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04 June 2013

Medicines and Poisons Scheduling Secretariat (MDP88)
GPO Box 9848
CANBERRA ACT 2601
Email: SMP@health.gov.au
Fax: 02 6289 2650

Dear Sir/Madam,

Re: Response to the Secretary to the Department of Health and Ageing Delegates May 2013 Invitations for further Submission concerning Interim Decisions and Reasons for Decisions

Aspen Pharma Pty Ltd agrees in principle to the Delegate's Interim Decision:

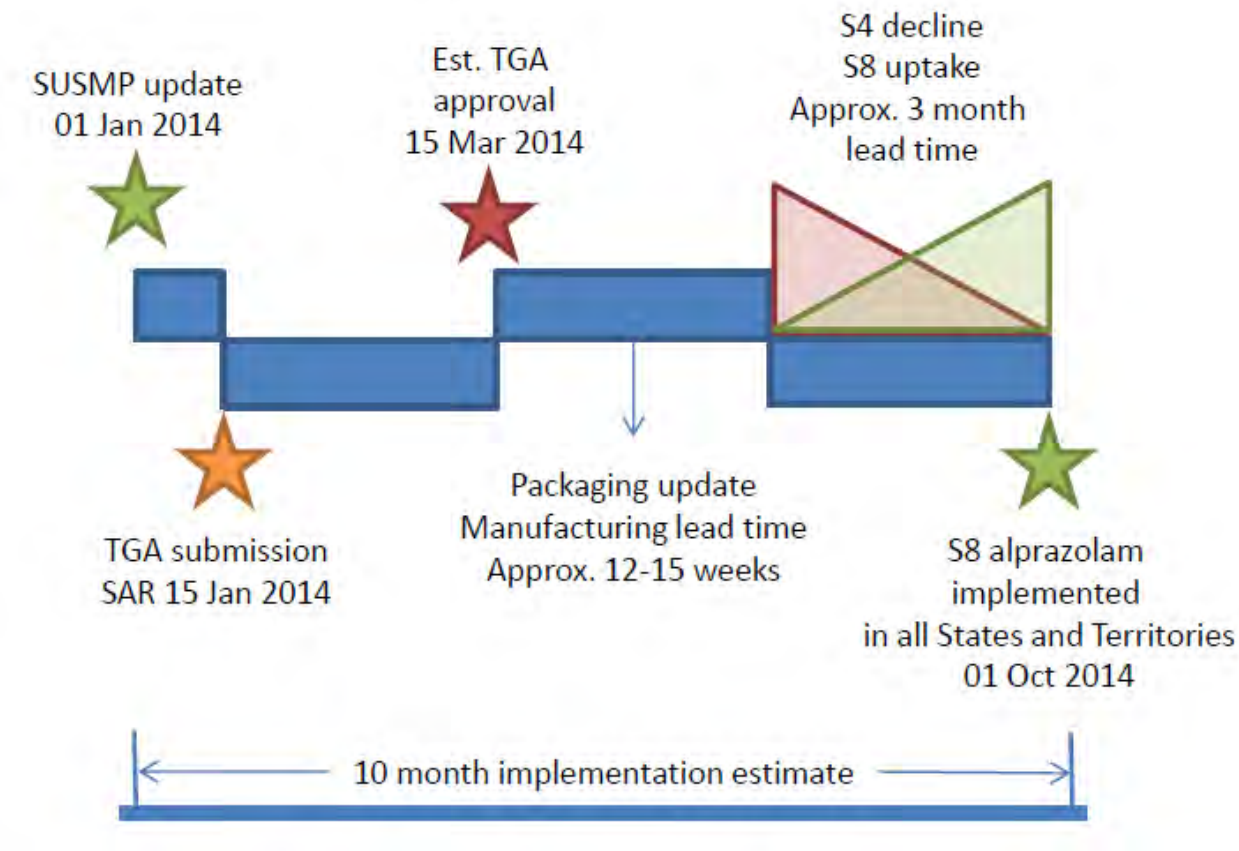
- that alprazolam be rescheduled from Schedule 4 to Schedule 8
- that the scheduling of the remaining benzodiazepines remains appropriate; and
- that benzodiazepines be included in Appendix D, paragraph 5.

However, we are concerned with the proposed implementation date of 01 January 2014. We believe that the Delegate could clarify that the implementation date is for the decision alone. Once the decision is ratified and the SUSMP is updated accordingly, there is still a long lead time required before S4 alprazolam products are exhausted from the market and S8 alprazolam are available and the individual States and Territories implement the changes in their jurisdictions.

One of the rate limiting factors to the full implementation of the rescheduling to S8 is the TGA decision timeframe from submission to approval of the artwork updates. A change to packaging is required to be submitted as a Self-Assessable Request and this includes a decision timeframe of 45 working days. A request to revise the product scheduling can only be submitted from 01 January 2014. TGA approval of the S4 to S8 labelling could therefore be estimated to occur by 01 March 2014.

Packaging lead times can take from between 12-15 weeks to implement from this approval timeframe. Therefore the earliest available S8 stock availability would be 01 June 2013. However, there would be a requirement to also run out the S4 stocks in the market, and a changeover of this magnitude would take approximately 3 months with an overlap required.

A diagrammatical representation of the implementation timeline is provided overleaf.



Aspen believes it would not be unreasonable to propose the Delegates decision date of 01 January 2014 include a further recommendation of the full implementation for the rescheduling of all alprazolam products as S8 from 01 October 2014 across all States and Territories.

Aspen will formally request consideration of this proposed timeline directly to the States and Territories Drugs and Poisons units.

Thank you for the opportunity to comment.

Yours sincerely,

Scott Pilarski
Regulatory Affairs Manager
Aspen Pharma Pty Ltd

Submission to

Advisory Committee on Medicines Scheduling

RE: Rescheduling of Alprazolam

6th June, 2013

Submitted to

Medicines and Poisons Scheduling Secretariat (MDP88)
GPO Box 9848
Canberra, ACT, 2601
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Authorised by

Damian Ferrie
Chief Executive Officer
Inner South Community Health Service
[redacted]

Contact

Sue White
General Manager
Inner South Community Health Service
[redacted]

1. About Inner South Community Health Service

Inner South Community Health Service (ISCHS) is a major provider of health and community services in the inner southern region of Melbourne, servicing the local government areas of Port Phillip and Stonnington. We also deliver a small number of regional and statewide programs.

ISCHS has particular expertise in working with marginalised population groups (including poly substance users, people who are socially isolated and people who have multiple and complex needs). Our Alcohol and Drug services span the spectrum of harm minimisation, case management and treatment / withdrawal. We also have a large Mental Health team and a number of services that target people experiencing homelessness. In March 2013, ISCHS established a GP service offering care to the entire community – including people with addiction issues.

2. Support for S8 Classification

Our work at Inner South Community Health Service indicates that there is a clear trend in the local community of problematic Alprazolam use. Associated adverse health outcomes impact significantly on both individuals and the broader community.

ISCHS has noted that inappropriate use of this medication can lead to increased morbidity and mortality amongst our local community. The real risk of overdose arises from poly-substance use, particularly when used with opioids (such as heroin) or alcohol. The short acting nature of Alprazolam results in increasing tolerance and the risk of addiction.

A Schedule 8 classification would enable a client with a clinical need for this drug to have a principal practitioner prescribing and managing their condition. For prescribers, this would allow for continued reinforcement to decline scripts whilst redirecting clients to their usual GP or engaging them with alternative treatment options.

Issues associated with Alprazolam misuse that impact on the local community include - the emergence of a street market for scripts and / or medication and associated behaviours such as violence.

3. Concerns / Potential Risks

Whilst there are no foreseeable significant risks with moving Alprazolam to Schedule 8, potential impacts may include:

- Impact on the street market if Alprazolam were less readily available (and the subsequent impact on the wider community);
- Risks of withdrawal with clients who are currently using Alprazolam would need to be managed.

4. Case study

Don is a 35 year-old man who was referred to the ISCHS Alcohol and Other Drug (AOD) Team for AOD Counselling in March 2012. Don presented with a history of poly substance use (primarily heroin, alcohol and benzodiazepines – including Xanax), anxiety (including panic attacks), homelessness, an overdose a few years ago requiring hospitalisation, and a broken hand from a recent fight. At assessment, Don reported that:

- he "wanted to get into less trouble", that he thought changes to his drug use may help,
- the manager of the housing service he was living in was warning him about possible eviction due to his aggressive behaviour,
- his parents worried about him and wanted to help, athough they could not live with him mainly due to his aggression.

Don was also concerned about the state of his teeth and requested support with accessing an appointment with a dentist.

Don agreed to work with a team comprising of an ISCHS AOD counsellor and Mental Health worker. Initial appointments were made at times of the day when Don was less likely to be substance affected. Don engaged well and appeared motivated to share the reality of his situation and was open to working on strategies with people in his support network to find a way forward. Don subsequently disclosed that he was using a second GP to access Xanax as well as being prescribed Valium by his primary GP.

Don has since managed to cease his use of Xanax and heroin, uses Valium as prescribed by his GP and occasionally uses alcohol. He reports feeling calmer and more able to manage his overall situation. His housing is stable and he is no longer at risk of homelessness. Don's's parents have a positive relationship with ISCHS staff and work in a respectful way that values inclusion and good communication. Don has also seen both the Dentist for regular appointments along with a Family Violence Counsellor. All services continue to work with Don on a regular basis.

5. Summary

As a major provider of health and support services to inner city communities, ISCHS fully supports the rescheduling of Alprazolam to Schedule 8. This move will result in public health benefits to both vulnerable individuals and the broader community.

SUBMISSION to the

ADVISORY COMMITTEE ON MEDICINES SCHEDULING

Therapeutic Goods Administration

RESCHEDULING OF ALPRAZOLAM

6 June 2013

Dr Hester Wilson **BMed (Hons), FRACGP, FAChAM**

Summary

The National Faculty of Specific Interest in Addiction in the RACGP supports the interim decision of the Advisory Committee on Medicines Scheduling to reschedule alprazolam. As General Practitioners with special interest in addiction we welcome the chance to participate in this decision and to meet at any future point in time with members of the Committee or their representatives to discuss issues raised in our submission.

We also provide further recommendations as we judge that alprazolam has little or no place on the Australian drug formulary. As a class, benzodiazepines are listed for short term, 2nd line pharmacological treatment of panic disorder and anxiety after psychological strategies and SSRIs. There is no evidence that alprazolam is more effective than other benzodiazepines in the treatment of this disorder and it is clear that the harms from alprazolam use greatly outweigh the benefit of use.

Key recommendations presented in this submission are as follows:

Recommendation 1: That alprazolam be rescheduled to schedule 8

Recommendation 2: That the 2mg dose be removed from the market

Recommendation 3: That the pack size be reduced from 50 tablets to 8 tablets

Recommendation 4: That GPs be supported to assist their patients who are dependent on alprazolam to transfer to long acting benzodiazepines to then undertake benzodiazepine withdrawal

Background

Benzodiazepines increase the effects of GABA receptors (gamma-aminobutyric acid) throughout the brain. These receptors are inhibitory and as a result, activation leads to sedation, decreased anxiety, increased seizure threshold, muscle relaxation and sleep. Benzodiazepines first became available in the 1960s and this class is one of the most commonly prescribed drugs in Australia.

Alprazolam is a potent benzodiazepine; highly lipophilic, with high binding affinity, it rapidly reaches peak levels in the brain and has a short half-life. These characteristics led to it being marketed for the treatment of panic attacks in panic disorder. The quick onset and short acting nature were seen to be perfect for managing panic attacks which came on quickly and lasted for a limited period of time. Over the last 10 years, scripts for alprazolam have skyrocketed and Xanax has achieved a high profile both in drug using communities and the general community.

Harms of use

Benzodiazepines were thought to be safe and non-addictive. The first concerns about abuse and dependency began in the 1980s (Hallstrom & Ladre 1981) and it is now clear that dependency, tolerance and withdrawal are common side effects. Benzodiazepines have also been shown to cause cognitive impairment even at therapeutic dose (Hindmarch, 2009) and in a recent paper, a longitudinal cohort study of over 10,000 subjects, therapeutic doses were linked to a 4-6 fold increase in risk of cancer and death (Kripke 2012).

Alprazolam with its quick onset and short half-life is a prime candidate for dependency, withdrawal and misuse (Pecknold 1993), (O'Brien, 2005). Like others of its class, alprazolam has the capacity to cause dependence, leading to tolerance with dose escalation, and withdrawal with significant symptoms on trying to reduce or stop the medication (Kline et al,

1994). Many of the withdrawal symptoms mirror those of anxiety, so it can be difficult for patient and clinician alike to delineate whether the symptoms are due to drug withdrawal or due to recurrence of anxiety symptoms (Pecknold 1993). In addition there have been reports of alprazolam actually inducing panic attacks (Bashir & Swartz 2002). Alprazolam has significant cognitive effects, in particular amnesia and in some patients leads to disinhibited behaviour. This can put the individual and the community at significant risk of harm.

The use of benzodiazepines, to accentuate the intoxicating effects of opioids is common practice amongst injecting drug users (IDUs). Alprazolam has also been shown to be more toxic in overdose (Ibister et al 2004). The concurrent use of benzodiazepines have been implicated in 40-80% of opioid related deaths (Darke et al 2010). While in a 2013 study in Victoria, alprazolam was implicated in 28% of heroin related deaths (Rintoul 2013). The 2012 Illicit Drug Reporting System (IDRS) national report found that 60% of a national sample had used alprazolam at some stage in their lives, 44% had used them recently and 6% had injected alprazolam.

Alprazolam is commonly used by clients attending the Medically Supervised Injecting Centre in Kings Cross. At this centre, drug users attend to inject drugs in a safe environment, where staff can resuscitate in the event of overdose. Clients ingest 10 to 20mg of alprazolam prior to attending the centre, then inject opioids and as a result accentuate the intoxicating properties of both drugs. These clients commonly become hypoxic and require intervention from the staff (Jauncey 2013).

A recent Illicit Drug Reporting System (IDRS) report concludes that drug users who use benzodiazepines are more likely to be unemployed, rate their physical and mental health as poor and be involved in violent crime (IDRS 2012). While those who take alprazolam are less likely to be in treatment for their dependency and report even higher levels of distress on the K10 (Kessler psychological distress scale) (MaIlwrath, 2012), (Darke et al 2010).

Anecdotally when patients cease their use, their health and psychosocial function improves. They often decrease other drug use, stabilise on treatment and rate their physical and psychological wellbeing as improved.

In our clinical experience in both general practice and public opioid pharmacotherapy settings, up to 30% of the patients in treatment for their opioid dependence either abuse or are dependent on alprazolam.

Alprazolam is obtained on the streets or from doctors. Some patients have described being given multiple scripts at individual consultations. This means that they are able to purchase large quantities of alprazolam, for example 150 tablets at a time. They also describe being given private scripts with 100-200 tablets per script.

Alprazolam is readily available and relatively cheap; 2 mg alprazolam tablets are the most popular and are easily available on the streets for $3-5 for each tablet. Given that a script of 50 tablets of 2mg Xanax costs $5.70 for health care card holders, the on selling of this prescription medicine is lucrative.

Benzodiazepines contribute to the chaos in IDUs lives and benzodiazepines, often alprazolam, commonly lead to the individual undertaking criminal behaviours ending in arrest and incarceration.

Patients describe risky behaviours while under the influence of alprazolam that include driving, assaults, drug use, other criminal behaviours or waking up after a period of amnesia and being frightened by what might have happened to them or what they might have done. Many patients describe alprazolam as ‘dangerous’, and wonder why it is so easily available. Characteristic of dependence, they express a desire to stop using alprazolam but find it difficult to change this behaviour. They find it very difficult to control their drug use and as a community we are letting them down but not acting to restrict access to alprazolam.

Patients who misuse alprazolam describe high levels of psychological distress and clinicians have a natural inclination to assist their patients and this may drive unhelpful prescribing. General practitioners tend to work in partnership with patients and respond to patient's demands. They may not be comfortable putting limits around scripts and patient behaviour nor in the habit of creating treatment agreements that limit the amount or duration of medicines. In addition patients who 'drug seek' can be very skilled at obtaining the medicine they feel they need and this can support poor prescribing.

In the general practice setting we see patients who do not have a history of drug addiction requesting help for alprazolam dependency. They give a history of alprazolam use for treatment of anxiety or panic attacks. Many of them have been on alprazolam for years. A number of these patients recount their experience of being given increasing doses of alprazolam by their doctor to assist with escalating symptoms.

It is almost impossible for patients to withdraw from alprazolam as they suffer debilitating withdrawal symptoms and rebound of anxiety and panic. They need to transfer to long acting benzodiazepines and then commence slow withdrawal. This whole process can take months to years to achieve. These patients need close monitoring, frequent review and staged supply of their medications. A good therapeutic alliance between the GP and patient is essential. This is time consuming, labour intensive and has significant cost to the individual, the GP, health services and our community.

A protracted withdrawal state has been recognised in the literature (Ashton 1991) and a significant minority of our patients have suffered or continue to suffer protracted withdrawal with ongoing debilitating symptoms for months to years after cessation of all benzodiazepines.

Indications for Use

Alprazolam is subsidized on the PBS in Australia and requires authority. It is restricted to use for 'panic disorder where other treatments have failed or are inappropriate' (PBS 2012). Since 2003 the Australian and New Zealand College of Psychiatry guidelines state that benzodiazepines are indicated as a second line **pharmacological** treatment for the short term management of panic disorder and that even the short term use of benzodiazepines must be weighed up against side effects including the difficulty withdrawing from the medication (RANZCP 2003).

The aim of treatment in the RANZCP guidelines is

(i) control and cessation of panic attacks;

(ii) control and cessation of fear-driven avoidance;

(iii) reduction in vulnerability to relapse.

While psychological treatments can achieve all three aims, there is no evidence that drugs can reduce vulnerability to relapse. (RANZCP 2003)

These guidelines compare psychological to pharmacological treatments in their meta-analysis and find that psychological treatment is more effective with smaller number needed to treat and larger effect size.

The 2011 NICE guidelines from the UK state that 'benzodiazepines are associated with a less good outcome in the long term and should not be prescribed for the treatment of individuals with panic disorder'.

In both the UK and Australian/New Zealand guidelines, SSRIs are first line pharmacological treatment with benzodiazepines as second line. In these guidelines alprazolam is not singled out as the benzodiazepine of choice for the treatment of panic disorder as there is debate

over whether this medicine is any more effective that others of its class (Moylan et al 2011) (Speigel 1998).

Prescribing Rates

Despite the changes to guidelines, prescribing levels of alprazolam continue to grow and Monheit (2010), taking estimates from the Australian Statistics on Medicines 2009, reported that levels of alprazolam prescribing have increased by 28% compared to other benzodiazepines where rates are falling. In addition 32% of the alprazolam scripts were private scripts. From 1997-2007 rates of alprazolam prescribing on the PBS increased by 93%, while private scripts increased by 99% (DOHA 2010). In 9009, 413, 526 scripts were written on the PBS while 103,715 private scripts were written.

The WHO has an internationally defined measure that corresponds to the average daily maintenance dose (defined daily dose per 1000 population per day; DDD) utilised for a drug's main indication. For alprazolam this is 1mg. In Australia the DDD for alprazolam has risen from 3.88mg in 2003 to 5.12mg in 2007 (Hollingworth & Siskind 2012). In addition the 2009 PBS data show that the most prescribed doses are the 1 and 2mg tablets. (DOHA, 2010)

Prescription rates of alprazolam are much higher in areas of Australia that have poorer access to illicit drugs such as heroin, for example, Tasmania, has a 100% higher prescription rate that the national average (Hooper et al, 2009) and concerns about the poor prescribing and misuse of this medication have led several states to issue warnings to prescribers (Department of Health and Families, 2010).

The idea that a medicine can 'fix' complex bio-psycho-social issues is a beguiling one but fallacious and risks leading to ongoing poor outcomes for patients. It is clear that levels of prescribing alprazolam are increasing despite changes to recommended treatments. This

prescribing is putting lives as risk and suggests that patients are not getting best evidence based care.

Rogers et al (2011) point to 7 main areas that would assist with improving prescribing. These include better monitoring and research into trends, assisting practitioners with structured responses to patient requests for inappropriate medicines, creating guidelines and assisting workforce development, improving patient health literacy, addressing harm reduction issues and managing commercial aspects. A real time prescription monitoring process would allow prescribers to check on previous scripts for their patients. These initiatives would be supported by greater limits on the prescribing of alprazolam.

Conclusions

Current trends in prescribing are leading to unacceptably high levels of harm in vulnerable groups in our community. Changing the schedule, indication, available doses and pack sizes will signal that a change in prescribing is needed.

Recommendation 1: That alprazolam be rescheduled to schedule 8

A change in listing to make alprazolam a Schedule 8 medication would signal to prescribers that this is a medication with significant risk, that needs thought before prescribing.

Recommendation 2: That the 2mg dose be removed from the market

2mg tablets are being disproportionately prescribed and are the favoured dose for misuse. Removal of 2mg alprazolam tablets from the market would assist to change this practice.

Recommendation 3: That the pack size be reduced from 50 to 8 tablets

Limiting pack size to 8 tablets without repeats suggests the role and amount of medication that is indicated and would make it more expensive for patients to obtain inappropriate amounts of the medication.

Recommendation 4: That GPs be supported to assist their patients who are dependent on alprazolam to transfer to long acting benzodiazepines to then undertake full benzodiazepine withdrawal

Prescribers need assistance to undertake more thoughtful and judicious prescribing. They need additional skills to assist them to undertake more realistic, collaborative, and time limited treatment planning. Doctors need ongoing education regarding the diagnosis of panic disorder and guidelines for best evidence based practice. General practitioners need greater support from their specialist colleagues.

Dr Hester Wilson is a Fellow of the Royal Australian College of General Practitioners, a Fellow of the Chapter of Addiction Medicine in the Royal Australian College of Physicians and has extensive clinical experience working with AOD and mental health co morbidity. She has worked in primary health care settings for the last 20 years including working in East London with the homeless as a primary health clinician and for 7 years at the Kirketon Rd Centre, a centre providing primary care for injecting drug users, street sex workers and at risk youth in Kings Cross, Sydney. She was Acting Medical Director at the Sydney Medically Supervised Injecting Centre in Kings Cross in 2009-2010. She currently works at the Langton Centre as an Addiction Staff Specialist and in private general practice in Newtown, Sydney, where she has a high case load of clients with AOD and mental health co morbidity.

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SIGMA

11th June 2013

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

Dear Secretariat,

Benzodiazepine

Sigma opposes the rescheduling of Alprazolam.

To reschedule Alprazolam will require all stock of Alprazolam to be relocated and stored on an ongoing basis in secure Drugs of Dependency cages and vaults.

To facilitate will require additional cost in space and administration.

Several of these facilities are nearing capacity accommodating current scheduled medicines and may result in new builds.

Any questions please advise.

[redacted]

Yours sincerely,

[redacted]

ALAN O'HARA
General Manager Supply Chain & Transformation
Sigma Pharmaceuticals

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3 June 2013

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SMP@health.gov.au

Further submission
Delegates' reasons for interim decision – adrenaline, bupivacaine, lignocaine

Dear Secretary

I am writing in response to the above interim decision of the Delegates.

I proposed the above schedule change while employed by the NSW Department of Primary Industries, and understand it was my submission which was forwarded to the Committee by the Australian Pesticides and Veterinary Medicines Authority. If that is not the case, I would still argue that it was my proposal which resulted in consideration of this issue by the Committee and therefore that I should be permitted to comment on it. A copy of my submission as previously forwarded is attached.

My main concern is that all the reasons put forward by the Delegates are in fact erroneous. The reasons, and my rebuttals, appear below.

- as mulesing is a regulated process, there is no evidence that rescheduling would improve the extent of use.

Mulesing is not a regulated process. Contractors who carry out mulesing are required to be appropriately qualified, but there is no oversight of mulesing nor is it restricted or regulated in any jurisdiction. No controls at all apply to producers who carry it out on their own sheep. See the attached document from Animal Health Australia downloaded from http://www.animalwelfarestandards.net.au/sheep/sheep_public_consultation on 27 May 2013.

- the toxicity of the local anaesthetic ingredients and the relatively narrow window of effectiveness in pain relief associated with mulesing, warrant appropriate supervision of treatment by a veterinarian.

The submission argued that the toxicity in the dose format in which these actives occur was not sufficient—to either sheep or users—to warrant "supervision of treatment by a veterinarian". This product is formulated and applied like thin paint.

Further, the fact that a product is included in Schedule 4, and must be supplied by a veterinarian, provides no more oversight than human consumption of antibiotics provided by a pharmacist on medical prescription. Any oversight of use, were any to occur at all, would apply only to the first and initial use of the product. Even in these cases it is highly unlikely a

veterinarian would attend the sheep. Also, in many cases, treatment is carried out by contractors who are very familiar with its use, rather than the owner of the sheep who is supplied with the product by the veterinarian.

- rescheduling to Schedule 6 could result in the product, currently available in 100 ml injection vials, being made available in much larger bulk containers, increasing the risk of inappropriate use.

My original submission made it clear that this product is already supplied in bulk containers – the smallest being 1L and the largest being 22L. Where did 100 ml (sic) come from?

Pack Sizes:	1, 2.5, 5, 10, 15, 20 and 22 L

Any risk of inappropriate use already exists. The question that needs to be addressed is what damage could result from "inappropriate" use, and the answer must be either "minimal or none". I am not aware of any such use or any adverse consequences of such use if it has occurred, since the product was first released for sale many years ago.

- rescheduling from Schedule 4 to Schedule 6 could increase the risk of the product being inappropriately used for purposes other than pair (sic) relief after mulesing.

This is much the same as the previous argument. All farmers who obtain this product and use it will invariably have surplus material on hand at the end of a mulesing season. To repeat, there have not been any reports of any misuse or any adverse consequences of such use if it has occurred.

- a broadening of use in pain relief for the practice of mulesing is a desirable outcome, but this can be achieved within existing scheduling arrangements, especially via advertising, which would remain restricted to professional journals and related sources.

If advertising of restricted substances is restricted to professionals (veterinarians) and they are already in receipt of such advertising, how can the product be further advertised to increase its use? Only by direct to user advertising could its use be increased, and this is illegal in most if not all jurisdictions.

I trust these comments will help allay the published fears of the Delegates in regard to this product. If these are their only concerns then it is obvious that they are not justified, and the re-scheduling as proposed can and should go ahead.

Thank you for considering this response.

Yours faithfully
(Signed)

[redacted]

[redacted]

Commercial-in-Confidence

Medicines & Poisons Scheduling
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e-mail SMP@health.gov.au

Dear Sir/Madam

[redacted] are the inventors and developers of the Tri-Solfen product (licensed to Bayer Animal Health Australia) that contains the actives Lignocaine, Bupivicaine, and Adrenaline that is currently under review for a schedule change from S4 to S6.

As a major stakeholder in the product and its future use we would therefore much appreciate if the delegates accepted our submission below that supports the original application for a schedule change.

[redacted] does not support the interim decision and instead supports the original application for re-scheduling of Tri-Solfen (including active constituents lignocaine, bupivacaine and adrenalin), from S4 to S6, as discussed further below.

[redacted] considers rescheduling is appropriate and would allow flexibility to increase information and practical accessibility of the product to a significant percentage of farmers who are remote from veterinary services, while still allowing provision and sale through veterinarians where services are readily accessed and available.

Background – [redacted] **Tri-Solfen product and use.**

[redacted] is a Research and Development Company which was responsible for inventing, developing and registering the Product “Tri-Solfen”, which is a topically applied spray-on pain relief and wound care agent registered for use to alleviate pain in lambs undergoing mulesing.

The product contains Lignocaine 5%, Bupivacaine 0.5%, Adrenalin 1:2000 and Cetrimide in a viscous gel base. It is applied topically to the mulesing wound immediately after the procedure using a spray-on applicator.

The procedure of “mulesing” does not require “diagnosis” or the attendance of a veterinarian. It is a surgical animal husbandry procedure legally performed by sheep producers on farm, on lambs that are considered to be otherwise vulnerable to a high life time risk of flystrike. It is a once-only procedure performed in lambs during the first weeks and / or months of life. It involves the removal of loose skin wrinkle in the breech region, usually undertaken at the same time as tail docking.

The application of Tri-Solfen to alleviate pain in lambs undergoing mulesing also does not require direct (on farm) veterinary supervision or monitoring. Due to the current S4 schedule, Tri-Solfen must be prescribed by a veterinarian. However, once prescribed the product is *applied by the farmer* to lambs with mulesing wounds

directly at the time of mulesing. It coats the wound, and the lamb is released to return to its mother in the field situation.

This “Veterinary prescribed - farmer-applied” pattern of use has been in evidence since the product first became commercially available in 2005, and has been safely and effectively used on an estimated 5 - 6 million lambs per year since this time.

[redacted] was unaware of the original application to reschedule Tri-Solfen from S4 to S6 and therefore did not make a submission. This submission is in response to the request for submissions on the interim decision.

Yours Sincerely

[redacted]

Submission in Support of Re-sheduling Tri-Solfen from S4 to S6

[redacted] supports the application for re-scheduling the product Tri-Solfen (including actives lignocaine, bupivacaine and adrenalin), for the following reasons – listed here and discussed in further detail below.

1. Schedule 6 is the most appropriate classification of the Product using the cascading principle and based on the specific indication for use, the low toxicity profile, and 8 year experience of use of the product.
2. A significant proportion of lambs undergo mulesing on remote properties where there is limited access to veterinarians / veterinary S4 restricted product information. The S4 scheduling is providing a significant barrier to uptake and use of the product in these locations, affecting an estimated 5-6 million lambs per annum born and raised on remote properties.
3. Rescheduling the product to S6, would provide greater flexibility to improve information, marketing and accessibility of the product to farmers in remote regions of the country, without significantly increasing the risk of harm or mis-use.
4. [redacted] considers that there are some errors in the factors used to develop the interim decision, and has provided information to address this.

Point 1

Schedule 6 is the most appropriate Schedule for the Product "Tri-Solfen" using the Cascading Principle.

According to the "Scheduling Policy Framework for Medicines and Chemicals", the model for making scheduling decisions embodies a "cascading principle". "For veterinary chemicals, assessment against the factors for Schedules 8 and 4, may be followed by assessment against Schedules 7, 6 and 5, as applicable. Veterinary chemicals will not be assessed against the criteria for schedules 3 or 2."

Animal Ethics considers that Tri-Solfen does NOT meet the conditions under assessment for S4 scheduling and should therefore cascade to S6 scheduling as outlined below. Animal Ethics Pty Ltd submissions are noted in blue.

"2. THE SCHEDULING FACTORS - FACTORS FOR PRESCRIPTION ONLY MEDICINES AND PRESCRIPTION ANIMAL REMEDY (SCHEDULE 4)"

1. **The ailments or symptoms that the substance is used for require medical, veterinary or dental intervention[2].**
   Diagnosis, management or monitoring of the medical condition is such that it requires medical, veterinary or dental intervention before the substance is used.
   Veterinary intervention is NOT required for the ailments or symptoms for which the product is used, nor for diagnosis management or monitoring before the substance is used.
   The substance (Tri-Solfen) is a farmer-applied topical anaesthetic formulation that is registered for use to alleviate pain in lambs following mulesing.
   "Mulesing" is an animal husbandry procedure legally performed on farm by farmers and does not require diagnosis, mangement or monitoring by a Veterinarian. The fact that mulesing causes pain to lambs also does not need diagnosis by a Veterinarian. It is well established in the scientific literature, and accepted by producers, the general public and veterinary profession that Mulesing causes pain to lambs.

[2] For the purposes of this document medical, veterinary or dental intervention is considered to include other authorised prescribers as described in relevant legislation of Australian states and territories.

2. **The use of the substance requires adjunctive therapy or evaluation.**
   Adjunctive therapy could include other medicines, non-pharmacological measures, or specialised medicine delivery devices. Evaluation could include laboratory tests or additional clinical assessments.
   Use of the substance does NOT require adjunctive therapy or evaluation. The substance is applied by spray-on topical application to the mulesing wound by producers on farm immediately following the procedure. The lamb is then released into the field to return to its mother. No additional interventions or evaluations are required.

3. **The use of the substance at established therapeutic dosage levels may produce dependency but has a moderate propensity for misuse, abuse or illicit use.**
   Control of access and duration of therapy by a medical, veterinary or dental practitioner is required.
   Control of access and duration of therapy by a veterinary practitioner is NOT required.
   The substance is used as a once-off application to a lamb following the mulesing procedure. There is no risk of producing dependency. The product does not contain actives such as sedatives or narcotics that have a moderate propensity for misuse, abuse or illicit use.
   The established history and pattern of use to date provides further evidence that there is an extremely low risk of misuse, abuse or illicit use.
   It has been commercially available and used on farm since 2005. It is typically prescribed by Veterinarians, and then supplied to producers in bulk packs (1L, 5L and 20L containers) sufficient to treat 150 – 3000 lambs at a time. The product is applied on farm without direct veterinary supervision. There have not been any cases reported of misuse, abuse or illicit use with an estimated 5–6 million lambs treated appropriately per annum during this time.

4. **The seriousness, severity and frequency of adverse effects are such that monitoring or intervention by a medical, veterinary or dental practitioner is required to minimise the risk of using the substance.**
   Intervention by a veterinary practitioner is NOT required to minimise the risk of using the substance.
   The substance is topically applied to lambs on farm by producers.
   There are no serious, nor severe or frequent adverse effects that require the intervention of a veterinary practitioner.

5. **The margin of safety between the therapeutic and toxic dose of the substance is such that it requires medical, veterinary or dental intervention to minimise the risk of using the substance.**
   The margin of safety between therapeutic and toxic dose is NOT such as to require veterinary intervention to minimise the risk of using the substance. The product is applied topically by farmers, in an amount sufficient to coat the wound. Any additional substance applied simply runs off the wound and onto the ground. Minimal levels of systemic absorption have been documented following topical application such that there is a very wide margin of safety between therapeutic and toxic doses of the substance.

6. **The seriousness or severity and frequency of the interactions of the substance (medicine-medicine, medicine-food, or medicine-disease) are such that monitoring or intervention is required by a medical, veterinary or dental practitioner.**
   There are NOT any documented serious, severe or frequent interactions of the substance (medicine-medicine, medicine-food, or medicine-disease) that required monitoring or intervention by a veterinary practitioner.

7. **The use of the substance has contributed to, or is likely to contribute to, communal harm.**
   For example the development of resistant strains of microorganisms. Appropriate use, and/or the decision to continue treatment, requires evaluation by a medical, veterinary or dental practitioner.
   Use of the substance is NOT likely to contribute to communal harm. Appropriate use is clearly defined, as a once-off single application of the substance to alleviate pain in lambs following mulesing. Lambs only receive one treatment per lifetime. There is no requirement to consider continuing treatment. Any potential risk to handlers, who may experience repeat exposure, can be prevented by proper labelling detailing handling and safety requirements (such as the requirement to wear gloves).

8. **The experience of the use of the substance under normal clinical conditions is limited.**
   Unexpected effects of the substance may only become evident after widespread use. Close monitoring of the patient is required by a medical, veterinary or dental practitioner to monitor for unanticipated effects.
   Experience of use of the substance is NOT limited. The substance has now been in widespread use for 8 years. There have not been any documented unexpected effects. Close monitoring by a veterinary practitioner is NOT required to monitor for unexpected effects.

FACTORS FOR LABEL USE OF "POISON" (SCHEDULE 6)

1. **The substance has a moderate to high toxicity, which may cause death or severe injury (including destruction of living tissue) if inhaled, taken internally, or in contact with skin or eyes.**
   Acute oral LD50 (rat) is between 50 mg/kg – 2000 mg/kg. Acute dermal toxicity is between 200 mg/kg and 2000 mg/kg. Acute inhalation LC50 (rat) is between 500 mg/m^3 and 3000 mg/m^3 (4 hours).

   Dermal irritation is severe. Eye irritation is severe. Skin sensitisation is moderate to severe.
   The substance does NOT cause this level of dermal eye or skin sensitization, however may cause death or injury if accidently ingested in large amounts.

   The substance has a moderate health hazard.
   The substance presents a moderate hazard from repeated use and moderate risk of producing irreversible toxicity.
   The substance is for single use, and does NOT have a moderate risk of producing irreversible toxicity in lambs.
   However, skin sensitization to lignocaine has been reported in the literature and thus poses a theoretical risk to farmers who handle the substance and who may be subject to repeated exposure. This risk can be addressed through preventing contact with the substance when applying it - via strong labelling and safe handling requirements such a wearing gloves.

2. **Reasonably foreseeable harm to users can be reduced through strong label warnings, extensive safety directions and child-resistant packaging (where appropriate).**
   Adequate packaging and labelling protects the consumer from the known danger(s) of the substance. Potential harm is reduced through labelling which informs the consumer about the safety measures to apply during handling and use (including safety directions) and child resistant packaging.
   This is correct. Forseeable harm to users (including handlers) of the substance includes accidental ingestion or inhalation of significant amounts of the substance and / or the potential for skin sensitization. This is best addressed through strong labelling and safe handling requirements as outlined above. It should be noted that the current label warnings, safety directions and packaging requirements have resulted in an 8 year history of safe and effective use of the product on farm, by producers, without direct veterinary application or supervision.

3. **The substance has a moderate potential for causing harm.**
   Potential harm is reduced through the use of distinctive packaging with strong warnings and safety directions on the label.
   This is correct as above.

POINTS 2 and 3 – S4 SCHEDULING IS PROVIDING A BARRIER TO APPROPRIATE USE FOR PAIN RELIEF IN LAMBS UNDERGOING MULESING IN REMOTE REGIONS. RESCHEDULING TO S6 WILL GREATLY IMPROVE INORMATION AND ACCESSABILITY FOR FARMERS IN REMOTE REGIONS.

A significant proportion of lambs undergo mulesing on remote properties where there is limited access to veterinarians / veterinary S4 restricted product information. The S4 scheduling is providing a significant barrier to uptake and use of the product in these locations, affecting an estimated 5-6 million lambs per annum born and raised on remote properties.

The percentage of lambs treated with pain relief at mulesing varies significantly by State. QLD and Western Australia, the two states in which woolgrowers graze sheep in some of the most remote regions of Australia, have the lowest uptake of use of pain relief for mulesing. Only 10.27% of lambs mulesed in Queensland, and 27.7% lambs mulesed in Western Australia are currently treated with Tri-Solfen pain relief. This compares with 57.70% in Victoria where farms are less remote. (Australian Wool Innovation survey data).

Access to veterinary services, and information from veterinary sources and journals can be extremely limited for many farmers in these States. For example Hyden in WA has no Veterinarian clinic or Vet, the closest is Merredin some 156km away (2 hour drive each way). Similarly, Blackall in Qld also has no rural Veterinarian clinic. The closest is in Longreach some 213km away (2h 16 m drive each way). Rural Outlet stores are much more accessible and are often a primary source of product supply and information. Both Hyden and Blackhall have a rural outlet stores (Elders & Landmark). Rescheduling to S6 would allow Tri-Solfen to be marketed and sold through rural outlet stores in regions where veterinary services are limited or unavailable – greatly improving information and accessibility for woolgrowers.

POINT 4 - Animal Ethics Response to Interim Decision Factors – Advice of the ACCS and ACMS

In making an interim decision the delegate took into consideration the advice of the ACCS and ACMS who recommended no change to the scheduling of lignocaine, bupivacaine and adrenalin – actives in the product Tri-Solfen .
The following reasons were noted:

- Insufficient data available to demonstrate that a change in Schedule will result in wider appropriate usage versus wider inappropriate usage.
- As mulesing is a regulated process, there is no evidence that rescheduling would improve the extent of use.
- Rescheduling would increase the risk of the product being inappropriately used.
- Rescheduling would increase the likelihood of larger quantities being available which could lead to misuse.
- Delegate's consideration

Animal Ethics responses and submission

[redacted] Considers that there is considerable evidence to indicate that a change in scheduling ***will*** result in wider appropriate use and will not result in an increase in inappropriate use.

Rescheduling will result in wider appropriate use principally because the majority of lambs undergo mulesing on regional and remote properties, where access to veterinary services is limited. The current S4 schedule restricts information flow and practical accessibility of the product to farmers in these circumstances. Rescheduling will allow more direct marketing and information supply, as well as improved practical access and affordability to farmers in regions remote from veterinary services.

Tri-Solfen (containing lignocaine, bupivacaine and adrenalin) is a topical anaesthetic spray-on formulation which is registered to be used for pain relief following mulesing in sheep. Mulesing is an animal husbandry procedure performed legally by producers on farm in sheep susceptible to flystrike. Veterinary presence or intervention is not required. It most commonly occurs in regional and remote parts of Australia. It is well documented and accepted that the procedure causes pain to lambs. Neither the procedure, nor the pain it causes needs "diagnosis" by a veterinarian.

Tri-Solfen is the only product that has proved safe and effective and is commercially available and registered for use to alleviate pain in lambs post mulesing. Currently, under S4 scheduling, it is almost universally used as a “Veterinary prescribed – farmer applied” product – that is, it is prescribed by veterinarians – however It is applied by farmers or mulesing contractors in the field – without the need for veterinary presence or monitoring.

However, the S4 scheduling places an onous and liablity on the Veterinarian to have a relationship with the farmer and to have viewed and assessed the sheep requiring the prescription. This is advantageous where it is available. Unfortunately a significant proportion of sheep producers live and work on remote properties where access to a veterinarian can be very difficult or time / cost prohibitive. For example it can require anywhere from 4-12 hours as a round trip for a farmer to visit a vet, or visa versa, which renders accessing the treatment (Tri-Solfen) either impractical or unaffordable for many farmers. Due to S4 advertising and marketing restrictions,

farmers who are remote from veterinary services are also less likely to have access to information about the availability of the product.

At present it is estimated that approximately 5-6 million lambs per year are mulesed with Tri-Solfen pain relief prescribed and applied, however this only represents an estimated 50% of total lambs mulesed. A significant proportion of those lambs that do not receive pain relief post mulesing are born on properties remote from veterinary services where access to Tri-Solfen is impractical / cost prohibitive under current S4 restrictions.

Continuing current sale arrangements (through veterinarians) is advisable where-ever good veterinary services and relationships are available, this would not be precluded by rescheduling to S6 schedule – however, re-scheduling to S6 would provide flexibility to improve information, access and affordability of Tri-Solfen to farmers in areas remote from veterinary services, through allowing marketing and supply of product through rural outlet stores. This has the potential to improve APPROPRIATE USE on an estimated 5-6 million lambs annually, that currently miss out on the pain relief treatment.

EVIDENCE THAT IT WILL NOT INCREASE INAPPROPRIATE USE

Tri-Solfen is approved and registered and marketed for use for a very clear, singular and specific indication. - i.e. - Pain relief following mulesing of lambs.
The directions for use and handling are clear, emphatic on the product labels and also easy for farmers to follow and adhere to. As discussed above it most appropriately fits under the S6 schedule under the cascading assessment regime.

As a topically applied product, Tri-Solfen has very poor penetration through in-tact skin and is thus largely in-effective except for use in large open wounds such as the mulesing wound. It is not clear what "inappropriate uses" are envisaged by the committee, however it should be noted that Tri-Solfen comes at some considerable cost to farmers, who are thus likely to use the product most judiciously for the intended purpose. This has certainly been the case to date, with 5-6 million lambs per year treated appropriately with Tri-Solfen for mulesing, and **no cases of inappropriate useage reported.**

In this regard it should be noted that the high level of appropriate use is NOT a function of the S4 schedule. This is because prescription by a veterinarian does not preclude an unscupulous farmer undertaking "inappropriate uses" of a medication once the product is prescribed and available on farm, as the veterinarian does not have any control or visibility over what happens to the medication once it is prescribed.

Instead, appropriate use is determined by the product information, directions and labelling, and farmer education regarding following product labeling instructions and safe and appropriate chemical handling.
Agricultural Industries have comprehensive farmer education and training programmes in place such as Chemcert - to educate train and promote the importance of appropriate chemical use and safe chemical handling to farmers - due to the high number of toxic chemicals, treatments and poisons used on farms.
In addition to this, (above and beyond the general farmer chemical training programmes) Bayer Australia, along with the Australian Wool Innovation, fund specific education and training for farmers on the proper and appropriate use and handling of Tri-Solfen when mulesing sheep. This is undertaken through mulesing accreditation training programmes.

Together these factors have resulted in the current history of extremely high levels of appropriate use, and low or absent levels of inappropriate use - and this pattern can be anticipated for Tri-Solfen regardless of S4 or S6 scheduling, as this is a function of strong labelling – which would continue unchanged under an S6 schedule.

It is therefore likely that changing the scheduling from S4 to S6 will vastly improve access to and useage of Tri-Solfen in regional and remote farms for the INTENDED purpose of pain relief post mulesing in up to 5-6 million lambs per year that are currently mulesed without appropriate pain relief treatment. This will far outweigh any theoretical increase in unintended use by any individual unscrupulous farmer.

POINT 4 (Cont) [redacted] Response to Delegates Interim Decision

"The delegates considered, and accepted, the advice of the joint ACCS & ACMS, advising that the specific uses of the veterinary product for pain relief in the practice of 'mulesing' sheep require veterinary supervision, and that changes to the existing Schedule 4 entries of the three active ingredients are not warranted. Accordingly, no scheduling changes are proposed in making an interim decision".

[redacted].

The specific use of the veterinary product for pain relief in the practice of mulesing sheep does not currently require "veterinary supervision".
Mulesing is an animal husbandry procedure performed on farm by producers legally, without veterinary supervision. Although the topical spray-on pain relief product Tri-Solfen must be prescribed by a veterinarian under the current S4 schedule, it is universally applied by farmers at the time of mulesing without veterinary presence or supervision. Rescheduling to S6 would improve information and practical accessibility and affordability of the product to farmers in regions remote from veterinary services.

"The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the Committee included; (b) the purpose, (c) the toxicity of a substance, (d) the dosage, formulation, labelling, packaging and presentation of a substance (e) the potential for abuse and (f) any other matters.
The following reasons were noted:

- As mulesing is a regulated process, there is no evidence that rescheduling would improve the extent of use.

[redacted] **Response**

As above, mulesing is not a "regulated process" in the sense that veterinary presence is required or mandated. It is an animal husbandry procedure undertaken legally by farmers (or mulesing contrators) without requirement of veterinary presence or oversight.

Mulesing is undertaken on farm - in many cases on properties that are remote from veterinary services. The current S4 scheduling is restricting information supply and practical accessability / affordability of the product to farmers in these areas.

- The toxicity of the local anaesthetic ingredients and the relatively narrow window of effectiveness in pain relief associated with mulesing, warrant appropriate supervision of treatment by a veterinarian.

[redacted] **Response**

a) The toxicity of the local anaesthetic ingredients is considerably less in topical formulations than in injectable preparations. It should be noted that lignocaine is widely available OTC in human medications, such as EMLA cream and xylocaine ointment 5% (http://shop.pharmacydirect.com.au/pharmacy/Lignocaine) Like these human medications, Tri-Solfen is a topically applied, local anaesthetic formulation. It is not an injected or injectable product.

b) The window of effect of pain relief post mulesing is not narrow – it is very wide. The product is applied to the wound immediately after the procedure. It coats the wound providing local anaesthetic effect which is evident within 1 minute of application to the wound, and continues for hours after the procedure. Most recently, studies have confirmed that an ongoing analgesic effect is still apparent even 24 hours after mulesing.

Lomax, S., Sheil, M., Windsor, P. (2013). Duration of action of a topical anaesthetic formulation for pain management of mulesing in sheep. *Australian Veterinary Journal*, 91, 160-167.

- Rescheduling to Schedule 6 could result in the product, currently available in 100 ml injection vials, being made available in much larger bulk containers, increasing the risk of inappropriate use.

[redacted] **Response**

Tri-Solfen is not available in 100ml injection vials. It is not an injected or injectable product. It is a topical local anaesthetic formulation that is applied using a spray-on applicator. The product is sprayed onto the surface of the mulesing wound to provide immediate post-procedural topical anaesthesia.

Mulesing is usually undertaken on all flystrike - susceptible lambs on one day, with 200 – 300 procedures performed at a time. Tri-Solfen is already prescribed and available to farmers in bulk containers (eg 5L) that contain sufficient medication to treat all lambs.

The container is worn as a back-pack and the Tri-Solfen is applied by metered spray-on topical application to each wound site immediately after the procedure.

Despite the “bulk” size of the containers, and the fact that the medication is farmer applied, without veterinary supervision - there is an extremely high record of appropriate use and no reports of inappropriate use to date. There is no reason to expect a change in this pattern should rescheduling occur to allow the product be more accessible to farmers in remote regions.

- Rescheduling from Schedule 4 to Schedule 6 could increase the risk of the product being inappropriately used for purposes other than pain relief after mulesing.

[redacted] **Response**

This has been discussed in answers above. It is much more likely that re-scheduling will increase appropriate use by farmers who are currently unable to access the product due to remoteness from veterinary services. An increase in inappropriate use is unlikely, and could just as easily occur under S4 schedule as S6 schedule. The incidence of inappropriate use is negligible to date – due to strong labeling and good training of farmers in safe chemical handling practices. This would still exist unchanged even if rescheduling occurred.

- A broadening of use in pain relief for the practice of mulesing is a desirable outcome, but this can be achieved within existing scheduling arrangements, especially via advertising, which would remain restricted to professional journals and related sources.

[redacted] **Response**

Farmers in regions that are remote from veterinary services have little access to information and products through vets, veterinary journals and related sources. Many / most rely on information and products through rural suppliers. The current S4 restrictions create a significant impediment to providing information and Tri-Solfen product to these producers.
S6 rescheduling would allow important information and accessibility of product through rural suppliers.

END

Tri-Solfen ***Submission 3 of 6 (including 3 attachments)***

Medicines & Poisons Scheduling
Secretariat (MDP88)
GPO Box 9848
Canberra ACT

AWGA Submission to TGA re rescheduling of Trisolfen from S4 to S6 Status.

Including 3 attachments

Dear Sir or Madam,

The Australian Woolgrowers Association (AWGA) is one of national peak bodies representing the Australian wool industry.

AWGA strongly recommends rescheduling of TriSolfen to S6 status as a matter of wool industry priority given that the industry is united behind such a sensible and timely move by the TGA.

Since 2005, the image and reputation of Australian wool has been under a barrage of international criticism over the controversial but necessary procedure of mulesing. Mulesing is a valuable on farm surgical procedure that effectively protects merino ewes from breech fly, performed by farmers with no vet supervision. Since the invention of Trisolfen, the wool industry has been afforded a level of international protection owing to the fact that mulesing can now be performed with effective pain relief and improved wound healing.

AWGA discussions with major international processors, fashion industry representatives and EU and USA national retail associations have consistently demanded that Trisolfen be increasingly adopted as best practice for mulesing, if Australian wool is to improve its international welfare credentials after so much negative publicity in international press, allowing their brands to be better protected in the market place from animal rights activity. (Please see 3 attachments).

In essence, the decision not to allow Trisolfen to be more easily purchased and administered could have further serious international trade implications via refreshed boycotts of wool soon to be reportedly implemented in 2014 by animal right activists. Thus, we strongly believe that Trisolfen must be moved to an s6 standard, allowing more ease of ordering, easier access, cost reduction, and increased uptake by the wool industry, thereby reducing the impacts of possible forthcoming threats to our international wool trade.

Further reasons why Trisolfen must be given an S6 status:

- Woolgrowers in remote regions on a regular basis complain about the difficulty in purchasing Trisolfen from vets. S6 status would allow over the counter sales through normal retails channels, would greatly ease tyranny of distance access to TriSolfen.
- Large percentages of lambs that are mulesed without pain relief every year are in remote areas without direct or easy access to Trisolfen. The current vet only Trisolfen distribution basis discriminates against those who are trying to improve best practice welfare.
- Woolgrowers are trying to do the right thing for animal welfare but it is unreasonable that growers in remote regions should have to carry a significant extra cost burden to travel to a vet to purchase a product that is not applied by or overseen by the vet when it is applied.
- Changing of the schedule would allow AWGA to undertake significant education and advertising to their members on the importance of using pain relief during mulesing currently this is prohibited under a S4 schedule.
- As a major grower organization we have not had one complaint or report of misuse since it became commercially available in 2006, in fact, all reports have been praiseworthy and of a highly productive nature of the product.
- All main stream welfare organizations are now calling for Trisolfen's use to be used by the entire industry, something that is impossible until it is available over the counter as are many other chemicals and pharma products. This can only be achieved via a s6 rescheduling.

We are sure that common sense will prevail and that your excellent organization will agree with us and all other wool bodies of the urgent and necessary need to reschedule Trisolfen, allowing more growers easier access and use, guaranteeing better welfare outcomes for our sheep, allowing for more competition in the market place, whilst boosting the welfare marketing credentials of the Australian wool clip, primarily giving much needed confidence to our customers overseas.

[redacted]

Paolo Zegna on mulesing and other wool related issues	29/11/2009

Woolnews.net spoke with Paolo Zegna in South Africa at the International Mohair Summit held last month. Mr Zegna is the Chairman of Ermenegildo Zegna, sponsor of the Ermenegildo Zegna Mohair Trophy. The company started in 1910 and today employs over 6000 people worldwide and is a leading multinational company with products from spinning and weaving and to retailing luxury clothing. The company supplies its products to 525 mono-brand stores of which 253 are directly operated under the Ermenegildo Zegna name in over 80 countries worldwide.

Mulesing

'I still believe that mulesing has been the best solution to flystrike to date. Millions of sheep would have died a horrible death if it was not for mulesing. But it is time to move on - I believe that pain relief is the best method at present. We use medication on humans for pain relief during medical procedures and it should be fully implemented in Australia during mulesing as soon as possible'. Mr Zegna said

Mr Zegna believes that Australian Wool Innovation (AWI) made a mistake when it promised to cease mulesing by 2010. It built expectations with customers that it could not fulfill, he said.

Zegna Group has calculated the number of lambs that are represented in the wool the company buys and will contribute toward pain relief to each of these lambs.

'At Zegna Group we take this issue seriously and we are prepared to pay for pain relief. It is very important to us that we do the right thing', says Mr Zegna.

'However, we need to be logical about this. Australia cannot just stop producing the finest world wool because of the mulesing issue. We all need wool, particularly fine Australia wool'. Mr Zegna believes that a genetic solution is probably the best solution to eradicate mulesing but it is a long term solution. At this stage pain relief is the best short term solution', he says.

Wool promotion

Mr Zegna believes that the customer needs "to be excited" about wool. The green image and environmental credentials that wool has is all good and well but what is really needed and what will really sell wool is if buyers are excited about wool and the products made from it.

He believes that re-igniting sales of Australia wool worldwide is a priority.

'In promoting wool we need to create excitement as well as value', he says. 'AWI needs to have a promotional plan and it must not take too long for this plan to be worked out and to be discussed with the industry'.

China

China is a rewarding market for Zegna Group. For the first time China will be the number one selling market for Zegna in 2010, out selling both Europe and the USA. The company continues to invest in China in updating its shops and showrooms and investing in personnel training.

Today Zegna has 73 stores across the Greater China region, with stores in mainland China, Hong Kong and Macau. ‘We will be putting a lot of resources into places like China and India and other emerging markets, because we believe that they help to overcome the reduction that everybody is facing in the so called ‘mature markets’’

‘We are looking to the young market where products must be both exciting and provide value. I am optimistic about the future of natural fibres as long as we do work to excite future buyers about wool’.

Tri-Solfen ***Submission 3of 6 – Attachment 2 of 3***

February 24, 2011

[redacted]

Dear [redacted]

Thank you for providing us the Australian industry response dated 7 February 2011 to the U.S. retail/brand position paper on mulesing. We appreciate the explanation of actions the Australian industry is taking to address the mulesing issue.

The letter did not, however, address many of the points in our position paper, including our proposed 2013 timeframe as a target date for the industry to adopt mulesing alternatives. Therefore, we restate our view that the wool industry should move toward the widespread adoption of alternatives to mulesing (suitable to particular environmental conditions) in an expedited fashion, and commit to achieve this objective within a reasonable timeframe. We again call upon the representative organizations of the Australian wool industry to provide a public report that maps out a strategy with measureable milestones to achieve this goal.

We also remain committed to two other goals. We are pleased to see in the wool industry response that the amount of wool sold at auction with an accompanying National Wool Declaration (NWD) has increased substantially. That said, we believe the only way to guarantee full and accurate participation is to make, filing of the NWD mandatory in the industry. Further, the information indentified through the NWD should be expanded by adding a category for "clips." Finally, we applaud the efforts of the Australian Wool Exchange (AWEX) to verify the information contained in the NWDs and encourage AWEX to expand these traceability and verification efforts.

Second, the wool industry response also notes that the use of pain relief on mulesed animals has also increased substantially as the analgesic, Trisolfen, has become widely available on a commercial basis. Therefore, we believe that use of post-procedure analgesia should now be adopted as an industry best practice and required of <u>all</u> growers who continue to mules their animals. In addition, this treatment should be expanded to include adoption of pre-procedure pain relief measures mentioned in the wool industry response, as soon as those treatments are approved and become commercially available.

We remain encouraged that our position paper facilitated the formation of the coalition comprising the broad range of wool industry stakeholders in Australia, and believe it was precisely what is required to meet our collective goal toward the widespread adoption of alternatives to mulesing. We hope that this coalition can provide the leadership needed to develop an industry consensus necessary to achieve a resolution to the mulesing issue that will be acceptable to all interested parties.

American Apparel and Footwear Association (AAFA)
National Retail Federation (NRF)
Outdoor Industry Association (OIA)
Retail Industry Leaders Association (RILA)
US Association of Importers of Textiles and Apparel (USA-ITA)
Wool Working Group

cc: Agforce Queensland
Australian Association of Stud Merino Breeders
Australian Council of Wool Exporters & Processors
Australian Wool Exchange
Australian Wool Testing Authority
Australian Superfine Wool Growers' Association
Federation of Australian Wool Organisations
Inland Woolbrokers Association
New South Wales Farmers Association
Pastoralists & Graziers Association of WA
Private Treaty Wool Merchants of Australia
South Australian Farmers Federation
Tasmanian Farmers & Graziers Association
The National Council of Wool Selling Brokers of Australia
Victorian Farmers Federation
Western Australian Farmers Federation
WoolProducers Australia

Tri-Solfen

Submission 3 of 6 – Attachment 3 of 3.

A message from major wool processors to Australian woolgrowers

We, the undersigned, the major processors of Australian wool, are concerned at the continuing decline of Australian wool production, which is the lifeblood of our businesses. We understand that many of you are considering a further reduction, or to stop altogether.

The Australian Wool Industry Taskforce has announced that mulesing will cease by the end of 2010, even though no commercial alternative is available to save sheep from deadly flystrike.

We sympathise with those of you who are caught between the PETA-driven demands of certain retailers and the potential death of your sheep and livelihoods. It appears that either way risks the end of the wool industry.

We will not allow this to happen. We believe there are solutions.

The long-term solution is to breed sheep which produce beautiful wool, yet which are naturally resistant to flystrike. This will take many years and we strongly encourage all of you to follow this course of action.

In the meantime we believe that growers should have the right to continue mulesing any sheep that are at high risk of flystrike, on condition that pain relief, as approved by the Australian Veterinary Association and other animal welfare groups, is applied.

We cannot understand how any retailer or its customer would object to the humane treatment of your animals, especially if your intention is to save their lives.

We therefore call upon you to intensify your efforts to breed sheep that are resistant to flystrike as soon as it is possible to do so, and to adopt the use of pain relief in the interim.

We also call on retailers to drop any and all boycotts of Australian wool from farmers who are undertaking this process and continue to support them beyond 2010 if necessary - for as long as it takes to eliminate the need for mulesing.

Without Australia there is no meaningful world wool industry. We must allow common sense and courage to prevail!

In no particular order:
CHINA
Reward (Ningbo) Wool Industry Co.,Ltd.
Heilan Group
Jiangsu Australia Harvest Group Co.,Ltd.
Zhangjiagang Free Trade Zone Concord Woollen Industrial Co.,Ltd.
Fine Wool Spinning Factory of Jiangsu Nijiaxiang Group
Tianyu Wool Industry (Zhangjiagang Free Trade Zone) Co.,Ltd.
Zhejiang Redsun Wool Textile Co.,Ltd.
Zhangjiagang Free Trade Zone, Zhongao Wool Combing Industry Co.,Ltd.
Zhejiang New Chuwa Wool Co.,Ltd.
Changzhou Wool-Top Factory
Zhangjiagang Aoyang Group
Changzhou Yuyang Wool Textile Industry Co.,Ltd.
Hebei Sanli Group
Kunshan Hengyi Top making Mill
Shanghai Hengyuanxiang Group
Zhangjiagang Golden Sun Wool-Spinning Co.,Ltd.
Tianjin Tianyang Wool Textile Group.(Tianjin No.2 Top Making Mill)
Zhangjiagang Free Trade Zone Xinle Wool Co.,Ltd.

INDIA
OCM India Limited

GERMANY
Suedwolle GmbH & Co Kg
Bremer Woll-Kaemmerei A.G.
Schoeller GmbH & Co KG
Gaenslen & Völter GmbH + Co KG
Zwickauer Kammgarn GmbH

ITALY
Associazione Nazionale del Commercio Laniero
Lanificio Policarpo S.p.A.
Lora e Festa S.p.A.
Filatura Botto Poala S.p.A.
E.ca.fil Best S.p.A.
Filatura e Tessitura di Tollegno S.p.A.
Pettinatura Italiana S.p.A.
Pettinatura Biellese S.p.A.

SWITZERLAND
G. Schneider S.A.

FRANCE
Segard Masurel S.A.
A. Dewavrin Fils & Cie.

UK
G. Modiano Ltd.

TURKEY
Aksu Iplik A.S. Istanbul
Altinyildiz Mensucat A.S.
Bahariye Mensucat A.S.
Boyner Sanayi Mensucat A.S.
Ormo Yun Iplik A.S.

BULGARIA
E. Miroglio AD

Tri-Solfen public submission 4 of 6

Scheduling Proposal for Adrenaline, Bupivacaine and Lignocaine [SEC=No Protective Marking]

[redacted]

to:
SMP@health.gov.au
06/06/2013 16:15
Hide Details
From: [redacted]
To: "SMP@health.gov.au" <SMP@health.gov.au>,
History: This message has been replied to.

Commercial-in-Confidence

Medicines and Poisons Scheduling Secretariat (MDP88),
GPO Box 9848
CANBERRA
ACT 2601
e-mail SMP@health.gov.au
Facsimile 02-6289 2650

Subject: Scheduling Proposal for Adrenaline, Bupivacaine and Lignocaine (Interim decision from March 2013 Meeting of ACCS & ACMS)

To the delegates,

Bayer Australia Ltd (Animal Health) (BAH) is the registrant and manufacturer of the product containing the abovementioned active ingredients, i.e. Tri-Solfen Topical Anaesthetic & Antiseptic Solution for Pain Relief in Lambs Following Mulesing (Tri-Solfen). BAH became aware of the proposal for the scheduling change only after the agenda for the committee's March 2013 meeting was published. BAH was not involved in preparation of any submissions made to the committee but feels it appropriate to provide comment on the interim decision recently published.

BAH is strongly in favour of the proposed change from Schedule 4 to Schedule 6 for this product. We are committed to promoting humane, science-based sheep production practices. For those lambs that require the mulesing procedure, the use of Tri-Solfen as a post-operative analgesic provides the best welfare outcome currently available to producers. Adoption of practices to support sheep welfare is of critical importance to the sustainability of the Australian wool-production industry.

We believe the proposed scheduling change would result in a significant increase in use of the product for its intended purpose by improving its availability to sheep producers and allowing the direct promotion of the product to end-users. To this end, we would like to provide comment on the "reasons noted" for the delegates' interim decision.

No data are available to demonstrate the likelihood or magnitude of increased appropriate usage due to the scheduling change. However, an increase in usage following the scheduling change is a very logical assumption. Currently, the product can be provided under veterinary prescription only. For many sheep producers the distance from a vet (e.g. to make a farm-visit) or the cost of veterinary services are significant hurdles and often voiced as concerns by industry stakeholders. Furthermore, the ability of BAH or other parties to promote the benefits of the product directly to sheep producers under the new scheduling classification would significantly increase the adoption of post-mulesing analgesia.

BAH is uncertain of what the delegates refer to as "inappropriate usage". Tri-Solfen has a very specific indication for use on lambs at mulesing. As for any veterinary medication, end-users are required to adhere to label directions and/or specific instructions provided by the prescribing veterinarian. We are not aware that changing the product schedule will in any way reduce the obligations (legal or otherwise) of the end-user to ensure appropriate use of the product (i.e. as per label directions). Furthermore, we are not aware of any demand for the product to be used for purposes other than the label indication that might be made legitimate or 'allowable' by the proposed scheduling change. It is difficult to determine what specific risks the delegates are considering in this instance.

The relationship between mulesing as a "regulated process" and the "extent of use" is unclear. BAH encourages the delegates to confirm what they consider to be 'regulation' of mulesing. BAH fully supports the

principles of mulesing operator accreditation to ensure the consistent adoption of best practice and, as a consequence, the best welfare outcome for lambs. However, the current code of practice* does not require the mandatory accreditation of mulesing operators (it is noted as a 'committed value' of the sheep industries). Furthermore, a new draft welfare guideline currently open for public consultation** has proposed that: "A person performing mulesing must have the relevant knowledge, experience and skills, or be under the direct supervision of a person who has relevant knowledge experience and skills".

It appears that the delegates have considered that the mulesing operation is restricted to 'licensed' operators only. And, it is assumed, that these operators maintain close links with the veterinarians who are being consulted by individual sheep producers to care for their flock – thus enabling high rates of prescribing of Tri-Solfen. This is simply not the case. As mentioned previously, the ability to promote use of Tri-Solfen directly to mulesing contractors/operators as well as sheep producers is expected to markedly increase the extent of use.

While the delegates' concerns regarding "inappropriate usage" are not clear, they have commented that the proposed rescheduling would "increase the likelihood of larger quantities being available which could lead to misuse". The very specific indication for this product's use was noted above. However, it should be emphasised that quantities of product are supplied based on demand through distribution channels. If the product were available without veterinary prescription, it would most frequently be sold through rural suppliers or veterinarians directly to sheep producers or mulesing operators. BAH does not anticipate any other off-label (i.e. inappropriate) uses for the product that will drive demand. Consequently, appropriate use will determine demand and this dictates the quantities of product available for sale.

It is noted by the delegates that the toxicity of the active ingredients and narrow window of effectiveness warrant appropriate supervision by a veterinarian. It is assumed that detailed data relating to the toxicity of the individual active ingredients are available for the delegates' consideration, with regard to their concentrations in the formulation. However, it should be noted that the product is only used at the time of the mulesing procedure (i.e. immediately after removal of the skin). This is because the young lambs are only handled once before being returned to the yard or paddock. Sheep producers will not re-handle the lambs following mulesing to treat them with Tri-Solfen at a time when the product is no longer effective. Furthermore, only in very rare circumstances would a veterinarian be present at the time of product use.

The delegates noted that the product is available in 100mL injection vials. This is not correct. The product is packaged in rigid plastic bottles/drums and, as per the APVMA's public product database (PUBCRIS), it is registered for supply in containers from 1L to 22L in volume. The product is applied by coarse spray to the mulesing wound where it forms a gel coating and exerts the analgesic and antiseptic effects – it is a topical formulation, not an injection.

It is very encouraging to note that the delegates see the increased use of Tri-Solfen for pain relief on mulesed lambs as "a desirable outcome". However, it is incorrect to state that the extent of use can be increased merely by promotion within the restrictions of the current scheduling arrangements. BAH has invested heavily in promotion of the product since registration in 2011 and it is not our belief (for the reasons stated above) that significant improvements in the frequency of use of this product can be achieved while it remains in Schedule 4.

We would like to thank the delegates for their consideration of the proposed change to scheduling of this product. Although BAH was unable to prepare a submission for the initial meeting, we hope that as the product registrant and manufacturer our comments on the interim decision will be considered.

Please let me know if I can provide any other information which may assist with the delegates' further consideration.

Best regards,

[redacted]

[redacted]

[redacted]

[redacted]

Please consider the environment before printing this email

*Primary Industries Standing Committee Model Code of Practice for the Welfare of Animals: The Sheep, 2nd edition, CSIRO Publishing 2006.
** Australian Animal Welfare Standards and Guidelines: Sheep, Edition One, Public Consultation Version 1.0, 21 February 2013, Standing Council on Primary Industries

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6 June 2013

Medicines and Poisons Scheduling Secretariat (MDP88)
GPO Box 9848
CANBERRA ACT 2601
e-mail SMP@health.gov.au

Notice under subsections 42ZCZP of the Therapeutic Goods Regulations 1990 (the Regulations)

Submission following March 2013 meeting of the joint Advisory Committee on Chemicals Scheduling (ACCS) and the Advisory Committee on Medicines Scheduling – ACCS & ACMS # 5 ADRENALINE, BUPIVACAINE AND LIGNOCAINE

As the research, development and marketing organisation for the wool industry, Australian Wool Innovation (AWI) wishes to take this opportunity to provide brief comment on the current review process, specifically the scheduling of Trisolfen. As the Industry Services Body for the wool industry, AWI does not have a policy development role, nor do we represent woolgrowers.

Since becoming commercially available to woolgrowers for the use in mulesing, the uptake of this product has been significant. AWI, like reputable animal welfare organisations, encourages woolgrowers to use pain relief if mulesing is required. Research trials clearly show welfare benefits and anecdotal reports from woolgrowers indicates an improved animal health outcome from the use of this product, hence the high adoption rate over a few years.

A move to make this product more readily available to woolgrowers is likely to result in an improved animal health outcome.

If you require any further information, please contact Dr Jane Littlejohn, GM On Farm R&D on 02 8295 3100.

[redacted]

Australian Wool Innovation Limited ABN 12 095 165 558
[redacted] www.wool.com
St, Sydney NSW 2000
GPO Box 4177, Sydney NSW 2001

WOOLMARK

Fw: Tri-solfen submission to ACCS . [SEC=No Protective Marking]

[redacted] to: smp 28/05/2013 15:42

Cc: [redacted]

History: This message has been replied to.

2 attachments

Covering letter to APVMA with Tri-Solfen rescheduling submission for the ACCS.doc

Final Submission to ACCS for Rescheduling of Trisolfen 5 March 2012.DOC

No Protective Marking

To Whom it May Concern

I wish to advise that the attached rescheduling application for Tri-Solfen (Adrenaline, Bupivicaine and Lignocaine) was originally sent to the APVMA by NSW to forward to the scheduling committee, in March 2012. There was apparently some difference of opinion as to whether it should have been submitted through the APVMA or directly to the scheduling committee. It was resubmitted directly to the scheduling delegate in August 2012 after receiving advice that jurisdictions could submit rescheduling requests directly. For some reason this was later disputed and as a result it appears that this submission was not considered in reaching the interim decision on the rescheduling request for Tri-Solfen.

The submission was submitted on behalf NSW with input from Victoria (both States being major sheep producing areas) after both feedback from sheep veterinary practitioners and with a full understanding of industry practices and the state legislation regarding dispensing of S4 products.

I am concerned that this submission was not taken into account and would like it to be given full consideration before any further decisions are made about Tri-Solfen. I have also attached associated emails following its original submission to show that it is genuine.

With reference to the comments made by Allen Bryce (Program Manager Veterinary Pesticides at the APVMA) at the end of these emails regarding this product, I'd also like to add the following points.

When the issue of rescheduling of this product was raised with sheep vets, it became clear that while sheep consultant vets were aware of its use by their regular clients, they had not dispensed it to them. It is therefore most unlikely that the veterinary practitioner who dispensed the product in that situation, had any knowledge about the flock structure, its management, health status, or even the number of lambs that are likely to be mulesed.
In Victoria, the requirement under Drugs Poisons and Controlled Substances regulations (Reg13), is that before dispensing a product, the veterinary practitioner must ensure that the drug or poison is for the treatment of an animal under his or her care; and, he or she has taken all reasonable steps to ensure a therapeutic need exists for that drug or poison. The only veterinarians who would be in a position to do this, would be specialist sheep consultants, as most private practitioners rarely if ever visit commercial sheep farms. However, consultants are generally not in the business of merchandising whereas private practitioners are. It is clearly not practical for a private practitioner to meet these requirements for dispensing Tri-Solfen and the only schedule that would

allow them to meet the legislative requirements without visiting the farms, would be a a schedule 2 or 3. However, I am advised by the APVMA that this is not possible, even if it was appropriate and necessary. Since the product is sold in pack sizes of up to 22 litres, there appears to be ample opportunity for its use other than on mulesed lambs as there is always likely to be product left over - that is if the producer wished to use it contrary to the label directions.

While the active constituents may be available only in small volumes and are scheduled S4, there have been a number of instances where scheduling has been changed to S5 or S6 to accommodate lower concentrations and larger volumes of S4 active constituents. This does not detract from the original scheduling of the active constituent.

Many products registered by the APVMA for use in livestock, have long withholding periods on the label directions for use but are not scheduled S4 to ensure that there is an ongoing educational program. Correct use relies on the producer reading and implementing the directions on the label. A good example would be the product Tussock Herbicide which has Flupropanate as the active constituent. It has a withholding period of 4 months after spraying on pasture, before stock may graze on it. Furthermore, stock must be removed and put on pasture that has not been sprayed with flupropanate for a further 14 days after grazing pasture previously sprayed with flupropanate, before they can be slaughtered or milk can be collected for human consumption. These requirements for withholding periods after grazing sprayed areas, are permanent. Similarly, Nitromec, a fukicide containing nitoxynil and ivermectin active constitiuents has a 56 day withholding period for meat and a 30 day withholding for milk. The requirements for Tri-solfen are relatively simple in comparison.

From an animal ethics point of view, the important issue is the use of the product, rather than the product being supplied by veterinarians. The aim is to have all lambs that are mulesed treated with Tri-solfen.

In summary, there is ample opportunity for misuse of this product, if a producer so wishes, even if it were supplied by a veterinary practitioner. The current scheduling of S4 for Tri-solfen means that in most cases, veterinary practitioners in Victoria are unable to meet legislative requirements when dispensing it. Many registered products have long withholding periods for meat and appear to be managed satisfactorily by producers. Finally, it would be advantageous from an animal ethics view point if all mulesed lambs were treated with this product. This could be achieved more simply if the product was not scheduled as S4 and could be advertised more generally.

Yours sincerely

Eubacterium sp public submission 1 of 1.

submission about the interim scheduling decision for Eubacterium sp.
[SEC=UNCLASSIFIED]
[redacted]
to:
'SMP@health.gov.au'
30/05/2013 15:42
Cc:
[redacted]
To: "'SMP@health.gov.au'" <SMP@health.gov.au>,
[redacted]
History: This message has been forwarded.

1 Attachment

EFSA_DSM11798_3203.pdf

UNCLASSIFIED

Dear [redacted]

This submission is in regard to the interim scheduling decision for Eubacterium Sp. (May 2013).

[redacted] has become aware of an EFSA (European Food Safety Authority) report on the Eubacterium in question (DSM 11798), this comprehensive report has only recently become available.

The report concludes that "although the additive is formulated to minimise exposure by inhalation some exposure of the respiratory tract remains possible and potential for respiratory sensitization cannot be excluded". As such, we thought it prudent to share this report with the delegate, as there is the possibility that it may add weight to the argument for Schedule 5 rather than Appendix B.

Please find the EFSA report attached as a PDF document. It is also publically available at the EFSA website: http://www.efsa.europa.eu/en/efsajournal/doc/3203.pdf.

[redacted]

UNCLASSIFIED