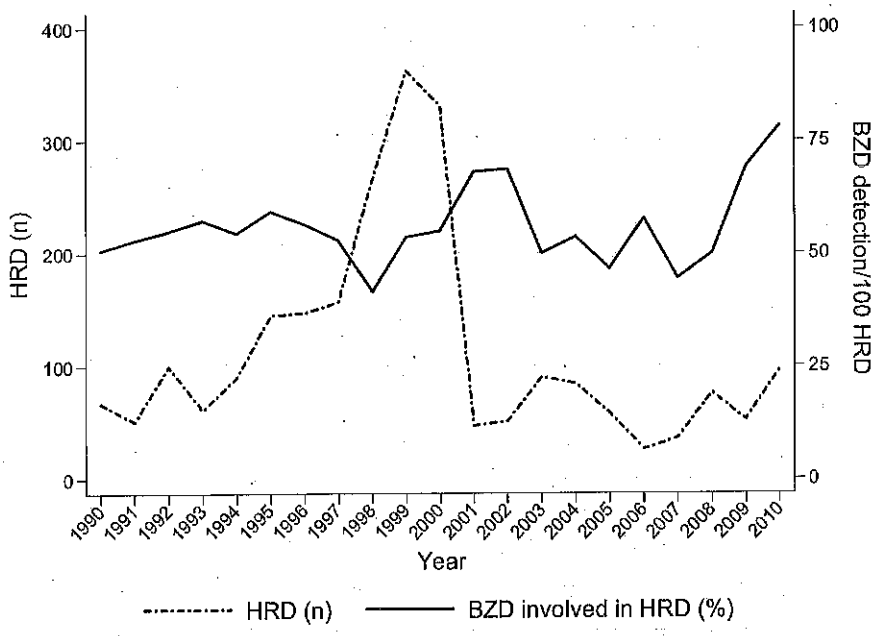
Table 1: Victorian heroin related deaths and detection of benzodiazepines from 1990 – 2010* - 78% of all Victorian HRD in 2010 involved at least one benzodiazepines

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Total no. HRD deaths	67	51	100	61	90	145	147	157	265	362	331	47	51	90	84	58	26	36	76	51	96
Total no. HRD where BZD detected	34	27	55	35	49	86	83	83	110	194	182	32	35	45	45	27	15	16	38	35	75
HRD involving a BZD (%)	50.7	52.9	55.0	57.4	54.4	59.3	56.5	52.9	41.5	53.6	55.0	68.1	68.6	50.0	53.6	46.6	57.7	44.4	50.0	68.6	78.1
Diazepam	19	10	29	17	33	55	54	57	90	160	152	26	26	36	37	24	13	15	31	20	46
Alprazolam	0	0	0	0	0	0	2	1	3	7	4	0	2	4	2	3	3	6	13	18	27
Oxazepam	15	7	13	8	14	16	14	19	16	35	23	5	3	6	8	1	2	2	3	4	10
Clonazepam	2	2	4	0	4	10	5	6	4	6	4	2	2	3	2	1	0	0	0	2	10
Temazepam	0	1	3	3	5	12	7	7	3	23	23	9	6	6	1	1	1	1	3	4	3
Flunitrazepam	16	11	25	10	8	16	22	12	9	1	1	0	1	0	0	0	0	0	0	1	0
Nitrazepam	1	2	0	2	2	4	5	2	9	24	16	1	6	0	2	0	0	1	1	0	2
Lorazepam	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Flurazepam	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0

* more than one benzodiazepine may have been detected meaning columns may sum > 100 %

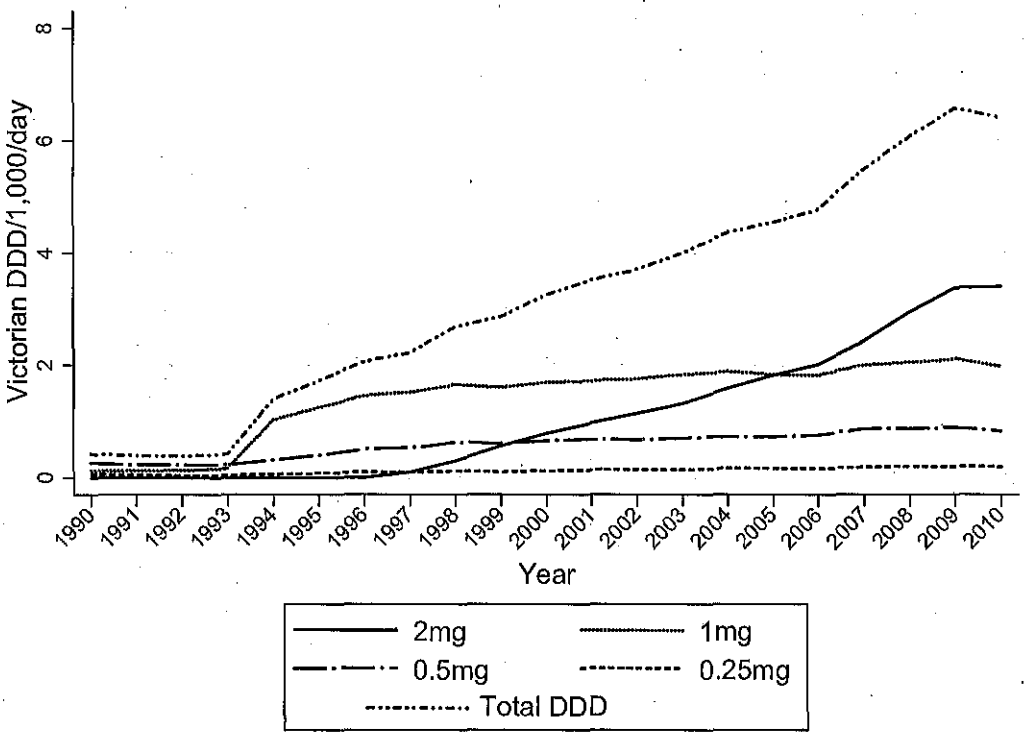
Benzodiazepines

Figure 1: Trends in HRD and the detection of benzodiazepines in HRD, Victoria 1990-2010



Appendix 2: Alprazolam base supply has increased 1,426% since 1990*, the 2mg formulation has increase disproportionately

Figure 2: Defined daily dose of alprazolam by dose formulation, Victoria 1990-2010



*Forthcoming article can be supplied upon request for detail on how Victorian DDD was calculated
Rintoul, A.C., et al., *Recent increase in detection of alprazolam in Victorian heroin-related deaths* Med J Aust, 2013 **(in press)**.

Appendix 3: Success in rescheduling problematic benzodiazepines, Victoria 1990-2010
Figure 3: When flunitrazepam was moved to Schedule 8 in 1993, detection in heroin related deaths rapidly decreased

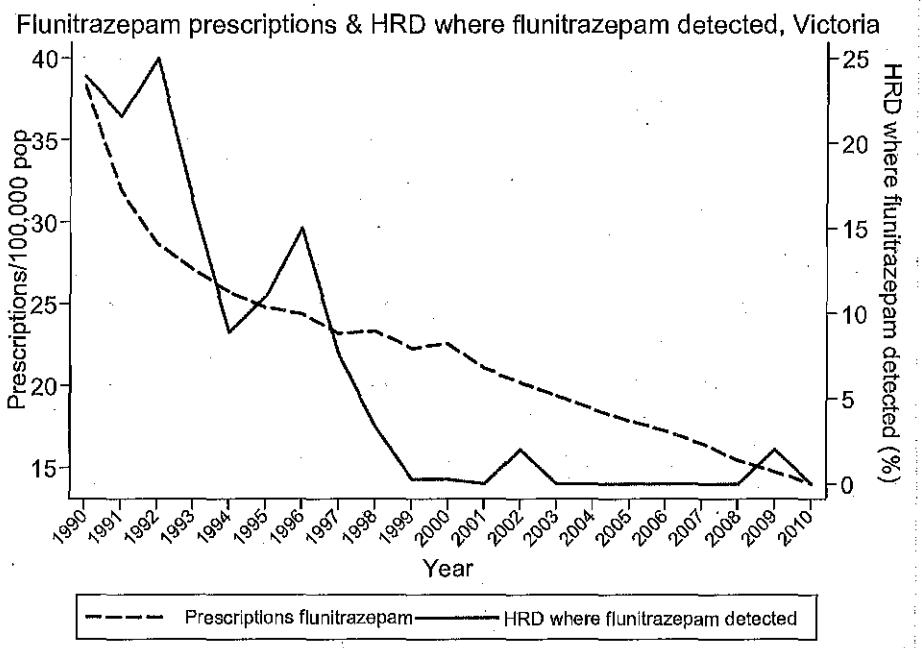
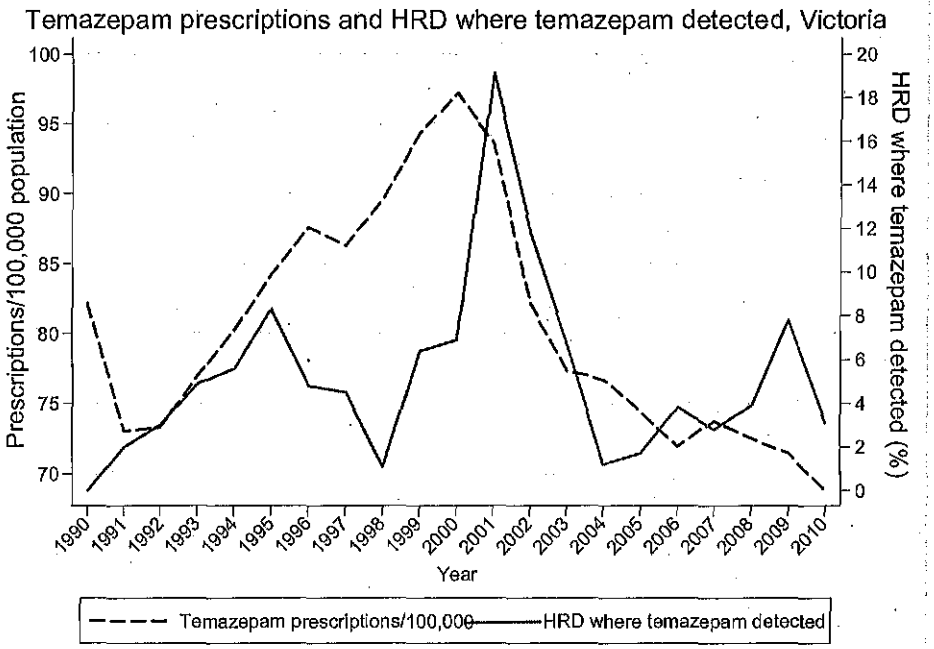


Figure 4: Heroin related deaths where temazepam was detected decreased rapidly when gel caps became authority required.



The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

17th January 2013

To The Secretary,

Re: Proposal to Reschedule benzodiazepines from Schedule 4 to Schedule 8

I write to give my support to the proposal to reschedule benzodiazepines from schedule 4 to schedule 8 under the relevant therapeutic goods administration articles.

I work as a psychiatric registrar in a community mental health service in Victoria, and also act as a researcher with Deakin University School of Medicine. Through the latter appointment I have undertaken research into the specific role of alprazolam, a short acting high potency benzodiazepine, in the treatment of panic disorder in Australia. Alprazolam is only supported for prescription in Australia for treatment of "Panic disorder where other treatments have failed or are inappropriate". Our research has clearly articulated that despite a limited recommended role for alprazolam in clinical practice, particularly since the introduction of selective serotonin reuptake inhibitors as first line pharmacological agents for treatment of panic disorder, the use of alprazolam has grown precipitously over the last decade. We discuss the potential reasons for this increase of prescription use in our review paper *The Role of Alprazolam in the treatment of Panic Disorder in Australia* published in the Australian and New Zealand Journal of Psychiatry[1]. Although there are many potential reasons for this increase in use, one that certainly conforms with clinical experience is that of inappropriate prescription to patients who are addicted to this medication.

Alprazolam is associated with a number of harms and side effects including increased risk of falls, accidents, and long-term cognitive deficits which are well articulated in the scientific literature. There is also recent data demonstrating that rates of alprazolam diversion and subsequent abuse are increasing. As an example, alprazolam use in conjunction with heroin appears to substantially increase the risk of death than when heroin is used alone.

The social consequences of this ready supply of alprazolam in the community are plain to see for clinicians working in the public mental health system. Although practitioners may differ on the relative merits of alprazolam and other benzodiazepines in the treatment of anxiety based disorders, international clinical guidelines (NICE, American Psychological Association) suggest use beyond the short term (4 weeks) is usually not appropriate. Unfortunately rates of prescribing in

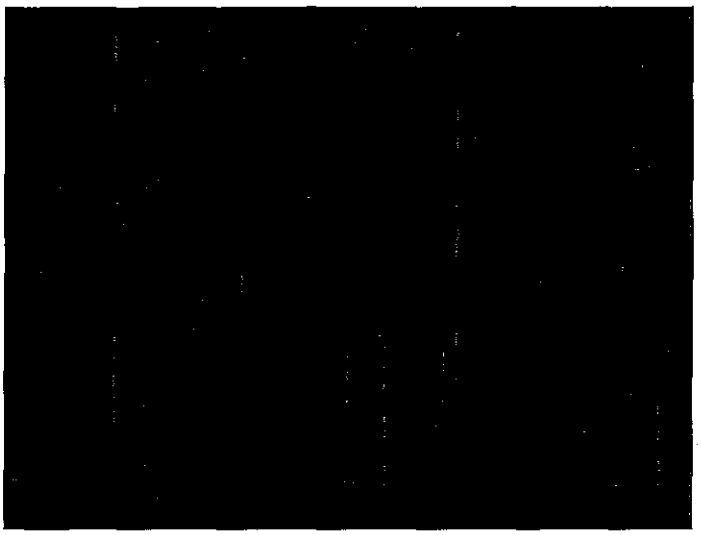
[1] **Moylan S**, Giorlando F, Nordfeam T, Berk M. *The Role of Alprazolam in the treatment of Panic Disorder in Australia.* Aust N Z J Psychiatry Mar 2012; 46(3): 212-224

Australia are disconnected from what would be expected if guideline based treatment practices were being followed.

A variety of measures will be required to bring prescribing practice in line with clinical practice guidelines, but one effective measure will be to identify and implement systemic measures that can be taken to increase oversight of prescribing. One mechanism that has shown effect in other areas of troublesome medical prescribing has been to elevate the status of a medication to schedule 8. I would strongly support this measure for benzodiazepines, particularly those with high potency and short half-lives (e.g. alprazolam), characteristics that make them likely to precipitate drug addiction.

Thank you for considering my submission,

With Kind Regards,



Central Support
56 Sylvan Road
Toowong Qld 4066
PO Box 1539
Milton BC Qld 4064
P: 07 3377 3377
F: 07 3377 3366
E: head.office@bluecare.org.au
www.bluecare.org.au

22 January 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 4061

Dear Sir/Madam

RE: Public Submission, Proposed Amendment: Proposal to reschedule Benzodiazepines from Schedule 4 to Schedule 8
(Regulation 42ZCZK, Therapeutic Goods Regulation 1990)

Blue Care welcomes the opportunity to provide the following comments regarding the proposed Amendment to reschedule Benzodiazepine medications from Schedule 4 to Schedule 8. Thank you for granting an extension to the closing date to 25 January 2013 (as advised on 15 January 2013) that has allowed us to do so.

Blue Care is the largest of several not-for-profit organisations forming part of UnitingCare Queensland, and is one of Australia's largest providers of community health and residential aged care. Blue Care provides care and support services throughout Queensland and Northern New South Wales from more than 260 centres, including residential services, in home care packages, day therapy, respite care, palliative care services, as well as other programs for carers. Blue Care also has a contractual arrangement with the Queensland Police Service (QPS) to provide nursing services to watch-houses.

While the proposed amendment may provide a control measure for illicit use, misuse or abuse of benzodiazepine medications, it will create many significant consequences for staff and work practices in residential aged care facilities and community services.

Background
Benzodiazepines, also known as 'minor tranquilisers', are most commonly prescribed by medical practitioners to relive stress and anxiety and to assist with sleeping. Common benzodiazepines used in aged care include Diazepam, Oxazepam, Alprazolam, Nitrazepam and Temazepam.

The benzodiazepines group of medications are commonly prescribed for older people who require care either in a residential aged care facility or in a community care service, in an appropriate manner, by the treating General Practitioner, a treating Medical Specialist or an authorised Nurse Practitioner. The decision to prescribe these types of medications is assumed to be done with full consideration and review by the prescribing officer.

It is known that regular use of benzodiazepines can develop dependence and tolerance. Dependence on benzodiazepines can be psychological, physical or both. The effect of benzodiazepines, as with any medication, depends on the amount taken and period of time over which use occurs. Use of any medication carries some risk as medications can produce unwanted side effects.

Blue Care acknowledges that current research is indicating that the use of benzodiazepine medications in the older person can have uncertain long term efficacy and potential serious side effects, including falls and fractures from falls, and that the use of this group of drugs in the older person should be carefully considered by the treating doctors. However the reduction in use will not be achieved by placing additional restriction on the storage and administration requirements imposed by the classification as a Schedule 8 drug.

It is of note that prescription of these medications is also reviewed regularly through the Medicare Australia Residential Medication Management (RMMR) and associated Quality Use of Medicines (QUM) reviews undertaken by an appropriately qualified Clinical Pharmacist in both residential and community care settings.

The inclusion of this group of medications to the Schedule 8 group poses a potential reduction in the quality of care for the older person because of the staffing impact of the required changes to work practices.

Impact on Aged Care Services
If the proposed change is implemented it will result in significant resourcing issues for Registered Nurses and care staff working in residential aged care facilities and community services, across all shifts. The impact of rescheduling benzodiazepine medications to Schedule 8 will require a change in practices related to receipt of drugs to a centre from the pharmacy, storage, recording, administration and monitoring of this group of medications.

Implications for work practices and staffing resources

- Reclassification of benzodiazepines will increase time taken to manage the delivery of medication from the pharmacy to the aged care facility, requiring counting at the time of delivery and checking in of the delivered medication into the site's controlled drug safe.
- The change in practice will require 2 staff having to check every episode of administration of a benzodiazepine medication, both regular and as required (PRN) doses. The Registered Nurse would be required to be present for the entire process of checking the medication from the secure storage cabinet, recording the details in Controlled Drug register and witnessing the administration to the client. This resourcing implication will be most significant during evening and night shifts when access to a Registered Nurse is usually reduced.
- The proposed change will have significant impact on the time taken for the medication count of schedule 8 drugs that occurs at staff shift changes as the number of medications to be counted will increase. The time taken by Service Managers to perform a weekly check of the controlled drug record will also increase.
- Clients in the community who have benzodiazepine medications prescribed and who have medications packed by a pharmacy would not have their benzodiazepine included and would require a Registered Nurse visit to administer.

- Many current Schedule 8 medications are managed in the Community setting using slow release medication delivery systems. Inclusion of benzodiazepine medications as Schedule 8, with the associated regulations, will require increased home visits by Registered Nurses.
- An increased number of Registered Nurse visits could be required for respite services if clients required administration of benzodiazepine medications.
- A significant amount of benzodiazepine medication is administered in the QPS watch house settings for the management of alcohol withdrawal symptoms and this change would impact on the time available for Registered Nurses with the additional checking and counting required for a Schedule 8 medication.

Implications for physical resources - storage

- The change in classification of benzodiazepines to a Schedule 8 drug will have significant impacts on medication storage.
- Regular benzodiazepine medication would have to be packed separately to other regular prescribed medications and stored accordingly.
- Imprest supply of benzodiazepine medication for emergency requirements would also have to be stored accordingly.
- Medication storage facilities are currently at capacity in most sites with those medications currently listed as Schedule 8.

In addition to the resourcing implications as a key challenge to this proposed change, are also the risks associated with the quality and timeliness of services provided. A subsequent consequence of the change to the Schedule for benzodiazepines, if not appropriately managed, will place older people at significant risk. Blue Care strongly requests reconsideration of the proposed rescheduling of benzodiazepine medications to Schedule 8 classification due to the impact that will be experienced in aged care settings.

Yours sincerely

[redacted]

LEADING AGE SERVICES
AUSTRALIA
QUEENSLAND

PO Box 995
Indooroopilly, QLD 4068
6 Pavilions Close
Jindalee, QLD 4074
Phone 07 3725 5555
Fax 07 3715 8166
info@qld.lasa.asn.au
www.qld.lasa.asn.au

16 January 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601
Email: SMP@health.gov.au

Dear Sir or Madam

Re: Proposed amendments referred by the delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling (ACMS). In particular, proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8.

Leading Age Services Australia Queensland (LASA Q) supports the submission to the ACMS from The Pharmacy Guild of Australia and is concerned about the impact such a proposal would have on the residential aged care sector.

LASA Q has identified a significant impact on prescribers and pharmacists and a further significant impact on residential aged care facilities (RACFs) should these changes take place.

Rescheduling Benzodiazepines to a Schedule 8 medication would significantly impact Queensland RACFs in the following ways:

- A significant increase in time would be required for Medication Administration rounds due to Schedule 8 regulatory compliance requirements. For example, medications are signed out and counted individually from Controlled Drug cupboards at the time of service and two staff are required to witness ingestion.
- Care delivery to residents would be affected as there will be no increase in funding to allocate additional resources for this task. The majority of Benzodiazepines are administered late afternoon, evening or overnight when the staffing ratio is generally reduced - therefore evening and overnight staffing levels would need to be increased at significant cost to the provider.
- Storage requirements would need to be expanded and additional Controlled Drug cupboards/safes will need to be provided to store the excess Schedule 8 medications.

- There would need to be a concomitant increase in resources to ensure required delivery documentation is completed. Schedule 8 medications must be signed into Controlled Drug registers at point of entry (therefore leading to an increased numbers of entries). This requirement would compound the issues associated with overnight staffing numbers and costs.
- Checking of Schedule 8 medications against the Controlled Drug register entries is required daily to ensure congruency and by virtue of the increase in the number of scheduled medications, additional time will be required.
- Further changes to the number of medications that require a script (once the national medication chart is implemented) will exacerbate the issues noted.

The level of use of benzodiazepines within RACFs is significant, for example there are residential aged care organisations which have approximately 60 – 70% of their residents medicated on regular or PRN orders for a Benzodiazepine. The rescheduling of Benzodiazepine as an S8 will have significant impacts on the storage, supply and administration capacity of these services with flow-on consequences and costs for an already under-resourced Residential Aged Care sector.

Although LASA Q acknowledges that there may be incidences of overuse/misuse of benzodiazepines, this will not be resolved by rescheduling. It would be better managed by other evidence-based approaches and mechanisms that are more consumer-centered with a focus on ensuring patients with a genuine need do not have their health and care needs compromised, and any examples of abuse/misuse are appropriately detected, managed and supported. This includes comprehensive education of health providers across the health care spectrum.

Yours sincerely

[redacted]

Benzodiazepines

[redacted]

[redacted]

15th January 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Re: Proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8.

We wish to state our objection to the proposed rescheduling of all benzodiazepines from Schedule 4 to Schedule 8.

The potential change of all benzodiazepine to schedule 8 will have significant adverse implications on the handling of medications within aged care facilities.

Including:

- Schedule 8 medications require increased staff handling and witnessing of administration in accordance with facility policy and state legislation.
- Increasing the number of schedule 8 medications with proposed changes to Benzodiazepine scheduling will greatly impact on nursing/care staff time requirements for administration of medications and documentation of schedule 8 transactions.
- Scripts for schedule 8 medications will still be required when using the new National residential medication chart therefore changing of Benzodiazepines to schedule 8 will minimize the benefits of reduced owing prescriptions with National residential medication chart.
- Increased number of medications requiring storage within existing and often small schedule 8 safe/cupboards.

Whilst we acknowledge that abuse of benzodiazepines may occur within the community, particularly with Alprazolam, we are uncertain of the benefits in changing the scheduling for all benzodiazepines. *We are well aware of the recommendation to minimize the use of benzodiazepines in the elderly, but they do remain useful and commonly prescribed medications for residential care patients.*

Wangaratta aged care Medication Advisory Committee members do not object to changing the scheduling for Alprazolam ONLY.

[redacted]

[redacted]

[redacted]

Proposed scheduled changes to benzodiazepines [SEC=No Protective Marking]

[redacted]

To Whomever it May Concern,

I write to you in regards to the proposed changes to the scheduling of benzodiazepines. I commend you for taking a bold stance against this known group of widely abused drugs. As a practising pharmacist working in Northbridge, WA, I see many of the direct consequences of irresponsible prescribing of benzodiazepines and I could not be more pleased that the time has come where some positive changes can be made.

I do however disagree with the proposed change of benzodiazepines to schedule 8. I believe this will create a myriad of problems in the pharmacy with the extra work created by recording every transaction as a drug of addiction. There are some pharmacies which dispense upwards of 300 scripts of diazepam 5mg alone per month and you can imagine how much extra time it will take to record every entry. In addition, I do not believe that up-scheduling benzodiazepines to schedule 8 will affect the prescribing habits of doctors in a meaningful way. Is it not possible to attach a requirement for the doctors to apply for a HDWA number before prescribing benzodiazepines to their patient, whilst still maintaining its position on schedule 4? This method was used very effectively to curb the use of Flunitrazepam since the early 90's, and I believe it can be used to the same effect for all general benzodiazepines. This way, prescribers will be prevented from writing out vast amounts of benzodiazepines, the Health Department can track usage by patients and prescribing by doctors, and private untraceable prescriptions will not longer be invisible to the health department. Doctor shopping by patients will no longer be possible as each and every transaction will be centrally monitored by the Health Department, regardless of whether the prescription was written as a PBS or as private.

While we are on the subject, it may be worth considering how much the PBS pays for the abuse of benzodiazepines. Does the PBS ever look into how many prescriptions of benzodiazepines a patient will have dispensed for them per year and how close the prescriptions are being collected? In my practice it is not uncommon to see a patient present with an Alprazolam prescription with 100 tablets with three repeats, all used up within a few days. There are also patients who reach the safety net by March/April purely with benzodiazepines alone, give or take a few other sedating drugs.

I look forward to your response and to the results of your final decision.

[redacted]

Benzodiazepines

[redacted]

To Whom it may concern at TGA,
As a Pharmacist I am strongly opposed to the proposed rescheduling of Benzodiazepines from S4 to S8.

I appreciate there may be many reasons for the change, however, from a Pharmacist point of view, it would involve MANY prescriptions having to be recorded MANUALLY, which would be more time consuming.
Scripts would expire in six months, not a year.
Scripts would not as easily be phone communicated for owings.
Pharmacists would have to spend a significant amount of time balancing medications, and count checking ,etc. which would detract from professional services.
S8s have to be stored in safes, which would be a significant cost, and result in decrease stock holding, and maybe limit stock availability.

Importantly, under the proposed changes for medication Profiles being a legal prescription, S8 medications will be exempt, so this will involve more prescriptions being required to be written.
This will significantly negatively affect Drs, Pharmacists, and Aged Care Facilities.
This will impact on time that can be better professionally used elsewhere.
Many Doctors in my experience are professional and only prescribe benzodiazepines after serious consideration, and do not prescribe them lightly.
To change the scheduling will impact negatively on Drs for time involved, Pharmacists for cost, (safes, and Staff time), and Clients who may not be able to access prescriptions in a timely manner. All of these factors have potential to negatively impact on patient care.
I request that this decision be not considered, or in the second case, perhaps be put to a much wider population for public comment, and that there needs to be much more advertising to allow people time to consider the full impact, and respond appropriately.

[redacted]

[redacted]

[redacted]

15/05/2013

Benzodiazepines

[redacted]

[redacted]

If you not an authorised recipient of this email, please contact Wizard/Prescription Plus Management immediately by return email or by telephone. In this case, you should not read, print, re-transmit, store or act in reliance on this email or any attachments, and should destroy all copies of them. This email and its attachments are confidential and may contain legally privileged information and/or copyright material of Pharmacy or third parties. You should only re-transmit, distribute or commercialise the material if you are authorised to do so. This notice should not be removed.

Benzodiazepines

[redacted]

To Whom It May Concern

I am writing this letter in regard to the proposal to reschedule benzodiazepines from schedule 4 to schedule 8. I am a community pharmacist, who in my work, supply medicines and other services to an aged care facility. From a logistical point of view this would be an unwelcome change for community pharmacy and I imagine for aged care facilities as well.

A major inconvenience that first and foremost springs to mind is the sheer volume of benzodiazepine stock that would have to be kept in a drugs safe. As a rural community pharmacy, we dispense anywhere from 110-170 benzodiazepine units per month. This would require a major refit to create enough space to legally store these medicines, as well as also most likely forcing a compromise where we are unable to keep as much stock on hand.

This change would also create more work for pharmacists in all fields and for the staff of the aged care facility in our community, which already struggles to retain enough registered nurses.

As I understand, this change is proposed to effect the need for prescriptions still to be written when legislation is passed allowing dispensing from medicines charts in aged care facilities. I would propose an alternative solution to this problem in the form of a new sub-schedule (not unlike the S4D group that benzodiazepines belong to) or recommending changes to the legislation for all schedule 4 medicines that carry further restrictions (benzodiazepines, anabolic steroids, etc) that require a prescription to be written still, once the new legislation has come into effect.

Regards

[redacted]

[redacted] 2013

Mercy Health
Care first

16 January 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

Dear Secretary

RE: Proposed amendments to the current Poisons Standard

I write in response to the proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8.

Mercy Health does not support this proposed amendment.

Mercy Health is a Catholic community provider of care founded and wholly owned by the Institute of Sisters of Mercy of Australia & Papua New Guinea. We offer acute and sub acute hospital care, aged care, mental health programs, specialist women's health, early parenting, palliative, home and community care, and health worker training and development.

While we understand the potential for abusive use of benzodiazepines it is our experiences as a provider of residential aged care which causes us to be unsupportive of this proposed amendment.

Rescheduling would result in tighter regulatory requirements throughout the distribution chain, impacting storage, security, reporting, records, authorisation of personnel and treatment.

All of these additional controls would impose significant additional costs to a health and aged care sector where costs need curbing.

The number of General Practitioners (GPs) who are willing to visit residential aged care facilities is decreasing as they face financial disincentives and increasing administrative work providing care to patients with high acuity and case complexity.

Mercy Health
Level 2, 12 Shelley Street, Richmond Victoria 3121 Telephone: (03) 8416 7777 Facsimile: (03) 8416 7888
mercyhealth.com.au ABN 77 191 901 062

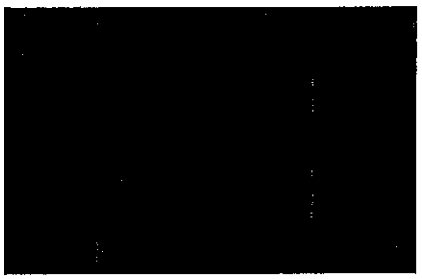
The additional administrative and compliance issues that would result from rescheduling benzodiazepines would further discourage GPs from providing care within residential aged care facilities. This could result in some of the most vulnerable people in our society not receiving timely medical care as required.

GPs are aware of the potential impact of sedatives, e.g. impaired cognition and gait, leading to falls, and consider these when prescribing them to the aged, particularly those experiencing dementia.

Rescheduling will also add to the work load of Registered Nurses working in residential aged care facilities, as they would no longer be able to include these medications in webster packs.

To reiterate, Mercy Health does not support the proposed rescheduling of benzodiazepines.

Yours sincerely



The Secretary
Scheduling Secretariat

Therapeutic Goods Administration

Thank you for the opportunity to comment on this proposal.

Problems arising from benzodiazepine dependence and misuse account for a significant amount of the work of Next Step and polydrug overdose involving benzodiazepines is a common cause of death in the patients we treat. Illicit drug users prefer the more sedating benzodiazepines and it is these benzodiazepines that are of greatest risk for overdose.

While from an addictions medicine perspective I would support all benzodiazepine being transferred to schedule 8 I am not sure how realistic this is given their widespread use in Australia.

Perhaps as a first step diazepam and temazepam could be left in schedule 4 and all the other benzodiazepines could be transferred to schedule 8.

Benzodiazepines

[redacted]

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

To whom it may concern,

Re: Proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8.

I was most concerned when I heard of this submission and the impact it will have on the staff who work in Aged Care.

Benzodiazepines are commonly used drugs in Aged Care Facilities.

If Benzodiazepines are rescheduled from Schedule 4 to Schedule 8 this will result in a major increase in time required for Registered and Enrolled Nurses to check these drugs and also to administer them. (Schedule 8 drugs must be given and checked by 2 staff).

This will largely impact on the time that RN/EN staff have to provide care to the residents.

Regards

[redacted]

[redacted]

[redacted]

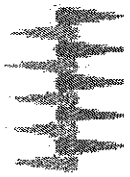
Notice inviting public submissions under Regulation 42ZCZK of the Therapeutic Goods Regulations 1990

I am a registered pharmacist in charge of a webster department in Albury NSW. I provide webster packs and pharmacy services to about 500 patients and am quite concerned about the very large effect that making Benzodiazepines Schedule 8 will have on myself and the nursing homes who I deal with.

Without going through my data base to fine the exact numbers i would guess that at leat 1/3 of my patients would be on some sort of regular or PRN Benzo, the amount of time and complexity that this would add to my day to day running is very substantial. As it is i spent up to 2 hours daily dealing with S8's and it can be very dificult getting scripts from Dr as the nursing home patients are numerous and time consuming. It would also have ramifications at the homes as far as storage and staff adminitering medications.

[redacted]

[redacted]



NATIONAL PHARMACEUTICAL SERVICES ASSOCIATION

24 January 2013

The Secretary
Scheduling Secretariat
GPO Box ACT 2601

NPSA Submission into the Proposal to reschedule benzodiazepines from Schedule 4 (S4) to Schedule 8 (S8)

The National Pharmaceutical Services Association (NPSA) which represents full line pharmaceutical wholesalers across Australia has concerns with the proposed rescheduling of benzodiazepines from Schedule 4 to Schedule 8.

The scale of this class of medicine is such that it is deserving of detailed consideration. The impact of the proposed change on the supply chain would be significant. NPSA recommends to the Advisory Committee that it give specific attention to the overlay of regulation that would follow from the rescheduling being considered and whether in fact the full breadth of the regulation is relevant to addressing the current concern with the misuse of benzodiazepines.

1. Scale of the class of medicines - benzodiazepines

NPSA estimates that benzodiazepines account for two million units of supply per annum - an estimated 2.2% of all medicines supplied by wholesalers to pharmacies and hospitals each year.

If all benzodiazepines were rescheduled to Schedule 8, the number of Schedule 8 medicines distributed to retail pharmacies by wholesalers would increase by over 50% to six million units.

2. Impact on Wholesalers

Wholesalers meet onerous obligations to ensure that medicine supply in Australia is safe and secure. These are outlined in State and Territory legislation as well as in the *National Coordinating Committee on Therapeutic Goods Australian, Code Of Good Wholesaling Practice for Medicines In Schedules 2, 3, 4 and 8* (effective date 1 April 2011) ("the Code") and need to be met by all wholesale suppliers of medicines in Australia.

Compliance with the Code is high as most medicines are supplied by CSO compliant wholesalers. These wholesalers are regularly audited for compliance with the Code by an Independent Administration Agency appointed by the Federal Government.

A summary of the minimum standards for supply of Schedule 4 medicines is set out in an Attachment to this letter. The security, warehousing, personnel, stock handling and control, transportation, records management and temperature control obligations are

extensive and effective at minimising diversion in the supply chain. Significant attention has been paid to security measures given the risk of diversion of pseudoephedrine from the supply chain.

When a Schedule 4 medicine is re-scheduled as Schedule 8 (Controlled Drugs - CD), further measures again are adopted in recognition of the higher risk of diversion for drugs of addiction.

Wholesalers need to meet various special obligations set out in State and territory legislation as well as additional obligations set out in the Code:

- CD (and CD waste) must be stored in a vault or safe in accordance with applicable State or Territory legislation.
- The vault or safe must be fitted with an alarm, seismic detectors and should be video monitored.
- The safe or vault should be located in a secure area of the building, out of public view, and kept locked except when in immediate use.
- Access to the safe or vault should be limited to authorised staff, controlled and monitored via appropriate measures to be determined by the Security Risk Management Plan.
- A Controlled Drugs register (which in most states still needs to be completed manually) should be maintained at each site in accordance with State and Territory legislation. These records should be subject to regular audits and verification by a responsible supervisor or manager.
- CD must be destroyed in accordance with State/Territory requirements.

There are a number of operational items that need to be considered:

- Operating costs will increase by approximately $1.5m due to the additional handling requirements within the warehouses.
- Freight costs will increase by approximately 2% ($500,000) due to the additional paperwork/ handling required by drivers and recipients within pharmacies. Drivers will be delayed at each pharmacy drop-off.
- Wholesalers charge CD fees per order line of about $2.50. This would equate to an additional $1.25m in fees passed to pharmacies ($500 per pharmacy per year).
- Wholesalers have capacity constraints in the vaults at each site and many vaults would need to be replaced with larger vaults or enlarged to cope with the additional volumes – this may not be feasible within existing infrastructure.

NPSA acknowledges current concerns regarding misuse of benzodiazepines and recommends consideration of measures that best address these concerns. NPSA believes that the rescheduling under consideration would impose a framework of costly measures on wholesalers that may not address the concerns seeking to be addressed.

NPSA supports retaining benzodiazepine scheduling as Schedule 4, the introduction of smaller pack sizes for benzodiazepines and / or the introduction of real time reporting of supply by pharmacists.

[redacted]

[redacted]

[redacted]

National Coordinating Committee on Therapeutic Goods Australian, Code Of Good Wholesaling Practice for Medicines In Schedules 2, 3, 4 and 8 (effective date 1 April 2011)	
	S4 Medicines
Security	• Surveillance and detection systems to be installed and monitored • Access restricted to required staff only • Regular security audits/ risk assessments undertaken with a senior manager to have overall site security responsibility • Overall site security in place to prevent unauthorised access • Procedures and conditions of work for employees and other persons having access to medicines should be designed and administered to minimise the possibility of pilferage, diversion or theft • Standard operating procedures for security, handling methods and reporting of theft or misuse of medicines should be developed and enforced • Systems in place to prevent theft of medicines • Wholesalers must have in place an adequate validation protocol that ensures that persons supplied with medicines are authorised appropriately under State or Territory legislation to be supplied with those medicines • Medicines for destruction should be enclosed in secure, opaque and sealed packaging or container. Destruction must be carried out by a licenced practitioner.
Buildings	• Warehousing of medicines should be carried out in buildings or parts of buildings that have been built for, or adapted to, this purpose • Buildings and storage facilities, including bays, docks and platforms used for the receipt or despatch of goods, should protect the medicines from contamination and deterioration. The conditions of storage should be in accordance with the storage conditions specified on their labels and their Material Safety Data Sheets (MSDS) where relevant • The facility should have appropriate perimeter fences, gates, lighting, signage and other systems that discourage attempted site penetrations and ensure security of the grounds and buildings and detection of site penetrations if they occur • Temperatures in facilities where (Temperature Sensitive Medicines) TSM are held should be monitored using suitable temperature recording devices and the results recorded and analysed so as to demonstrate the suitability of these areas for their purposes
Personnel	• Appropriate policies and procedures should be in place for the selection of staff and contractors, as well as requirements for ethical conduct of staff and contractors. • Standard operating procedures should be developed for use by all staff. Staff should be trained in the operating procedures relevant to their responsibilities in such a way that individual responsibilities are clearly understood. • Specific training should be given for medicines with specific risks, e.g. medicines requiring special storage conditions, fragile products or medicines containing substances that pose high risk to personnel and/or to product quality if package integrity

National Coordinating Committee on Therapeutic Goods Australian, Code Of Good Wholesaling Practice for Medicines In Schedules 2, 3, 4 and 8 (effective date 1 April 2011)	
	S4 Medicines
	is breached or spillage occurs, e.g. dangerous goods, cytotoxic drugs
Stock Handling & Stock Control	• Storage areas should be adequate and organised to enable segregation and identification of the various materials and products stored, and should enable stored medicines to be easily maintained in a clean, dry and orderly condition. • Medicines should be stored off the floor (e.g. on pallets or shelves) to reduce exposure to dust and moisture, and to help facilitate cleaning. • Handling and storage of medicines should be in accordance with established procedures designed to prevent contamination or deterioration of the goods Goods inward: • Upon arrival, stock should be inspected and examined for correctness against order, acceptable period of time before stock expiry date and absence of damage or evidence of tampering. • There should be a system for the recognition and prompt handling of medicines that require special handling or care.
Transport	• Containers for delivery of medicines should be clean and provide adequate protection from damage or deterioration for the medicines delivered. • A system should be in place to give assurance of the trustworthiness of employed and contracted delivery personnel, for example, through proof of identity and criminal records, employment history and reference checks. • A system of identification for delivery personnel should be in place. • Delivery personnel should be required to keep vehicles secured when unattended. • A system should be in place to enable the return of signed receipts obtained from the authorised recipients of the goods in paper or electronic form. • There should be standard operating procedures for employed delivery personnel to ensure safe, secure and timely delivery of medicines and for dealing with incidents such as accidents which result in loss or destruction of a load, or part of a load, of medicines in transit.
Management of records	• An accurate record of all receipts and sales transactions must be kept. • All records should be stored and maintained in such a way that they are accessible and readily retrievable. • Records should be stored in facilities that provide a secure environment which minimises damage or deterioration and prevents loss through inadequate storage and/or control. • Computer records must be secure and protected from unauthorised access and tampering. Procedures should be in place to ensure data integrity of computer records.

National Coordinating Committee on Therapeutic Goods Australian, Code Of Good Wholesaling Practice for Medicines In Schedules 2, 3, 4 and 8 (effective date 1 April 2011)	
	S4 Medicines
	Standard Operating Procedures • A register of standard operating procedure documents should be kept. • Standard operating procedures should be: o clear, concise, comprehensible and readily available to those needing to use them; and o numbered, dated, have a title, identify the name or position of the person responsible for the standard operating procedures; and o include detailed instruction on the subject and a date for review.
Cold Chain Medicines	• Refrigerated areas for the storage of cold chain medicines should be correctly set up and operate continuously. • Temperature monitoring equipment should be installed within facilities used to store cold chain medicines • Maximum and minimum temperatures should be recorded, either electronically • Procedures should be in place detailing the actions to be taken in the event of continued power failure or an excursion outside the defined temperature range. • If cold chain medicine storage temperature is found to have deviated from the sponsor's recommended conditions, the sponsor of the medicines should be contacted and the suitability of the medicine for use should be resolved and the outcome recorded. Inwards Cold Chain Medicines from Suppliers • Cold chain medicines with a defined temperature range should not be stored in a temporary stock location that could expose them to temperatures outside the specified range Order Assembly and Dispatch of Cold Chain Medicines • Packaging of cold chain medicines should be undertaken in an area specifically set aside for this purpose and be performed under conditions that minimise the risk of medicine temperature excursions • Validated temperature-control systems shall be used to ensure integrity of the cold chain is maintained between wholesaler and customer. • For each delivery, assessment of the delivery method and validated temperature-controlled system to be used should consider the time required for delivery, weather conditions and any foreseeable exposure risks. • Special delivery procedures, transport and packaging should be established for cold chain medicines likely to be exposed to an unfavourable environment. • The external packaging/shippers containing cold chain medicines should be suitably labelled • Cold chain medicines should be clearly identifiable from other goods in the same delivery.

National Coordinating Committee on Therapeutic Goods Australian, Code Of Good Wholesaling Practice for Medicines In Schedules 2, 3, 4 and 8 (effective date 1 April 2011)	
	S4 Medicines
	• The packaging and handling of cold chain medicines should seek to alert the receiver that the order contains cold chain medicines and that the receiver should place these medicines in appropriate storage facilities as soon as possible. Transport of Cold Chain Medicines • Cold chain medicines should be transported under conditions that have been validated or are monitored

LEADING AGE SERVICES
AUSTRALIA
Helping older Australians to live well

Unit 4, 21 Torrens Street
Braddon
ACT 2612
Phone 02 6230 1676
Fax 02 6230 7085
info@lasa.asn.au
www.lasa.asn.au
ABN 71156349594

17th January 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

Re: Proposed amendments referred by the delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling (ACMS)

Proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8.

Leading Age Services Australia (LASA) would like to submit the following response to the proposed amendments to the current Poisons Standard.

LASA supports the submission to the ACMS from The Pharmacy Guild of Australia in regards to the proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8 and highlights the impact such a proposal would have on the residential aged care sector.

LASA suggests that not only would such a change have a significant impact on prescribers and pharmacists, but it would also have a significant impact on residential aged care facilities (RACFs).

Given the level of use of benzodiazepines within RACFs, it would likely impact on storage, supply and administration capacity of these medicines and have flow-on consequences and costs to many elements of an already under-resourced provider sector. Extra security procedures may be required and would certainly impact on the administrative burden for staff in storing and handling another S8 medication.

Acknowledging that there are issues with overuse/misuse of benzodiazepines, LASA is concerned that the proposed 'blanket' approach may have a number of unintended consequences and that the issue would be better managed by other evidence-based mechanisms that are more consumer-centred with a focus of ensuring patients with a genuine need are not compromised and those with abuse/misuse issues are appropriately supported.

Should you have any questions please do not hesitate Ms Kay Richards, National Policy Manager on 02 6230 1676.

[redacted]

CATHOLIC HEALTH
Australia

17 January 2013

Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

By email: SMP@health.gov.au

Dear Sir/Madam

I refer to your notice of 29 November 2012 inviting public submissions under Regulation 42ZCZK of the Therapeutic Goods Regulations 1990.

Catholic Health Australia is the peak member organisation for some 550 aged care facilities operated by different bodies of the Catholic Church within Australia in fulfillment their mission of care.

Our submission concerns the proposal to reschedule Benzodiazepines from Schedule 4 to Schedule 8.

We note that under 52E (1) (a), the Secretary of the Department must take into account, inter alia, "the risks and benefits of the use of a substance".

We are advised by our membership that risks for the effective care of aged care recipients could arise from rescheduling because of the additional resources that would be required to administer benzodiazepines as a result of the regulatory arrangements governing Schedule 8 drugs. In particular, the need for two qualified staff to check the administration of every episode and increased time to administer each episode. The additional resources need to be considered in the context of the tight labour market for nursing staff in many regions of Australia (especially after hours staff), and the highly regulated financing arrangements in aged care which inhibit the capacity of many service providers to attract and retain nursing staff.

A potential consequence of the combined effects of these circumstances is that aged care homes may be constrained in their capacity to effectively administer legally and competently prescribed medications.

We therefore urge that in considering the proposed change, the Committee addresses the potential risks for aged care recipients.

Yours sincerely

[redacted]

Level 1, 10 Thesiger Court, Deakin ACT 2600. PO Box 330, Deakin West ACT 2600. T 02 6203 2777 F 02 6260 5488
Catholic Health Australia Incorporated | ABN 30 351 500 103

www.cha.org.au

17 January 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601
Email: SMP@health.gov.au

Invitation for public comment – ACMS and ACCS meetings, March 2013:
Proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8

The **Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT)** is the professional and independent Society in Australia and New Zealand with expertise in the use and toxicity of medicines and chemicals. ASCEPT welcomes the opportunity to comment on the proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8. This submission will address ASCEPT'S views about some key issues, noting that individual members may make their own more detailed submissions to the proposal.

Given the evidence of abuse of benzodiazepines and the risks of withdrawal and overdose[1] associated with these drugs, ASCEPT believes a change in schedule to S8 (alongside drugs like morphine and oxycodone) would be a positive public health measure. Specifically, this change in regulation would increase the controls on prescribing, potentially restrict duration of prescribing and raise prescriber awareness of the risks of benzodiazepine use.

The objectives of scheduling are to reduce the level of accidental or intentional poisonings

[1] There is a growing body of research supporting the status of benzodiazepine use as a significant risk factor for opioid overdose.

through inappropriate access to drugs, provide expert intervention to ensure consistency of information between consumers and the pharmaceutical industry and provide a mechanism whereby the inappropriate use of medicines for unsafe or criminal use are minimised.

Further, rescheduling usually occurs when there is a need for maintaining consistency with comparable products under a different schedule or there has been a perception that the risk profile of the product has either been increased or decreased (thus necessitating a move to a higher or lower schedule). **It is within this context that ASCEPT supports the rescheduling application.** ASCEPT further notes that zopiclone and zolpidem are very similar to benzodiazepines and should be similarly considered.

While the dangers of benzodiazepines are well documented, their efficacy is limited. With continuous use the efficacy of benzodiazepines decreases and tolerance and dependence increases. They widely prescribed for indications with uncertain efficacy. Their harms are well documented and they are widely abused. Benzodiazepine addiction is a physical and psychological addiction. Tolerance to the hypnotic effects of benzodiazepines develops in week-months, but the adverse effects on physical and cognitive function persists throughout the treatment period.

In summary, ASCEPT supports rescheduling of benzodiazepines to S8, noting the issues of harms from inappropriate use and abuse are similar to other S8 drugs.

[redacted]

Benzodiazepines

[redacted]

Hello,

I am one of the RN working in the aged care facility. I am writing this email to state my opinion of against this proposal of reschedule benzodiazepines from Schedule 4 to Schedule 8.

Benzodiazepines is a common medications across all over Australia. Many people have easy access to this type of medications. It is not a very strong sedation for the dosage and its effects as well. In general it has been classified as schedule 4 medication which has been regulated by RN and EN when administrating this type of medications. It is relatively safe when resident administrate this medication. This is no point to reschedule it to DDA. I personally do not see any concern of overuse in the public of this particularly medications and it would has the great negative social effects as the other DDA medications as morphine. Furthermore every nursing home has more than 60% of residents are taking this medication for their sleep problem or their anxiety. It has been taken great amount of time for nurses to count the regular DDA medications already for each shift. It generally took 15 to 30 minutes for two nurses to count medication each shift. It took 30 mins for two nurses to count the schedule 4 medications. Despite of adding this type of medications into DDA, there would be a time consuming work. It not merely add up more workload for nurses, but also take great part of nursing time on counting medications. We more willing to put more time on nursing care on resident rather than spend on merely on medications count.

So I personally strongly against this proposal.

[redacted]

[redacted]

15/05/2013

ALPHAPHARM RESPONSE TO THE THERAPEUTIC GOODS ADMINISTRATION PROPOSAL TO RE-SCHEDULE BENZODIAZEPINES FROM PRESCRIPTION ONLY MEDICINES (S4) TO CONTROLLED DRUGS (S8).

PLEASE NOTE – ALL SECTIONS HIGHLIGHTED WITH A GREY BACKGROUND ARE COMMERCIAL-IN-CONFIDENCE AND SHOULD NOT BE DISCLOSED

BACKGROUND

Benzodiazepines were introduced into clinical practice in the 1960s and have now largely replaced older and less safe sedative-hypnotic agents such as the barbiturates. They have many important roles in pharmacotherapy particularly for disorders such as anxiety and insomnia, epilepsy, anaesthesia, muscle spasticity and spasm, and substance withdrawal. They also have the potential for misuse and abuse.

Alphapharm has eight benzodiazepines included on the Australian Register of Therapeutic Goods, most of which are scheduled as Prescription Only Medicines (Schedule 4), except for Hypnodorm (flunitrazepam), which is a Controlled Drug (Schedule 8). Alphapharm believes that the current scheduling of benzodiazepines provides the appropriate level of control over access and availability of the medicines, without unnecessarily restricting access to the vast majority of patients who use them appropriately. Benzodiazepines have many clinical advantages and if used as recommended are considered highly efficacious medicines with a rapid onset of action and a low level of toxicity.[1]

The scope of this report will focus on the six Alphapharm benzodiazepines that are primarily indicated for use as hypnotic or sedative medicines. These include Alepam™ (oxazepam), Alodorm™ (Nitrazepam), Antenex™ (diazepam), Hypnodorm™ (flunitrazepam), Kalma™ (alprazolam) and Temaze™ (temazepam). Alphapharm also markets Paxam™ (clonazepam), most commonly used as an anticonvulsant, and midazolam injection, used as an adjunct in anaesthesia and related procedures. We assume that the rescheduling proposal also applies to clonazepam and midazolam.

RECOMMENDATIONS

Alphapharm does not support the proposal to reschedule benzodiazepines from Prescription Only Medicines (S4) to Controlled Drugs (S8).

Our view is that the current scheduling arrangement applied to this class of medicine provides an appropriate balance between the benefits derived from appropriate prescribing and use of these medicines by the great majority of health professionals and consumers, against the possible risks to a few, often associated with intentional abuse or misuse.

We believe that the proposal to reschedule the medicines will significantly impact on the appropriate and justified therapeutic use of the agents, significantly increase the administrative burden associated with the prescribing, dispensing and administration of the medicines and significantly impact the capacity of manufacturers, wholesalers and pharmacies to securely store the medicines and to appropriately account for stock movements.

Furthermore we are not convinced that rescheduling the medicines will offer a greater disincentive to those consumers intent on misusing or abusing them, than that currently provided by Prescription Only status.

The question therefore remains: will rescheduling benzodiazepines appreciably alter the current societal risk/benefit balance provided by the agents, or simply impose additional hurdles to the safe and effective use in the vast majority of those patients who use the

medicines according to the principles of quality use, and who consequently derive great benefit with minimal risk to health?

Alphapharm believes that it will not, and such an imposition will inappropriately restrict access to a group of medicines with a long history of safe and effective use.

Our recommendation is based on the following information, which is discussed more extensively in the main body of our submission.

- Benzodiazepines are used in a wide range of conditions and indications, apart from the management of anxiety disorders and insomnia. Many of the indications are medically important, with few alternative therapeutic options. They include use as anticonvulsants, antispasmodics in nerve damage, adjuncts to anaesthesia and the management of nausea, in the management of major psychoses, and alcohol and substance withdrawal.

- When used according to directions, they have a wide margin of safety, with few cases of fatal overdose associated solely with excessive benzodiazepine intake.

- Benzodiazepines have a well established and predictable side effect profile, which is predominantly non-life-threatening.

- Benzodiazepines have a very low Fatality Toxicity Index, ranging from 1.1 to 7.1 deaths per one million prescriptions.

- Compared to analgesics, the level of non-medical use is low.

- Of those people who had used tranquilisers/sleeping pills for non-medical purposes in the past 12 months, the source of supply was from a prescription for a medical condition in 30.1% of cases, whereas in 32.4% of cases it was obtained from a friend or acquaintance.

- The scheduling of opioid medicines as Controlled Drugs does not in itself prevent the misuse or abuse of these agents.

RESPONSE TO SECTION 53E CRITERIA

(a) The risks and benefits of benzodiazepines

Benzodiazepines have important treatment indications in the management of a wide range of clinical conditions. These include the short term treatment of insomnia, the management of anxiety disorders (generalised anxiety disorder, panic disorder with or without agoraphobia), short term relief of symptoms of anxiety and the management of agitation associated with acute alcohol withdrawal. Benzodiazepines are also used as anticonvulsants and skeletal muscle relaxants, for preoperative relief of anxiety and provision of sedation, for light anaesthesia, for continuous sedation in intubated and mechanically ventilated patients undergoing treatment in a critical care setting (e.g., ICU) and for induction and maintenance of anaesthesia. [2]

Benzodiazepines are also used in a wide range of unregistered indications, for which evidence of benefit is available, including the use in the management of schizophrenia either alone or together with antipsychotic agents, for the management of nausea and vomiting associated with cancer chemotherapy alone or in combination with $5HT_3$ receptor antagonists, delirium, drug induced cardiovascular emergencies [2], add on therapy with SSRIs for Obsessive Compulsive Disorder and adjunctive therapy in treating patients with acute mania or acute agitation. [3]

In general, the side effects of benzodiazepines are rarely troublesome and can largely be prevented by keeping dosages at minimal effective levels, courses short (ideally up to a

maximum of four weeks) and through careful patient selection [1]. Benzodiazepine side effects include drowsiness, psychomotor impairment - especially in the elderly, and occasional paradoxical excitement. Other side effects that have been reported include dry mouth, blurred vision, behavioural changes including confusion, agitation, hyperexcitability, decreased inhibition, memory impairment, gastrointestinal complaints, sensitivity reactions, respiratory depression, and sleep related behaviours. [2, 4]

Dependence, tolerance and withdrawal effects, which are considered the major disadvantages with benzodiazepines, generally result from long term use.[1]

Dependence rarely develops in patients taking normal therapeutic doses of these drugs for short periods (1-2 weeks). However about a third of patients on long term treatment may have difficulty in reducing or ceasing benzodiazepines. Severe benzodiazepine dependence is seen in some poly-drug dependent patients (who make up only a very small proportion of total patient numbers) [4, 5]

Tolerance to sedative and hypnotic effects appears to develop more quickly than other effects associated with benzodiazepine use. For example, there is little evidence of tolerance to the anxiolytic effects developing within 6 to 12 months of continued use. [4]

Abrupt treatment cessation must be avoided particularly after long term treatment. Symptoms of abrupt treatment cessation can include increasing anxiety, rebound insomnia, aching limbs, nervousness and nausea, and the severity of withdrawal symptoms is usually related to dose and duration of treatment. Abrupt treatment cessation from very high doses can result in seizures. [4] If the drug is to be discontinued, the dosage should be tapered gradually.[2,6] After short term use, benzodiazepines can usually be ceased without any problems [4]

Benzodiazepines are generally thought to be safe in overdose when consumed on their own. Death after admission is rare and usually due to respiratory depression and aspiration of gastric contents. [7] Overdose is most dangerous when benzodiazepines have been combined with other sedative drugs such as alcohol, opioids or barbiturates. [4]

- **levels of abuse seen with these medicines**

Although one of the main concerns with benzodiazepines is abuse and misuse, it is in fact only a small minority of the population that misuses this class of drug. According to the National Drug Strategy Household Survey, in 2010, 3.2% of the Australian population had used tranquilisers/sleeping pills (including benzodiazepines) for non-medical purposes* at some stage in their life and 1.5% had used them in the past 12 months. [5]

This is in contrast to pain relievers/analgesics and opiates, where 4.8% and 1.0% had used them for non-medical purposes at some stage in their life respectively. Pain relievers/analgesics were the class of drugs most likely to be used for non-medical purposes in the previous 12 months, the majority (72.7%) being obtained over the counter (Pharmacy medicine or Pharmacist Only medicine). [5]

In 1993, the percentage of the Australian population that had ever used tranquilisers/sleeping pills for non medical purposes was 0.9%. There was a peak in 1998 to 3% and fell again to 1.5% in 2010. [5] This demonstrates only a very slight overall increase in usage over time.

Of those people who had used tranquilisers/sleeping pills for non medical purposes in the past 12 months, the source of supply was from a prescription for a medical condition in 30.1% of cases, whereas in 32.4% of cases it was obtained from a friend or acquaintance.

**non medical purposes refers to the use drugs in ways that induced or enhanced a drug experience, enhanced performance.*

- **therapeutic benefits**

The main therapeutic benefits of benzodiazepines are their rapid onset of action, high efficacy and low toxicity. [1] They are well tolerated and have a low risk of dependence, tolerance or withdrawal effects, if taken as directed.

Benzodiazepines have a wide plasma concentration therapeutic range meaning that the difference between the therapeutic level and toxic level of the drug is large. Therapeutic ranges of benzodiazepines are as follows.[8,9]

Drug	Therapeutic range
Diazepam	100-1000ng/mL
Clonazepam	15-60 ng/mL
Alprazolam	10-50 ng/mL
Lorazepam	700-1000ng/mL
Oxazepam	0.2-1.4 mcg/mL

- **Fatalities**

There have been only a few deaths directly attributed to benzodiazepine poisoning reported in the medical literature [7]

No fatalities due to benzodiazepine overdosage have been reported to Alphapharm over the past 10 years.

In a retrospective study carried out in Sweden over 14 years, there were 702 admissions to an intensive care unit due to benzodiazepine overdose. Among these cases, 144 had ingested a benzodiazepine alone, 200 had taken benzodiazepine with alcohol and 358 had taken benzodiazepines with other miscellaneous drugs. Only five of these cases were fatal and three were attributed to benzodiazepine alone. [10]

In another study in Britain in the 1980s, fatal poisonings attributed to benzodiazepines taken alone or with alcohol were calculated at an overall rate of 5.9 deaths per million prescriptions for benzodiazepines. [10.] During this period, 265.5 million prescriptions were issued and 1576 fatal poisonings were attributed to benzodiazepines. Of these, 891 (56.5%) were linked to a single compound alone, another 591 (37.5%) to a single compound with alcohol, and the remaining 94 (6%) were attributed to a combination of different benzodiazepines with or without alcohol. The categories of death were 848 (53.8%) suicides, 406 undetermined deaths (25.8%) and 322 accidental deaths (20.4%)[11.]

Fatality Toxicity Index for the following benzodiazepines were reported as follows: [11]

Drug	**Death Per Million prescriptions** (with or without alcohol)	**Death Per Million prescriptions** (Alcohol not involved)	**Estimated deaths per million patients** (with or without alcohol)
Alprazolam	5.9		24
Diazepam	4.0	1.5	16
Flunitrazepam	8.1		49
Nitrazepam	4.4	2.8	26
Oxazepam	2.3	1.1	9
Temazepam	11.9	7.1	71

- **Reported Side Effects**

Dose dependent CNS effects are common including drowsiness, oversedation and light-headedness. Many other benzodiazepine adverse reactions are considered infrequent or rare.

There were only 26 benzodiazepine adverse events reported to Alphapharm and four reported to the Therapeutic Goods Administration (TGA) for Alphapharm branded benzodiazepines during 2010 and 2011. This equates to 0.0003% of all domestic sales of Alphapharm benzodiazepines.[12] The lack of adverse events reported to Alphapharm and the TGA appears to support the relative safety of benzodiazepines established in the studies previously reviewed in this document.

- **General recommendations for use**

To help ensure the safe and efficacious use of benzodiazepines and to help minimise the concerns regarding dependence, withdrawal and abuse potential, the following general principals should be followed when prescribing and dispensing benzodiazepines. This advice is readily available to healthcare professionals through the Psychotropic Therapeutic Guidelines, Australian Medicines Handbook and Product Information, all well known medicine reference sources.

- Treatment with benzodiazepines should be part of a broader treatment plan and in general should not be considered as first-line treatment.

- Proper counselling should be given to patients by doctors or pharmacists, cautioning them about the risk of dependence, abrupt withdrawal and side effects such as the potential to cause residual day time drowsiness.

- Sedation may persist the following day after benzodiazepine dosing and the effects of alcohol and other CNS depressants e.g., opioids, can be potentiated. Patients should be warned that this may affect their ability to drive and operate machinery safely.[4]

- As stated in all benzodiazepine Product Information, the continuous long term use is not recommended, and should be limited to the smallest effective dose for the shortest time possible and a definite limited duration of use agreed with the patient (2-4 weeks). If longer term use is required, the patient must be advised to consult their doctor before abruptly discontinuing benzodiazepine therapy. Manifestations of withdrawal, especially the more serious ones, are more common in those patients who have received excessive doses over a prolonged period. In these situations, the benzodiazepine should be terminated by tapering the dose to minimise occurrence of withdrawal symptoms.[2,6,13]

- Patient selection is very important. Benzodiazepines should be avoided in people who have a history of drug or alcohol abuse or are addiction prone. The elderly also must be prescribed these medicines with caution as they may be more susceptible to the sedative effects of benzodiazepines and associated giddiness, ataxia and confusion, which may increase the possibility of a fall. [13]
- The need for continued therapy with benzodiazepines should be monitored periodically and large dosages or quantities must not be prescribed for patients. [13]

(b) The purposes for which benzodiazepines are used and the extent of use of benzodiazepines

Registered indications for benzodiazepines include significant medical conditions unrelated to their anti-anxiety and hypnotic activity.

The utilisation of these medicines over the past two full years for which sales data are available has remained relatively consistent.

(c) Toxicity of benzodiazepines

The most common side effects associated with benzodiazepines in routine clinical use are manifestations of excessive depression of the CNS; adverse effects related to other physiological systems are rare.

The side effects of benzodiazepines occurring most frequently include drowsiness, muscle weakness, light headedness, vertigo, ataxia, dysarthria, diplopia, blurring of vision, confusion, apathy, and vertigo. The relative risk of such effects varies with individual patient susceptibility; because of pharmacokinetic changes associated with aging, for example, the elderly may be at increased risk. [13]

Adverse CNS side effects usually occur in the first few days of benzodiazepine therapy and may diminish with continued therapy or reduction in dosage. [2]

The relative safety of the benzodiazepines is most clearly evident in cases of overdose. [10] Even massive overdoses, if taken without other CNS depressants, are rarely fatal. Morbidity and mortality associated with drug overdoses declined dramatically as benzodiazepines replaced older sedative–hypnotics; this has been one of the most important advantages of this drug class.

Overdosage of benzodiazepines is usually manifested by degrees of CNS depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion, lethargy, dysarthria and paradoxical reactions. In more serious cases, symptoms may include ataxia, CNS depression, hypotonia, hypotension, respiratory depression, cardiovascular depression and coma, and very rarely proves fatal. It must be borne in mind that multiple agents may have been taken.[13]

(d) The dosage, formulation, labelling, packaging and presentation of benzodiazepines

The recommended dosage depends on the type of benzodiazepine, its strength, and the condition for which it is being taken. [13]

Drug	Presentation	Packaging	Dose [13]
Alepam	15mg, 30mg tablet	(25) Bottle	7.5 – 30mg three to four times a day
Alodorm	5mg tablet	(25) Bottle	2.5-20mg at bed time
Antenex	2mg, 5mg tablet	(50) Bottle, (30), (90) blister pack	Adults: 5 to 40 mg daily. Ambulatory patients. Average dosage is 2 mg three times daily or 5 mg in the evening and 2 mg once or twice during the day. Muscle spasm. 10 to 30 mg daily. Elderly or debilitated: 2 mg twice daily or half the usual adult dose. Hospital treatment of tension, excitation, motor unrest: 10 to 15 mg three times daily until the acute symptoms subside.
Hypnodorm	1mg tablet	(30) Bottle with CRC	Adults: 1 to 2 mg on going to bed. Elderly: 0.5 to 1 mg.
Kalma	0.25mg, 0.5mg, 1mg, 2mg, tablet	(50) Bottle	Anxiety: 0.5-4mg daily (in divided doses) Anxiety with depressive symptoms: 1.5-4.5 daily (in divided doses) Elderly patients in the presence of debilitating disease: 0.5-0.75mg daily (in divided doses and increase as needed)

			Panic related disorders: Start at 0.5-1.0mg at bed time and increase as needed
Temaze	10mg Tablet	(25) Bottle	10-30mg one hour before bed

All Alphapharm benzodiazepines have Consumer Medicine Information (CMI) leaflets, which contain the following relevant warnings:

Under the heading **"What ... is used for."**
"In general, benzodiazepines such as (insert name) should be taken for short periods only (for example 2 to 4 weeks). Continuous long term use is not recommended unless advised by your doctor. The use of benzodiazepines may lead to dependence on the medicine."

Under the heading **"How long to take ... for."**
" Usually, (insert name) should be taken for short periods only (for example 2 to 4 weeks). Continuous long term use is not recommended unless advised by your doctor. The use of benzodiazepines may lead to dependence on the medicine."

(e) The potential for abuse of benzodiazepines

Although benzodiazepines are less likely to be abused than previously available sedative/hypnotics, they are not free from abuse potential. Drug abusers are often poly-drug dependent patients, and their drug use patterns tend to be chaotic with benzodiazepines used to augment or substitute for other drugs, notably opiates. Benzodiazepines may also be used to terminate a stimulant binge.[4]

According to an AIHW report, only 3.2% of the Australian population have ever abused or misused tranquilisers/sleeping pills in their life time and in only 30% of these cases the drugs where obtained from a prescription from a doctor. In the majority of cases, drug abusers were obtaining the medicines by other means, usually from friends or an acquaintance. [5]

Death from overdose is rare[10], and in the absence of a history of substance abuse, patients are not likely to either increase the dose or to use the drugs for recreational purposes. [14,15]

Proper patient selection and adherence to clinical guidelines can minimise benzodiazepine misuse and abuse.

As a general rule, it is recommended that prescriptions should not be issued to patients not well known to the doctor and should be issued on a short term basis only.[4]

(f) Other Matters for consideration

THE ROLE OF THE HEALTH PROFESSIONAL IN MEDICINES UTILISATION

Benzodiazepines must be used rationally to best maximise their advantages and minimise their disadvantages.[1]

All prescription medicines in Australia have a Product Information (PI) document summarising all relevant information necessary for the safe and efficacious use of the medicine. The document is designed to assist doctors, pharmacists and nurses in their decision to prescribe and supply the medicine to an individual patient, so they can appropriately balance the risks and benefits of the medicine relevant to the individual.

It is the prescriber's responsibility to weigh the risks and benefits of a medication for an individual patient and the pharmacist's role in providing expert professional advice about the use and effects of medications.

It may therefore be argued that any decision to prescribe a benzodiazepine is based on this information, in the context of individual patient consultation, rather than the schedule applied to the agent.

Alphapharm also makes available a Consumer Medicines Information (CMI) leaflet for all its benzodiazepines providing the consumer with important information that they should consider before, during and after taking the medicine. The CMI also helps the patient discuss the use of the medicine with their doctor or pharmacist and raise any questions or concerns they may have with the medication with their health care professional.

Both the PI and CMI clearly caution that benzodiazepines should be taken for short periods only (for example two to four weeks), that continuous long term use is not recommended unless advised by the doctor and that the use of benzodiazepines may lead to dependence on the medicine.

The quality use of medicines in Australia is dependent on doctors and pharmacists prescribing and supplying medicines in a responsible manner.

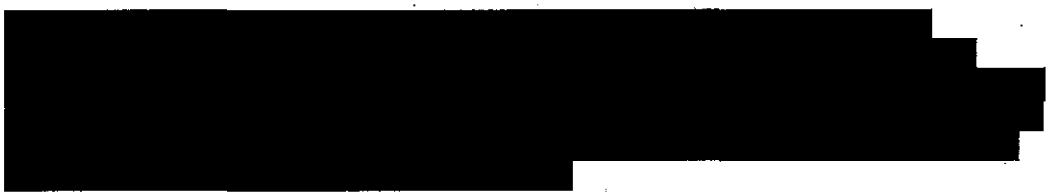
"Schedule 8" (Controlled Drug) applies to medicines that should be available for use but require restriction of manufacture, supply, distribution, possession and use to reduce abuse, misuse and physical or psychological dependence. Narcotic analgesics are "Schedule 8" medicines, however this restricted schedule has failed to fully prevent the abuse and misuse of this class of drugs. In the AIHW report on Drug Use in Australia, the percentage of Australians that had ever used an opioid for non medical purposes was 1% (~ 220, 000 people).[5] It is well documented in the literature that these medicines are widely misused and abused all over the world. In North America, oxycodone contributed to the largest number (5548) of all drug related deaths during the period 1998 to 2005 and in Australia, there were 465 oxycodone related deaths between 2001 and 2009.[16]

Therefore, restricting the schedule of medicines to S8 does not necessarily prevent the abuse and misuse of these medicines.

THE ADMINISTRATIVE AND LOGISTICAL IMPACT

State and federal legislation proscribes specific requirements on the packaging, labelling, procurement, storage, delivery, recording and validation of controlled medicines, beyond the requirements for other medicines.[18]

In particular, controlled drugs must be stored separately in mild steel plate, lockable and securely fixed safes at manufacturer, wholesaler and pharmacy level. The current volume of sales of benzodiazepines, even if substantially reduced by the proposed legislation, will significantly exceed current storage capacity, particularly at community and hospital pharmacy level.



The prescriber of controlled drugs must record and retain specific details of the person to whom the prescription is issued, and details of the dose, frequency and directions for use of the medicine.

The pharmacist must verify the authenticity of the prescriber before dispensing the controlled medicine.

Rescheduling of benzodiazepines will significantly increase the administrative workload and logistical requirements of health professionals and others involved in the supply pathway.

CONCLUSIONS

In summary, benzodiazepines are very effective in relieving the signs and symptoms associated with a wide variety of disorders including generalised anxiety, panic disorder, and insomnia. In addition, benzodiazepines have important roles in other more critical medical conditions such as epilepsy, anaesthesia, substance abuse and psychiatry. Furthermore, they have few troublesome side effects and are considered relatively "safe" in terms of direct fatal poisoning in overdose and the frequency of severe reactions.[10,11]

Concerns regarding dependence, withdrawal, and abuse potential with benzodiazepines can be largely limited by following strict guidelines for the use of these agents. This includes using the smallest effective dose and limiting duration of use, providing proper counselling to patients on side effects and the potential for dependence, and appropriately selecting which patients are the most likely to benefit from these agents and avoiding use in patients who have a history of abuse or are addiction prone.

Rescheduling medicines cannot on its own achieve these goals, as they rely on education designed to implement effective prescribing practices and appropriate support and information if consumers are to continue to use these medicines safely and effectively.

Inappropriately restricting benzodiazepines, may lead to the substitution of alternative medicines that may have decreased efficacy and greater safety concerns. [17]

Although there is a need for the careful prescribing and dispensing of benzodiazepines, we do not believe that rescheduling benzodiazepines to "Schedule "8 will reduce the relatively small amount of abuse seen with these drugs, but will make it more difficult to access for the overwhelming majority of patients who use them appropriately, conservatively and responsibly.[15,17]

References.

1.Ashton H. Guidelines for the Rational Use of Benzodiazepines. When and What to Use. Drugs. 1994 Jul 48(1):25-40

2.American Society of Health System Pharmacists. AHFS Drug Information MD, USA. Authority of the Board of American Society of Health System Pharmacists American Hospital Formulary Service 2012

3. Chouinard G. Issues in the clinical use of benzodiazepines: potency, withdrawal, and rebound J Clin Psychiatry 2004;65 Suppl 5:7-12

4. Psychotropic Expert Group. Therapeutic Guidelines. Psychotropic Version 6. Melbourne:Therapeutic Guidelines Limited;2008

5. Australian Institute of Health and Welfare 2011: Drugs In Australia 2010: tobacco, alcohol amd other drugs.Drug statistics series no.27.Cat. no. PHE 154. Canberra:AIHW

6. Australian Medicines Handbook 2012.13th Edition. Australian Medicines Handbook PTY LTD;2012

7. Buckley NA, Dawson AH, Whyte IM, O'Connell DL. Relative Toxicity of Benzodiazepines in Overdose BMJ 1995;310:219-21

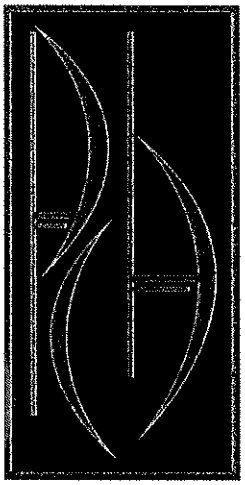
8. Kratz A, Ferraro M, Sluss P, Lewandrowski KB. Case Recored of the Massachusetts General Hospital. Laboratory Reference Values N Engl J Med 2004;351: 1548-63

9. Tietz NW (Ed): Clinical Guide to Laboratory Tests, 3rd Edition. WB Saunders 1995

10.Hojer J, Baehrendtz S, Gustafsson L. Benzodiazepine Poisoning: Experience of 702 Admissions to Intensive Care Unit during a 14 year period. Journal of Internal Medicine 1989:226:117-122

11. Serfaty M, Masterton G. Fatal Poisonings attributed to benzodiazepines in Britain during the 1980s.BJP 1993;163:386-393

12. Data on File. Alphapharm Domestic Sales on Alepam, Alodorm, Antenex, Hypnodorm, Kalma, Temaze.2010-2011
13. Product Information leaflets for Alepam, Alodorm, Antenex, Hypnodorm, Kalma, Temaze.
14. Ciraulo DA. Abuse Potential of Benzodiazepines. Bull NY Acad Med 1984 61:8;728-741
15. Piper A. Addiction to Benzodiazepines-How Common? Arch Fam Med. 1995;4:964-970
16. Roxburgh A, Bruno R, Larance B, Burns L. MJA 2011 195:280-284
17. Moller H. Effectiveness and Safety of Benzodiazepines. J Clin Psychopharmacol. 1999 Dec;19 (6) (Suppl 2):2S-11S.
18. Poisons and Therapeutic Goods Regulations 2008. Sydney, NSW.



Palliative Care Australia

Submission to the Therapeutic Goods Administration

on

Proposed reclassification of benzodiazepines to Schedule 8

on behalf of
Palliative Care Australia

Contact:

[redacted]

January 2013

Overview

Palliative Care Australia (PCA) welcomes the opportunity to discuss the prescribing of benzodiazepines and issues of concern about the use and misuse of this class of drugs.

PCA does NOT support the proposed reclassification of benzodiazepines.

PCA would, however, support exploration of a range of methods of addressing the potential misuse of these drugs that does not include reclassification. The conduct of a review of prescribing patterns, and development of a comprehensive educational program to improve understanding of best practice prescribing could valuably complement this.

Background

On 29th November 2012, the Australian Government Department of Health and Ageing – Therapeutic Goods Administration (TGA) issued a public notice inviting submissions regarding a proposal to reschedule certain medications, including benzodiazepines, from Schedule 4 to Schedule 8.

Benzodiazepine use, misuse and adverse effects

Benzodiazepines are a group of medications that are generally prescribed to treat insomnia, anxiety and panic disorders, but also have indications for seizure management, acute behavioural disturbance, alcohol withdrawal, muscle spasm, premedication and sedation for procedures and in intensive care units. Benzodiazepines available in Australia include:

Generic Name	*Brand Name*
Alprazolam	Alprax, Kalma, Xanax, Zamhexal
Bromazepam	Lexotan
Clobazam	Frisium
Clonazepam	Paxam, Rivotril
Diazepam	Antenex, Ducene, Valium, Valpam
Flunitrazepam	Hypnodorm
Lorazepam	Ativan
Midazolam	Hypnovel
Nitrazepam	Alodorm, Mogadon
Oxazepam	Alepam, Murelax, Serepax
Temazepam	Normison, Temaze, Temtabs
Triazolam	Halcion

The Australian Medicines Handbook 2012 lists potential common adverse effects of benzodiazepines as drowsiness, over-sedation, light headedness, memory loss, hypersalivation, ataxia, and slurred speech, and potential less frequent adverse effects as headache, vertigo, disorientation, confusion, paradoxical excitation, euphoria, aggression and hostility, anxiety, decreased libido, anterograde amnesia, respiratory depression and hypotension.

There has been much documentation and many studies into the use and misuse of benzodiazepines in Australia and other countries. Along with opioids they are also the prescription drugs most commonly associated with illicit use. While recommended only for short term use, they are commonly prescribed long term particularly in the elderly, and studies have shown their use correlates to an increased rate of falls[1].

While benzodiazepines can be effective for short term management of insomnia or anxiety, non-drug treatments (eg behavioural therapy, cognitive therapy, light therapy) are considered first line treatments offering better long term outcomes. Relaxation techniques and good sleep hygiene strategies are also of benefit.

Long term use of benzodiazepines may result in the development of tolerance and dependence. Tolerance results in reduced efficacy and hypnotic effect. Dependence can develop in some patients where drug seeking behaviour and craving may occur. Sudden cessation of benzodiazepines may produce withdrawal symptoms such as anxiety, dysphoria, irritability, insomnia, nightmares, sweating, memory impairment, hallucinations, hypertension, tachycardia, psychosis, tremors and seizures.

Benzodiazepine use in palliative care

Benzodiazepines are a class of drugs used widely in the control of problematic symptoms in palliative care patients. It is commonly used in the management of nausea and vomiting, panic attacks and anxiety, acute dyspnoea, acute pain (associated with anxiety), catastrophic haemorrhage, seizures and in the terminal phase to treat agitated delirium.

Reclassification of benzodiazepines to Schedule 8 (S8) will mandate that all drugs of this class be locked away in designated drugs cabinets and exact quantities listed in log books for each drug. S8 classification would also exert limits to the quantity of benzodiazepines prescribed on a single prescription or mandate the need to write authority prescriptions for more than a month's supply.

Benzodiazepine use in residential aged care

Benzodiazepines are widely used in residential aged care facilities in Australia as prescribed treatments for sleeplessness and anxiety and to assist in managing the behavioural and psychological symptoms of dementia. Guidelines are in place relating to the use of this class of drug in residential aged care[2].

[1] Rossat A, Fantino B, Bonque B, Colvez A, Nitenberg C, Annweller C, Beuchet O *Association between benzodiazepines and recurrent falls: a cross-sectional elderly population-based study*, J Nutr Health Aging 2011 Jan; 15(1): 72-7

[2] Blogg LC, Suzuki N, Roberts M, Clifford RM, *Prescribing Benzodiazepines In Residential Aged-Care Facilities*, J Pharm Pract Res 2012; 42: 287-90

Potential impact of benzodiazepine rescheduling in palliative care and aged care

The proposed reclassification of this class of drug to S8 will restrict access to these drugs for palliative care patients needing urgent treatment of acute symptoms. For example, in the hospital or residential care setting at present, drugs such as lorazepam, clonazepam or even midazolam may be available in a locked cabinet by the bedside of patients with unpredictable, acute dyspnoea or panic attacks. These symptoms are often very severe, and produce physical, mental and emotional distress.

Appropriate medical management of these symptoms requires that treatment be administered as soon as possible to avoid harm to patients. In the current situation, a severely distressed patient would call for attention and await response by a nurse. The nurse would unlock the drawer in the bedside cabinet and dispense the dosage according to the order in the medication chart.

S8 classification will impact on patient care as when a patient requires a benzodiazepine for extreme dyspnoea for example, a nurse would firstly respond to the patient "call bell", then locate the medication chart where the drug is prescribed, locate another nurse (usually two Registered Nurses (RNs) are required – exceptions may exist in residential aged care facilities that may only have one RN and one Enrolled Nurse (EN) present during a shift) with the keys to the designated drugs cabinet, both nurses have to identify the correct drug, dosage and formulation, cross check the quantity in the log book and subtract the dose dispensed, as well as record the patient's details in the log according to S8 regulations, take the drug to the patient, confirm the patient's details on medication chart and wrist band, dispense the drug to the patient and observe the dose being consumed.

The delays created by this process are unacceptable in situations of extreme patient distress. In some facilities, for example in low care residential aged care facilities, there might only be one nurse rostered on a shift – resulting in S8 drug dispensing not occurring on that shift.

S8 classification would exert limits to the quantity of benzodiazepines prescribed on a single prescription or mandate the need to write authority prescriptions for more than a month's supply. This added layer of bureaucracy is a disincentive for doctors to prescribe these medications and may create situations where patients will run out or not have the medications available when it is most needed.

PCA also notes that pharmacies must store S8 medicines in a medicine safe that meets jurisdictional legislative requirements. Such medicine safes have a limited storage capacity and with more products being restricted to S8, pharmacies must assess and resolve any storage issue. Replacing a safe or installing an additional one can be costly, and some pharmacies may not have the space for such measures without a significant refit of the dispensary. The proposed change is likely to have a similar impact on aged care facilities with the extra security and administrative burden for staff in storing, handling and administering benzodiazepines as an S8 controlled medicine.

PCA would be most concerned should changes in the Schedule lead to difficulty in accessing benzodiazepines locally on prescription for people receiving community based palliative care. If community access becomes restricted, the result will be fewer people being able to access appropriate drugs to control pain and anxiety as they approach end of life.

Alternatives to rescheduling

PCA recognises that benzodiazepines are a class of drug that is open to misuse.

However, PCA argues that other mechanisms for control, including improvements in prescribing and the use of current tracking systems available through pharmacies, should be explored prior to rescheduling, which should only be a last resort.

PCA notes recent Australian research indicates that there is scope for improving prescribing and monitoring of the use of benzodiazepines in residential aged care[3,4]. PCA believes that benzodiazepines are drugs that are vital for palliative care, aged care and community care and supports their appropriate prescribing and use.

PCA believes it is also appropriate to regularly review the appropriate use of these drugs in aged care, noting that to do so will result in cost implications for aged care staff.

PCA would be pleased to work with the TGA and the Department of Health and Ageing to examine a range of control mechanisms that could be used to improve the prescribing and use of benzodiazepines in palliative care and aged care.

[3] Blogg et al, op cit

[4] Westbury JL, Jackson S, Peterson GM, *Psycholeptic use in aged care homes in Tasmania, Australia* J Clin Pharm Ther 2010 Apr;35(2):189-93

Benzodiazepines

[redacted]

All mail to:
P.O Box 6178
Sussex Inlet NSW 2540

Suite 2, Level 1
The Macey Building
144 Junction St
Nowra NSW 2541
Ph/Fax 02 4421 3439

Friday, December 07, 2012

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

By email

Dear Sir/Madam,

I am a physician practising only in the area of Addiction Medicine in Nowra, on the south coast of New South Wales. I wish to respond to the proposed rescheduling of all benzodiazepines to Schedule 8.

I trust that this is an ambit claim where an over-reaching goal hides the more specific intent of attaining a particular outcome - in this case, most likely and hopefully – the placement of **alprazolam** on Schedule 8.

I have worked in this field for more than 25 years and have firm views based on experience, both mine and others in regard to the Benzodiazepines. More recently my opinions were reinforced by discussion with colleagues and peers at the recent conference in Melbourne of the Australian Professional Society on Alcohol & other Drugs.

I am aware of the issues with BZD use in the elderly specifically as well as the issues of abuse with this group of drugs. For many years I supported the idea that Diazepam in the long term had no real place in treatment. Now, however, I note many working in Drug and Alcohol have modified and mollified their earlier hard-line position on this matter. I also now belong to this group.

Thus, I believe there would be scant professional support for the placement of all Benzodiazepines in Schedule 8. The inconvenience that this would create for no real gain would be widespread and extend well outside of the area of Addiction Medicine. The number of patients who have sustained long term benefit from the sensible use of many of the drugs in this category is legion. Indeed in

my practice, I have a number of patients whose life is markedly altered for the better by controlled dosing by the dispensing pharmacy in parallel with either methadone or buprenorphine.

If the conditions for prescribing all these drugs were to change, then I expect that it would cause a great deal of anxiety at many levels in the community. That said, I doubt it would have much of an impact on the use of temazepam for night sedation and diazepam for occasional anxiety.

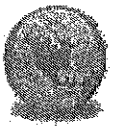
However, I do believe that there would be almost universal support for the removal of **alprazolam** form the 4th Schedule to the 8th by professionals working in the Drug and Alcohol sector. Almost every person I know who prescribes or works in an Opioid Replacement Program has experience of one or all of the following: episodes of violence, other criminal offences, accidents and occasional deaths associated with the concurrent use of alprazolam and other narcotics. This particular drug is without doubt the most highly prized and sought of all the Benzodiazepines at this time and like many I would like to see it follow the path of Clonazepam and Flunitrazepam onto Schedule 8.

Of course, much of this problem would disappear if doctors took a more proactive role when faced with doctor shoppers and refused to prescribe drugs with abuse potential to first-time patients or known abusers. When a patient on a methadone program travels from Nowra on the south coast to suburban Burwood in Sydney for an alprazolam script, you know something is not as it should be.

The fact that sustained release oxycodone is on the S.8 has not prevented it from becoming the most abused drug in Australia, let alone the world. Placing **alprazolam** on the 8th Schedule will not dissuade doctor shoppers, but it might just raise in the prescribing doctor's mind that he/she is doing something more significant than distributing jelly babies and liquorice.

We can only live in hope.

Yours sincerely



BENZODIAZEPINES [redacted]

[redacted]

Dear Sir

We are writing to inform you our strong affirmation to reschedule Benzodiazepines from Schedule 4 to Schedule 8 medications. We as community pharmacist and GP who are involved in opioid replacement program over the past 10 years have seen the easily availability, prescribing and misuse of Benzo's in the community. They have a very significant impact on the health and well-being of a number of people and their families. All current evidence have pointed out that the therapeutic place for benzo's prescribing is very limited, however they are wildly prescribed by GPs in community and aged care settings. In order to prevent the wide misuse of these drugs, it is imperative that they be restricted and a change in schedule will be the first and most important step in this regard. We have seen the changes they have cause in the personalities of long term users and the impact they have on families of benzo's users. We have seen generations of families addicted to benzo's, households having mum, dad, grand-parents and children all on benzo's.

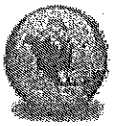
We will strongly recommend to restrict benzo's prescribing and develop guidelines for GPs.

Thank you

[redacted]

[redacted]

Benzodiazepines



[redacted]

To whom it may concern,

I am writing as I am against the proposal to reschedule benzodiazepines from schedule 4 to schedule 8. There is a lot of extra paperwork associated with schedule 8's. As a pharmacist, it would really slow me down having to write all the schedule 8 medicines into the controlled drugs register and it would mean we would have to get a new safe to fit all the benzodiazepines in it.

In addition, the doctors at my clinic are already very pressed for time and it would increase their workload substantially if they have to do extra paperwork organising permits for benzodiazepines. I believe that rescheduling benzodiazepines will not affect prescribing of them too much, but it will affect the time health professionals have to spend improving patient health, as they will be doing schedule 8 administration work instead.

Regards,

[redacted]

[redacted]

[redacted]

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

My submission as a Consultation Community Pharmacist who has worked as an employee, employer, locum pharmacist for > 40 years

Rescheduling of all Benzodiazepine Medication to Controlled Drugs (CD)

Rescheduling will not address any QUM issues
Education, dissemination of appropriate information to Health Professionals & the general community will impact more significantly- prohibition simply does not achieve the desired outcomes in the Quality Use of Medication (diversification, drug seeking behavior in regard to illicit use of Fentanyl patches is an excellent example of the failure to limit or reduce access and harm)

Rescheduling **will**

- Increase recording, secure storage burden, for pharmacists without any real immediate Quality Use of Medicines (QUM) benefit
- CD requirements have not reduced or stopped illicit drug use, drug seeking behaviour or diversion

In Victoria Benzodiazepine drugs are in Schedule 11 and this imposes a requirement to report to the Dept Health all unusual drug useage of these medications (Doctor shopping or excessive use)

- Money spent in changing the scheduling and consequential education of Health Professionals could be more effectively diverted to increasing the disbursement & monitoring the current scheduling requirements and consequential data collection
- rescheduling may restrict access (eg Rohypnol use) but will not address the fundamental issues about the drug seeking behaviour, over use, inappropriate use situations and treating the UNWELL population will still not become a priority

[redacted]

[redacted]

15/05/2013

Benzodiazepines

[redacted]

Hi
I am a registered pharmacist. I am also qualified to do medication review. I work at a private pysch hospital in Sydney.
I feel that the rescheduling of benzo's from S4 to S8 would greatly impinge on nursing and pharmacy time, disadvantaging patient care in a system already strapped for time.
I would be grateful if you would consider leaving the benzo's as S4.

regards
[redacted]

APS Australian Psychological Society

Level 11, 257 Collins Street
Melbourne VIC 3000
PO Box 38
Flinders Lane VIC 8009
T: (03) 8662 3300
F: (03) 9663 6177
www.psychology.org.au

January 17, 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA 2601

Dear Sir

Re: Proposal to reschedule Benzodiazepines from Schedule 4 to 8

The Australian Psychological Society (APS) represents the interests and standards of care of Australian psychologists. It has over 20,000 members which represents nearly two-thirds of registered psychologists. A large number of its members work in the health domain and engage with the Australian community members in various aspects of their physical, psychological and social well being; a section of these practitioners work specifically with clients with mental health and mental illness issues. All of them will at times have reason to work with clients for whom benzodiazepines have been a source of assistance or at times a focus of abuse. For these reasons the APS has noted the intention to alter the accessibility of the group of medications referred to as benzodiazepines and to register the views of its members.

The APS recognises the concerns of the TGA with regard to the abuse of these drugs and applauds the intention to find ways to reduce this harm to the well being of community members. At the same time, it must raise misgivings about the possible interference in the ready access to these medications where they are used effectively to reduce the pain and suffering of individuals and thereby contribute as stand alone or adjunct therapies for a range of physical and psychological disorders.

A good example of such situations is the extensive work done by psychologists, often in multi-disciplinary teams, to reduce and assist with the management of chronic pain that can result from a range of social, occupational and/or physical disorders. A second group for whom benzodiazepines have often been a helpful adjunct to recovery or management have been those with sleep disorders. This is particularly relevant for post-traumatic disturbed sleep among veterans and victims of disasters. For both these groups, and other similar conditions, any further restriction on their access could be counterproductive.

While the APS concedes that more rigorous monitoring of the usage of such medications may assist with reducing the prevalence of misuse and

abuse, it finds the process a rather blunt one and observes that it fails to be coordinated with other initiatives and measures that may assist those whose reasons for abuse and misuse are not effectively acknowledged or managed. Once again, a good example would be many community members who struggle with untreated, or unsuccessfully treated, chronic pain. Another example would be untreated depression. Many of these may find themselves abusing/misusing benzodiazepines out of desperation rather than miscreant behaviour. Many such persons are already often disadvantaged and with limited resources and may find this rescheduling another example of the alienation and confined access to services that their circumstances have prompted them to perceive as real.

The APS therefore suggests that accompanying the rescheduling should be measures and initiatives as part of a broader health package to address the health needs of those for whom the drugs have been a very effective palliative or treatment and for whom tighter access may become a real barrier to care. The APS would suggest that the current groups of users, and the conditions for which they seek these medications, could be identified and alternative ameliorating interventions be promoted. From a psychological perspective, it has been well established by rigorous research in recent years that a number of psychological interventions (CBT, ACT and pain management techniques) are as effective as medication and could assist such patients to enhance the effectiveness of medication or reduce their reliance on it. This would seem to be one added way of encouraging good clinical and health practice and reduce the appearance of blunt administrative interventions.

The APS would welcome the opportunity to engage in further consultation on this matter if a broader health initiative was to accompany these changes. Specific initiatives and proposals could be provided and expertise accessed through its membership.

Yours Faithfully

[redacted]

AMA

AUSTRALIAN MEDICAL ASSOCIATION
ABN 37 008 426 793
T | 61 2 6270 5400
F | 61 2 6270 5499
E | info@ama.com.au
W | www.ama.com.au
42 Macquarie St Barton ACT 2600
PO Box 6090 Kingston ACT 2604

10/224
D13/152

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601

email: SMP@health.gov.au

TGA proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8

Thank you for the opportunity to comment on the proposal to reschedule benzodiazepines from Schedule 4 to Schedule 8 medicines which is due to be considered by the Advisory Committee on Medicines Scheduling at its meeting in March this year.

Our comments are general given the lack of any background information or rationale provided by the TGA for the proposal.

The AMA supports evidence-based and responsible use of medicines.

In considering any proposal to move medicines from Schedule 4 to Schedule 8, the AMA urges the TGA to carefully assess the balance between the potential for abuse and the need for availability and access in the event of urgent clinical need, such as in hospitals.

The administrative burden, for both hospital staff and general practitioners, of benzodiazepines moving to Schedule 8 would be significant.

The AMA acknowledges that these medicines are at risk of abuse and illegal trade. However there are a range of existing mechanisms that seek to control this including patient and medical practitioner education, electronic tracking of dispensing, auditing of prescribing, and prosecutions.

Therefore the decision to move benzodiazepines to Schedule 8 should be supported by evidence that a Schedule 8 classification is necessary and will be beneficial.

In the absence of evidence, the AMA supports benzodiazepines remaining under Schedule 4.

[redacted]

Yours sincerely

[redacted]

[redacted]
Chair, AMA Therapeutics Committee

15 January 2013

gd:gm

1.1 Adrenaline, bupivacaine and lignocaine

WOOLPRODUCERS AUSTRALIA

25 January 2013

Veterinary Medicines Program
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
KINGSTON ACT 2604

Via email: SMP@health.gov.au

Dear whom it may concern,

RE: **Proposal to reschedule a veterinary preparation containing adrenaline, bupivacaine and lignocaine (Tri-Solfen) from Schedule 4 to Schedule 6.**

I am writing to provide WoolProducers Australia's (WPA) submission to the rescheduling of the above product. The attached includes a statement about WPA's role and how this relates to issues surrounding the rescheduling of the product named above.

WoolProducers Australia also greatly appreciates the extension of time granted for this submission.

Please feel free to contact me if you require further information.

Yours sincerely

[redacted]

PO Box E10, Kingston ACT 2604
NFF House, 14-16 Brisbane Avenue, Barton ACT 2600
T 02 4836 7369
E woolproducers@nff.org.au
www.woolproducers.com.au
A Member of the National Farmers Federation

Proposal to reschedule a veterinary preparation containing adrenaline, bupivacaine and lignocaine (Tri-Solfen) from Schedule 4 to Schedule 6.

1. BACKGROUND - WOOLPRODUCERS AUSTRALIA

WPA is the national Peak Industry Council representing and promoting the needs of Australia's wool growers.

The objectives of WPA are -

- To represent all Australian wool growers by providing them with a unified policy forum on national wool issues.

- To promote and carry on those activities necessary or advisable for the benefit and advancement of Australian wool growers social and economic well-being.

- To maintain WoolProducers Australia Ltd as the recognised peak national body for the Australian wool growing industry.

WPA represents all wool growers in Australia and provides an efficient mechanism to bring a diverse range of issues and needs to the policy making process. The Board draws on many formal and informal processes to achieve this. Principle amongst these is input from the state farming organisations, which have extensive networks across their jurisdictions

WPA is led by a National Executive made up of woolgrowers from around Australia. Each state farmer organisation member is represented on the Executive, while another three members are directly elected by growers Australia-wide. Democratically elected independent members gives anyone involved with wool growing in Australia the opportunity to be a part of the leadership team. This sets WPA apart from other grower groups and gives it the mantle of the true democratic voice of the Australian wool industry.

WPA plays a key role in working with the companies that are funded by grower funds - whether they are compulsory levies or fees for service - to develop constructive and profitable outcomes for industry. WPA carries the responsibility of appointing a director to the Australian Wool Exchange and the Australia Wool Testing Authority, promoting good corporate governance and ensuring that the interests of growers are paramount.

WPA maintains a close working relationship with Australian Wool Innovation (AWI) as the voice on behalf of their shareholders. WPA aims to contribute to AWI's programs for the benefit of growers, promoting responsible use of levy funds and ensuring good corporate governance.

WPA is the sole wool industry member of Animal Health Australia, and as such, carries a significant responsibility for decision making on behalf of the industry in the event of an emergency animal disease outbreak. WPA also provides advice to AHA on behalf of the wool

industry on a day to day basis through its representation on national animal health and welfare committees.

WPA also works closely with the Federal Department of Agriculture, Fisheries and Forestry on key issues such as animal health, emergency animal disease outbreak preparedness and industry development.

As the only woolgrower organisation with membership of the National Farmers' Federation, WPA is responsible for providing key policy advice on behalf of our members to Australia's peak farm body.

2 – MATTERS RELATED TO THE RESCHEDULING OF TRI-SOLFEN TO AN S6

The wool industry has been involved in a protracted debate regarding industry's ability to continue mulesing. Initially WPA supported the proposed 2010 phase out of mulesing however in light of the fact that no universally accepted alternative has been developed, WPA's current policy reflects the need to have a viable alternative before this practice is ceased.

In recognition that mulesing is an essential practice for many wool growers across Australia and that the welfare of sheep must be considered in all husbandry procedures, WoolProducers current policy surrounding mulesing also supports the use of pain relief for mulesing.

While figures suggest that around 70% of Merino lambs mulesed receive pain relief, the current S4 scheduling means the producers must employ the services of a veterinarian in order to obtain Tri-Solfen. This leads to an impediment in uptake for those producers who are in remote locations or do not employ veterinarian services on a regular basis.

The rescheduling of Tri-Solfen to an S6 could potentially see an increase in adoption of the use of Tri-Solfen for mulesing, ultimately leading to improved welfare outcomes for lambs undergoing mulesing.

As Tri-Solfen is currently only registered as *'a local anaesthetic and antiseptic gel spray for use on lambs to provide pain relief following mulesing'*, WPA acknowledges the concerns that if rescheduled to an S6 that there may be a greater chance that Tri-Solfen could be used 'off label' other than as *a one-off treatment for lambs that are to be kept for wool production.* WPA believes that the strict container and labelling required as part of the S6 requirements would provide an adequate safeguard to ensure that producers followed any prescribed protocols.

The 90 day withholding period also provides an adequate safeguard for any residue concerns of Tri-Solfen entering the food chain. A number of factors should also be considered surrounding the risks associated with residues from Tri-Solfen entering the food chain:

- Merino lambs are not usually sold for slaughter as they do not reach slaughter weights in optimal time.

- Under the Model Code of Practice for the Welfare of Animals: The Sheep, it is recommended that lambs are mulesed between 2 and 12 weeks, the 90 day withholding period would be adequate time for any Merino lambs that were sold for slaughter if Tri-Solfen was used between 2 and 12 weeks of age.

Under the application for registration of Tri-Solfen in October 2012, the applicants agreed to deliver an on-going program to ensure that 90-day withholding period is observed. It should also be noted that any residue risks would be just as likely to occur regardless of scheduling status.

3 – CONCLUSION

WPA has supported research and development into pain relief for sheep husbandry procedures, and alternatives to mulesing. The industry acknowledges that mulesing is an essential animal husbandry procedure and accepts that there is a need on the basis of animal welfare for a registered product to relieve pain post-mulesing.

WPA believes that the positives of rescheduling Tri-Solfen to an S6, including greater uptake and better welfare outcomes far outweighs any concerns such as off label use and residue issues.

The rescheduling of Tri-Solfen from an S4 to an S6 will enable greater access to producers, leading to greater uptake by producers resulting in higher animal welfare outcomes and aligns with WPA's policy of supporting the use of pain relief for mulesing.

RSPCA

for all creatures **great** & **small**

1 March 2013

The Scheduling Delegate
c/- The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Dear Sir/Madam

Proposal to reschedule a veterinary preparation containing adrenaline, bupivacaine and lignocaine from Schedule 4 to Schedule 6

We have just become aware of a notice on the Therapeutic Goods Administration website regarding an invitation to comment on a proposal to reschedule a veterinary preparation containing adrenaline, bupivacaine and lignocaine from Schedule 4 to Schedule 6. The closing date for public comment is 17 January 2013. The footnote, however, points out that 'Notice inviting public submissions for the agriculture and veterinary chemicals and delegate initiated scheduling applications will be published on 7 February 2013 with the public comments due on 7 March 2013.' We trust that you will accept this submission.

Unfortunately, the only information provided on your website is that this proposal is to reschedule a veterinary preparation. As far as we are aware, there is only one veterinary preparation which contains the actives for which rescheduling is proposed and that is 'Tri-solfen'. This product is a local anaesthetic and antiseptic gel spray for use on lambs to provide pain relief following mulesing.

Mulesing is performed without anaesthesia and, prior to the introduction of Tri-solfen, generally also without pain relief. The operation is quick; however the acute pain is long lasting - up to 48 hours. Mulesed lambs will socialise less, lose weight in the first two weeks post mulesing, exhibit behavioural indicators of pain including prolonged standing and less time lying and feeding, and stand in a hunched position. The effect on gait and growth may be apparent for up to three weeks following the procedure.

The RSPCA believes mulesing should only be carried out in areas where there is a high risk of fly-strike and when it is in the long-term welfare benefit of the animal. Mulesing must only be performed as a measure of last resort and where alternative humane options are not viable. We believe that mulesing must always be performed by an accredited operator using pain relief as per the instructions on the product label. When using Tri-solfen, this latter aspect is important as the timing of application influences the efficacy of the product.

Under the current scheduling arrangements, Tri-solfen has been readily taken up by over 70% of woolgrowers who continue to mules their lambs, resulting in a significant reduction in animal suffering.

RSPCA Australia Inc.

ABN 99 668 654 249

P 02 6282 8300
F 02 6282 8311
E rspca@rspca.org.au
W rspca.org.au

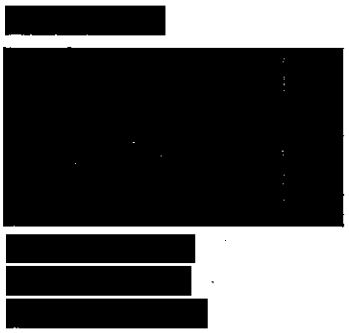
PO Box 265
Deakin West ACT 2600

As Australia's leading animal welfare organisation, we know that the general public have less and less tolerance of husbandry procedures that cause pain, suffering and distress to the animal concerned - particularly those so visually confronting and obviously painful as mulesing. And, as you may be aware, this global trend is becoming increasingly evident in the purchasing behaviour of retailers and consumers - including those that purchase Australian wool or wool products.

To this end, RSPCA Australia supports the continued availability of Tri-solfen and similar pain relief products, to ensure that, where a painful procedure is carried out, it is conducted with appropriate pain relief.

RSPCA Australia is not opposed to the rescheduling of the named active ingredients, as long as it does not result in Tri-solfen no longer being available to woolgrowers for the purpose of alleviating the pain associated with the mulesing procedure and as long as the scheduling requirements ensure that the product continues to be used in the manner intended and described on the product label.

Please don't hesitate to contact us should you require further information.



Proposal to reschedule a veterinary preparation containing adrenaline, bupivacaine and lignocaine (Tri-Solfen) from Schedule 4 to Schedule 6.

February 2012

NSW Farmers' Association
Level 25, 66 Goulburn Street
Sydney NSW 2000

BACKGROUND – NSW Farmers Association

The NSW Farmers' Association is Australia's largest State farmer organisation representing the interests of its farmer members – ranging from broad acre, Livestock, wool and grain producers, to more specialised producers in the horticulture, dairy, egg, poultry, pork, oyster and goat industries. It is the largest representative body for wool producers in NSW and is a member of many peak bodies including WoolProducers Australia, Sheepmeat Council of Australia and the National Farmers Federation.

THE RESCHEDULING OF TRI-SOLFEN TO AN S6

NSW Farmers' policy seeks the development of cost effective and sustainable alternatives to mulesing and an increase research and development of new technologies to reduce incidence of, and increase protection from breech strike. At present, however, there is no universally accepted alternative to mulesing and as such it is imperative that affordable pain relief is available to farmers with a minimum of regulatory and other restrictions.

While figures suggest that around 70% of Merino lambs mulesed receive pain relief, the current S4 scheduling means the producers must employ the services of a veterinarian in order to obtain Tri-Solfen. This leads to an impediment in uptake for those producers who are in remote locations or do not employ veterinarian services on a regular basis.

The rescheduling of Tri-Solfen to an S6 could potentially see an increase in adoption of the use of Tri-Solfen for mulesing, ultimately leading to improved welfare outcomes for lambs undergoing mulesing.

As Tri-Solfen is currently only registered as 'a local anaesthetic and antiseptic gel spray for use on lambs to provide pain relief following mulesing', NSW Farmers acknowledges the concerns that if rescheduled to an S6 that there may be a greater chance that Tri-Solfen could be used 'off label' other than as a one-off treatment for lambs that are to be kept for wool production. NSW Farmers believes that the strict container and labelling required as part of the S6 requirements would provide an adequate safeguard to ensure that producers followed any prescribed protocols.

The 90 day withholding period also provides an adequate safeguard for any residue concerns of Tri-Solfen entering the food chain. A number of factors should also be considered surrounding the risks associated with residues from Tri-Solfen entering the food chain:

- Merino lambs are not usually sold for slaughter as they do not reach slaughter weights in optimal time.
- Under the Model Code of Practice for the Welfare of Animals: The Sheep, it is recommended that lambs are mulesed between 2 and 12 weeks, the 90 day withholding period would be adequate time for any Merino lambs that were sold for slaughter if Tri-Solfen was used between 2 and 12 weeks of age.

Under the application for registration of Tri-Solfen in October 2012, the applicants agreed to deliver an on-going program to ensure that 90-day withholding period is observed. It should also be noted that any residue risks would be just as likely to occur regardless of scheduling status.

Recommendations

NSW Farmers supports research and development into pain relief for sheep husbandry procedures, and alternatives to mulesing. The industry acknowledges that mulesing is an essential animal husbandry procedure and accepts that there is a need on the basis of animal welfare for a registered product to relieve pain post-mulesing.

NSW Farmers believes that the positives of rescheduling Tri-Solfen to an S6, including greater uptake and better welfare outcomes far outweighs any concerns such as off label use and residue issues.

The rescheduling of Tri-Solfen from an S4 to an S6 will enable greater access to producers, leading to greater uptake by producers resulting in higher animal welfare outcomes and support industry best practice which is the use of pain relief for mulesing.

Elanco Animal Health response to re-scheduling application for Tylosin

Elanco Animal Health

A Division of Eli Lilly and Company

112 Wharf Road, West Ryde

May 10, 2013

Elanco response to rescheduling application of tylosin

Executive Summary

Elanco requests the joint committees and delegates consider the five pillars of discussion Elanco raises in response to the scheduling application under review. These fivepillars are:

1) **Inconsistent scheduling decision process** - The submission of tylosin for a re-scheduling application in the manner proposed is inconsistent with the process used by the NDPSC to re-schedule other antibiotics as the JETACAR recommendations have been enacted. In previous applications to the NDPSC, advice was gained from EAGAR who assessed the resistance data currently available at the time and provided recommendations to the NDPSC for a decision.

2) **Failure to complete the macrolide review** - The failure by the APVMA to complete the macrolide review as required by JETACAR (Note response to Recommendation 2 from APVMA) has not been helpful to the animal health and veterinary industry in managing the development of prudent use guidelines. The lack of a rigorous scientific review on all macrolides means that this re-scheduling application will be undertaken in the absence of an overall understanding of macrolides as opposed to focusing on individual compounds. Elanco requests that the APVMA acts immediately to **complete** the macrolide review as stated in Recommendation 2 of the JETACAR report and also as outlined in the minutes of the NDPSC meeting 39.

3) **Expert review of new data** - Elanco has compiled significant new data related to the impact of macrolide use on macrolide resistance patterns across a variety of species and generated specific hazard/risk assessment documents on the specific concern of human failure of treatment due to a macrolide resistant organism. Elanco welcomes the opportunity to provide an extensive dataset as a response to a re-scheduling application but considers that an expert review is the appropriate procedure for valid scientific assessment to be undertaken and ensure a consistent decision making process across this complex area.

4) **Reasons used to support the re-scheduling application of Tylosin**

   Elanco has re-stated from the APVMA submission the basis that NDPSC made rescheduling decisions following JETACAR. These are:
   - the possibility of resistance generation in animals being transferred to humans,
   - co-selection of resistance to unrelated classes of antibiotics
   - the importance of the agents as therapeutic agents in some animal species
   - to protect their value in the treatment of mycoplasma and brachyspira in pigs
   - to protect the value of the macrolides in human health, and
   - to protect the value of tylosin in animals.

Elanco does not believe that the process proposed to review the scheduling status of tylosin will permit the current scheduling committee to meet the previously stated re-

scheduling decision objectives of NDPSC due to the lack of provision of an expert report to consider the aspects listed.

5) Senate Review of JETACAR

The intention to conduct this review was announced Dec 5, 2012 and the Terms of Reference taken from the announcement are outlined below.

SENATE FINANCE AND PUBLIC ADMINISTRATION REFERENCES COMMITTEE

TERMS OF REFERENCE

Inquiry into the progress in the implementation of the recommendations of the 1999 Joint Expert Technical Advisory Committee on Antibiotic Resistance

On 29 November 2012, the Senate referred the following matters to the Finance and Public Administration References Committee for inquiry and report by 21 March 2013:

Progress in the implementation of the recommendations of the 1999 Joint Expert Technical Advisory Committee on Antibiotic Resistance, including:

(a) examination of steps taken, their timeliness and effectiveness;

(b) where and why failures have occurred;

(c) implications of antimicrobial resistance on public health and the environment;

(d) implications for ensuring transparency, accountability and effectiveness in future management of antimicrobial resistance; and

(e) any other related matter.

Elanco asserts that given the announcement of this review, it is inappropriate to continue the re-scheduling assessment of tylosin until such time as the Senate review is completed. Elanco believes it is possible that during the Senate review some of the original recommendations proposed by JETACAR may be reviewed and amended. These changes will need to be formalised and communicated to industry with appropriate timelines and guidance as to what is expected from impacted applicants. The basis of the APVMA re-scheduling application for Tylosin is driven from JETACAR recommendation 6 but JETACAR recommendation 2 is also closely linked to this application. This recommendation includes the need to undertake the macrolide review as outlined in JETACAR as part of the risk analysis approach.

The APVMA have indicated that re-scheduling is a process that can occur outside of the macrolide review but Elanco wishes to reinforce the views expressed in pillars two and four of the executive summary of the previous Elanco submission sent in June 2012.

Elanco respectfully requests that the scheduling delegate continue to defer the tylosin re-scheduling application until such time as the outcomes of the senate review are confirmed.

Conclusion

Elanco wishes to contribute to this review to the same level of scientific rigour as previously conducted during rescheduling applications and all antibiotic reviews during JETACAR. Elanco welcomes the opportunity to submit the significant quantities of contemporary data that could be of value during this the assessment and would greatly appreciate an opportunity for this data to be fully reviewed.

To confirm the five pillars of the Elanco submission, these are listed in bullet point format below:

- Inconsistent scheduling decision process
- Failure to complete the macrolide review
- Expert review of new data
- Reasons used to support the re-scheduling application of Tylosin
- Senate review of JETACAR

1.2 Tylosin

DEBENHAM
Australia Pty Ltd ACN 100 242 526 ABN 14 100 242 526

PO Box 187 (Compass Arcade)
Leongatha VIC 3953 AUSTRALIA
Telephone: + 61 3 5662 5317
Facsimile: + 61 3 5662 5348
Email: office@debenham.com.au

Specializing in soil, crop, pasture and livestock nutrition
Treating mineral deficiencies at their source.

8th January 2013

Medicines and Poisons Scheduling Secretariat (MDP88)
GPO Box 9848
CANBERRA ACT 2601

Dear Secretariat

Re: TYLOSIN – Scheduling Submission

We offer the following submission regarding the rescheduling of TYLOSIN PHOSPHATE used at current label rate guidelines from its current Schedule of S5 to a Prescription Only Medication in the S4 Category.

As consultants to the dairy industry, we have substantial concerns over the resulting issues which will arise from the rescheduling of Tylosin phosphate as per the current label guidelines.

We would like to confirm for the committee that while tylosin phosphate is registered for the treatment of liver abscess in cattle, that Tylosin phosphate when fed according to label guidelines combined with Monensin sodium, is highly effective against gram negative microbes associated with the acidosis/rumenitis complex, including those which produce lactic acid. Tylosin alters the rate of fermentation, which helps to optimise rumen pH, contributes to a stable rumen environment and prevents ruminal and abomasal ulceration. This has a positive effect on the problem of acidosis in cattle.

If tylosin phosphate is rescheduled, other antibiotics with greater risk profiles for antimicrobial resistance would need to be used. The consequence is greater cost (as veterinary consultation would be needed) and the risk that antimicrobials which can induce cross-resistance with those used in humans may be used for legitimate therapeutic use. Tylosin in this respect is a very favourable option and significant amounts of data have been provided over the years to substantiate that antimicrobial resistance and cross-resistance is much lower with tylosin than many of the alternatives.

By using the combination of monensin-tylosin to optimise rumen stability, means that it becomes unnecessary to use and recommend the only registered product currently available to treat acidosis, being Virginiamycin. Our concern is that if the use of Tylosin is rescheduled, it will reduce our ability to provide our clients with a low cost preventive measures that are not related to human application to be used as a control of acidosis.

The only product registered for the direct treatment of acidosis in cattle is Virginiamycin. Virginiamycin has been demonstrated to have far greater risks of antimicrobial resistance that could impact humans and as a consequence, its use has already been substantively reduced when the APVMA recommended removal of all growth promoting claims and varying the approval to restrict use on Virginiamycin.

Being able to control this common problem in cattle by the use of tylosin phosphate reduces the use of virginiamycin or other antibiotics in the feed. The alternative, in the event of the rescheduling of the low concentrations of Tylosin phosphate in feedstuffs will be the greatly increased use of higher risk antimicrobials or to promote a system of off-label prescription which is less desirable for an S4 category medication.

If the objective of the committee is to review the potential for antibacterial resistance in humans, it should take into account that by rescheduling Tylosin based on current label guidelines, the dairy and feedlot industries will be forced to use Virginiamycin with inherently greater risks if used widely.

We contend that the use of antibiotics will not be reduced by rescheduling. What will happen is that the specific antibiotic used will change from Tylosin phosphate to Virginiamycin. Currently, we as Dairy consultants see only minimal use of Virginiamycin at farm gate level, dairy cows are milked in 300 day lactation, and Virginiamycin would need to be scripted for the duration.

Preventive management is needed to avoid rumenitis and acidosis in high yielding dairy cows. Failure to address this on a herd basis can lead to ulceration, death and severe economic impact to the industry.

We ask that the committee take this into account in their decision on the rescheduling of this antibiotic at low concentrations in stockfeed, specifically for the dairy and feedlot industries. We feel that the full consequences have not been fully considered and not all stakeholder views fully represented.

Yours Truly

[redacted]

1.2 Tylosin

Animal Health

18th January 2013

Scheduling Secretariat
Office of Chemical Safety
Office of Health Protection
Department of Health and Ageing
MDP 88
GPO Box 9848
Canberra 2601

Attention: Scheduling Secretariat, Office of Chemical Safety
Re: Possible Rescheduling of Tylosin phosphate

Good afternoon,

[redacted]

Doxal Australia Pty. Ltd. is the major supplier of Tylosin phosphate into the Australian market.

We ask that in the event the Committee makes the decision that Tylosin phosphate in low addition rates is re scheduled to an S4, that, at the discretion of the delegate, we are permitted an extension period in order to deplete any stockholding that we may have at the time.

We are required to carry sufficient stock of this medication to cover the forward requirements of our clients and any abrupt halt to the sales leaving us with unsaleable product would severely financially disadvantage our company.

We ask that consideration be given to our position in the event of a rescheduling.

[redacted]

DOX-AL AUSTRALIA PTY. LTD. ABN: 76 079 454 265
HEAD OFFICE: 21 Terrara Road, Vermont, Victoria AUSTRALIA 3133, Tel: +61 3 9874 1892 Fax: +61 3 9873 4194
NEW SOUTH WALES OFFICE: 15 Railway Parade, Balmoral Village, NSW, AUSTRALIA 2571, Tel: +61 2 48 899 003 Fax: +61 2 48 899 004
WESTERN AUSTRALIA OFFICE: 3 Peirse Way, Marmion, Western Australia, AUSTRALIA 6207, Tel: 0402 270627, Fax: +61 89243 5039

2.3 Part 1, Interpretation

Re: public comment - part 1 interpretation [SEC=No Protective Marking]
[redacted]
to:
SMP
24/02/2013 22:26
Hide Details
[redacted]
To: SMP@health.gov.au,
History: This message has been replied to.

Hi,
in addition to the above, I'd like to make an additional observation concerning isomers and stereoisomers.

Firstly, stereoisomers can exhibit distinct pharmacological and pharmocokinetic properties. For instance, I refer you to the recent intellectual patent decision concerning the difference between the drug citalopram (racemic) and escitalopram. It was decided in this case that escitalopram be designated a seperate scheduling status and intellectual patent on the basis of a significant pharmacological difference.
Therefore it is not obvious that stereoisomers be neccessarily included in the definition of "analogue" or "derivative".
Secondly, isomers that have the same linear chemical designation but a different conformation almost 100% of the time exhibit vastly different physichochemical and pharmacological properties, and therefore should be excluded from falling under the designation of "analogue" or "derivative".

In conclusion, I support the consideration of international intellectual patent laws in defining what might exclude something from being an analogue or derivative.
My final suggestion is that

: Stereoisomers and Salts exhibiting no substantially different pharmacological properties (both pharmacokinetic AND pharmacodynamic) from the parent molecule should be considered analogues or derivatives. Any broadening of this definition seems to run aground against intellectual patent law.

[redacted]

On Sun, Feb 24, 2013 at 4:10 PM, [redacted] wrote:

> Hi,
> here's my public comment relating to the interpretation of the terms synthetic, analogue and derivative.
>
> 1) I understand that the current understanding of "analogue" and "derivative" encompasses "ethers, esters, and salts". This definition may be too broad.
> I give the following reasons:
>
> a) ethers and esters of scheduled drugs may in fact fall under seperate intellectual patents, your legal advisory will need to confim that. Therefore it is unwise to include ethers and esters as analogues or derivatives, as this may stimie intellectual patents for new drugs, especially if the ester or ether has novel pharmacological actions.
>
> b) even "salts" may be too broad. For example, I cite the instance of hyocine butylbromide compared to hyocine hydrobromide.
> The former salt has a distinct and seperate pharmacokinetic profile.: it is not absorbed into systemic circulation, whereas hyocine hydrobromide and other related salts do. It is therefore

unwise to propose that all "salts" are analogues or derivatives of existing substances, given that some salts may exhibit distinct pharmacological properties. These distinct properties may also fall under seperately regarded intellectual patents.

Therefore, I support a narrowing of the definitions of "analogue" and "derivative" to include ONLY salts that exhibit a similar pharmacological profile.

As for the definition of "synthetic" I believe this is straightforward: anything made in a stepwise fashion requiring formation of the parent molecule is to be regarded as "synthetic". Any minor modifications made to naturally derived products, such as salts, ethers, esters and prodrugs should be regarded as "nonsynthetic", especially if the pharmacological profile is substantially similar to the naturally derived product. There is an issue as to simple modifications of natural products that result in drugs of substantially different pharmacological profiles, and such substances may indeed be granted a seperate intellectual patent. It might be wise in such a circumstance to consider such a substance "synthetic".

[redacted]

[redacted]

17/05/2013

Proposed amendments to the poisons standard referred by the delegate for scheduling advice [SEC=No Protective Marking]

[redacted]

to:
SMP
07/03/2013 13:24
Cc:
[redacted]
To: <SMP@health.gov.au>,
[redacted]

Dear Sir/Madam,
The increasing prevalence and detection of new analogues of existing illicit drugs in the Australian illicit drug marketplace is of high interest to both Law Enforcement and Health Agencies in Australia. On the 21st and 22nd February 2013 the Australian Federal Police(AFP), in cooperation with the National Institute of Forensic Science (ANZPAA/NIFS) and the Senior Managers of Australian & New Zealand Forensic Laboratories (SMANZFL), hosted a workshop in Canberra to derive a consistent definition of "drug analogue". I write to you as Chair of that workshop and on behalf of that consortium of Federal and State Agencies/Departments.

Representatives involved in the workshop and in agreement with the new definition were from the following agencies, included is their jurisdictional responsibilities.

AFP, Forensic & Data Centres – Illicit Drug Analysis Coordination for AFP and border seizures
Aust, National Measurement Institute – Illicit Drug Analysis for AFP and Australian Customs
WA, ChemCentre – Illicit Drug Analysis for WA Police
Victoria Police, Forensic Services Department – Illicit Drug Analysis for Victoria
NT Police, Forensic Science Branch – Illicit Drug Analysis for NT
Queensland, Department of Health, Forensic and Scientific Services– Illicit Drug Analysis for Queensland
ACT, Government Analytical Laboratory – Illicit Drug Analysis for ACT
Tasmania, Forensic Science Service Tasmania – Illicit Drug Analysis for Tasmania
NSW Police Force, Forensic Services Group – Illicit Drug Coordination & Analysis for NSW
NSW Health, Forensic & Analytical Science Service – Illicit Drug Analysis for NSW
SA, Forensic Science SA – Illicit Drug Analysis for SA

A broad range of input was considered by the group including community health, chemistry, pharmacology, toxicology, policing policy and AG initiatives. This additional input to the workshop was sourced from AG's, NZ health and forensic science agencies, NSW's Westmead Hospital Emergency Dept., NSW Police, Univ of SA and the Victorian Institute of Forensic Medicine.

I have attached a document, an AFP Minute, which summarises the intent and output of the workshop. Following the introductory preamble three sections provide information of direct relevance to your proposed amendments.

- **Section 1: Explanation of the existing analogue clauses** of the Commonwealth *Criminal Code Act 1995* (Sections 314.1(2) and 314.4(2))

- **Section 2: Potential issues / restrictions with the existing clauses** and reasons for making adjustments for the general definition
- **Section 3: Proposed general definition for "drug analogue"**

It was proposed by the workshop that the new definition of a drug analogue, included in section 3 of the attachment, should replace the existing definition in the Commonwealth *Criminal Code Act 1995*. Furthermore it was intended that this new drug analogue definition should be used in its entirety either by inclusion into or by reference from the various Australian jurisdiction drug or poisons Acts.

Thank you for the opportunity to contribute constructively to your proposed amendment. [redacted]

[redacted]

DRUG AND ALCOHOL OFFICE

Government of **Western Australia**
Drug and Alcohol Office

7 Field Street
MT LAWLEY WA 6050
Tel: (08) 9370 0333
Fax: (08) 9272 6605

Notice inviting public submissions under Regulation 42ZCZK of the Therapeutic Goods Regulations 1990

The following submission is presented on behalf of the Western Australian Emerging Psychoactive Substances Review Group.

The Western Australian Government's Drug and Alcohol Office has established an interagency Government group to coordinate action and provide advice to Government about synthetic cannabinoids and other synthetic psychoactive substances that may emerge. The core membership of the Western Australian Emerging Psychoactive Substances Review Group includes the:

- Western Australian Drug and Alcohol Office
- Western Australian Police
- Western Australian Department of Health – Pharmaceutical Service Branch
- Western Australian ChemCentre
- Western Australian Department of Commerce – Consumer Protection

In response to the Notice inviting public submissions under Regulation 42ZCZK of the Therapeutic Goods Regulations 1990, the Group wishes to provide comment on the following proposed amendments:

- Part 1, Interpretation – Advice on inclusion of terms, such as synthetic, analogue and derivative, to the Part 1, Introduction in order to better define these terms, their intent and purpose.

The issue of drug analogues, and the definition of such, is currently being debated across a number of jurisdictions, both nationally and internationally, in particular within the forensic drug chemistry forum.

The appearance of new analogue drugs, including synthetic cannabinoids, is one of the major emerging challenges being faced by both health and law enforcement organisations.

In Western Australia the *Poisons Act 1964* and *Misuse of Drugs Act 1981* reference the Poisons Standard (SUSMP) for the status of compounds in a particular schedule. As such, both health and law enforcement agencies are dependent on the use of the term 'derivative' as defined within the SUSMP in order to determine whether or not a new drug is covered within the existing schedules. This can often rely on an individual's expert opinion that can be challenged or difficult to determine, and may require comment from experts in the fields of chemistry, pharmacology and toxicology for each new compound.

At a recent workshop, attended by representatives from each state and territory forensic drug laboratory and Commonwealth laboratories, the Australian Federal Police and the Attorney-General's Department recommended that a harmonised approach to the definition of 'drug analogue' be taken.

This approach should lead to greater consistency between Commonwealth and state legislation, and support actions such as the *National Drug Strategy 2010-2015*, which has as one of its key objectives to *identify and respond to emerging issues* to reduce the supply of drugs.

A definition for the term 'analogue' already exists within Australian legislation, as found in the Commonwealth *Criminal Code Act 1995* Sections 314.1(2) and 314.4(2). This definition has previously been used for determining the legal status of new drugs and is currently being reviewed and updated.

The current use of the term 'derivative' in the context of the SUSMP includes a balanced consideration of the toxicology and pharmacology of a new drug, in addition to the chemical structure. Any adoption of a uniform analogue definition would potentially need to be complemented by a similar consideration of the toxicology and pharmacology aspects of new drugs.

The Western Australian Emerging Psychoactive Substances Review Group consider that a consistent approach to scheduling of drugs, along with harmonised definitions of terms including 'drug analogues' across the different jurisdictions is a worthy objective. The adoption of an agreed definition for 'drug analogue' based upon the existing definition as found in the Commonwealth *Criminal Code Act 1995* is an important and achievable step towards this goal.

I trust that this submission is of assistance to the Committee in its consideration of the proposed amendments as outlined in the TGA Delegate's notice paper.

Yours sincerely

Neil Guard
Executive Director
Drug and Alcohol Office

20 May 2013