REASONS FOR FINAL DECISIONS BY DELEGATES OF THE SECRETARY TO THE DEPARTMENT OF HEALTH AND AGEING FOR AMENDMENTS TO THE POISONS STANDARD

MARCH 2011

Delegates' final decisions on scheduling matters:

- Initially referred to the December 2010 joint meeting of the Advisory Committee on Chemicals Scheduling (ACCS) and the Advisory Committee on Medicines Scheduling (ACMS) [**ACCS-ACMS#1**];
- Initially referred to the December 2010 meeting of the ACMS [**ACMS#1**]; or
- Considered as delegate-only matters i.e. were not referred to an advisory committee.

Notice under subsections 42ZXZS and 42ZCZX of the Therapeutic Goods Regulations 1990 (the Regulations)

A delegate of the Secretary to the Department of Health and Ageing hereby gives notice of delegates' final decisions for amending the Poisons Standard (commonly referred to as the *Standard for the Uniform Scheduling of Medicines and Poisons* – SUSMP) under subsections 42ZCZS and 42ZCZX of the Regulations. This notice also provides the reasons for each decision and the date of effect of the decision. Edited versions of further submissions on matters referred to ACCS-ACMS#1 or ACMS#1 are also available at http://www.tga.gov.au/industry/scheduling-decisions.htm.

Matters referred to ACCS-ACMS#1 and ACMS#1

Delegate's interim decisions on recommendations by ACCS-ACMS#1 and ACMS#1 were published on 16 February 2011 at http://www.tga.gov.au/industry/scheduling-decisions.htm. This public notice also invited further comment from the applicant and parties who made a valid submission in response to the original invitation for submissions (published 29 September 2010 at http://www.tga.gov.au/newsroom/consult-scheduling-acmcs.htm).

In accordance with subsection 42ZCZR of the Regulations, if a delegate makes an interim decision on an application, that delegate may make a final decision confirming, varying or setting aside the interim decision only after considering any further valid submissions. If no further submissions were received then the delegate may choose to confirm the interim decision as the final decision.

Further submissions from parties other than those who made a valid submission in response to the original invitation or the applicant, or those received after the closing date, need not be considered by the delegate.

Matters not referred to an advisory committee

A delegate may make a final decision on matters the delegate did not choose to refer to an advisory committee. Guidance for the delegate when deciding not to refer a matter to an advisory committee is set out in the Scheduling Policy Framework (SPF) accessible at http://www.tga.gov.au/industry/scheduling-spf.htm.

Implementation

The amendments arising from this notice will be incorporated into the SUSMP through an amendment which will be available for purchase from National Mailing and Marketing Pty Ltd, telephone (02) 6269 1035. The SUSMP and its amendments are also available electronically at the ComLaw website, a link to which can be found at http://www.tga.gov.au/industry/scheduling-poisons-standard.htm.

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GLOSSARY

ABBREVIATION	*NAME*
AAN	Australian Approved Name
AC	Active Constituent
ACCC	Australian Competition and Consumer Commission
ACCS	Advisory Committee on Chemicals Scheduling
ACCM	Advisory Committee on Complementary Medicines (formerly Complementary Medicine Evaluation Committee [CMEC])
ACMS	Advisory Committee on Medicines Scheduling
ACNPM	Advisory Committee on Non-Prescription Medicines (formerly Medicines Evaluation Committee [MEC])
ACPM	Advisory Committee on Prescription Medicines (formerly Australian Drug Evaluation Committee [ADEC])
ACSM	Advisory Committee on the Safety of Medicines (formerly Adverse Drug Reactions Advisory Committee [ADRAC])
ADEC	Australian Drug Evaluation Committee (now Advisory Committee on Prescription Medicines [ACPM])
ADI	Acceptable Daily Intake
ADRAC	Adverse Drug Reactions Advisory Committee (now Advisory Committee on the Safety of Medicines [ACSM])
AHMAC	Australian Health Ministers' Advisory Council
APVMA	Australian Pesticides and Veterinary Medicines Authority
AQIS	Australian Quarantine and Inspection Service
ARfD	Acute Reference Dose
ASCC	Australian Safety and Compensation Council

ASMI	Australian Self-Medication Industry
ARTG	Australian Register of Therapeutic Goods
CAS	Chemical Abstract Service
CHC	Complementary Healthcare Council of Australia
CMEC	Complementary Medicine Evaluation Committee (now Advisory Committee on Complementary Medicines [ACCM])
CMI	Consumer Medicine Information
COAG	Councils Of Australian Governments
CRC	Child-Resistant Closure
CTFAA	Cosmetic, Toiletry & Fragrance Association of Australia
CWP	Codeine Working Party
DAP	Drafting Advisory Panel
ECRP	Existing Chemicals Review Program
EPA	Environment Protection Authority
ERMA	Environmental Risk Management Authority (NZ)
FAISD	First Aid Instructions and Safety Directions
FDA	Food and Drug Administration (US)
FOI	Freedom of Information Act 1982
FSANZ	Food Standards Australia New Zealand
GHS	Globally Harmonised System for Classification and Labelling of Chemicals.
GIT	Gastro-intestinal tract
GP	General Practitioner
HCN	Health Communication Network

INN	International Non-proprietary Name
ISO	International Standards Organization
LC_{50}	The concentration of a substance that produces death in 50% of a population of experimental organisms. Usually expressed as mg per litre (mg/L) as a concentration in air.
LD_{50}	The concentration of a substance that produces death in 50% of a population of experimental organisms. Usually expressed as milligrams per kilogram (mg/kg) of body weight
LOAEL	Lowest Observed Adverse Effect Level
LOEL	Lowest Observed Effect Level
MCC	Medicines Classification Committee (NZ)
MEC	Medicines Evaluation Committee (now Advisory Committee on Non-Prescription Medicines [ACNPM])
MOH	Ministry of Health (NZ)
NCCTG	National Coordinating Committee of Therapeutic Goods
NDPSC	National Drugs and Poisons Schedule Committee
NHMRC	National Health and Medical Research Council
NICNAS	National Industrial Chemicals Notification & Assessment Scheme
NOAEL	No Observed Adverse Effect Level
NOEL	No Observable Effect Level
NOHSC	National Occupational Health & Safety Commission
OCM	Office of Complementary Medicines
OCSEH	Office of Chemical Safety and Environmental Health
ODBT	Office of Devices, Blood and Tissues
OOS	Out of Session

OPM	Office of Prescription Medicine
OTC	Over-the-Counter
PACIA	Plastics And Chemicals Industries Association
PAR	Prescription Animal Remedy
PBAC	Pharmaceutical Benefits Advisory Committee
PEC	Priority Existing Chemical
PGA	Pharmaceutical Guild of Australia
PHARM	Pharmaceutical Health and Rational Use of Medicines
PI	Product Information
PIC	Poisons Information Centre
PSA	Pharmaceutical Society of Australia
QCPP	Quality Care Pharmacy Program
QUM	Quality Use of Medicines
RFI	Restricted Flow Insert
SCCNFP	Scientific Committee on Cosmetic and Non-Food Products
SCCP	Scientific Committee on Consumer Products
STANZHA	States and Territories and New Zealand Health Authorities
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
SVT	First aid for the solvent prevails
TCM	Traditional Chinese Medicine
TGA	Therapeutic Goods Administration

TGC	Therapeutic Goods Committee
TGO	Therapeutic Goods Order
TTHWP	Trans-Tasman Harmonisation Working Party
TTMRA	Trans-Tasman Mutual Recognition Agreement
WHO	World Health Organization
WP	Working Party
WS	Warning statement

PART A – FINAL DECISIONS ON PROPOSALS REFERRED TO AN ADVISORY COMMITTEE

1. MATTERS INITIALLY REFERRED TO ACCS-ACMS#1

1.1 5-AMINOLEVULINIC ACID

DELEGATE'S REFERRAL TO EXPERT ADVISORY COMMITTEE

The delegate considered the scheduling of 5-aminolevulinic acid (5-ALA) and decided to seek advice from the December 2010 ACCS-ACMS joint meeting on the following:

5-aminolevulinic acid (5-ALA) – proposal to include in Schedule 4. This proposal is a result of a recommendation from the June 2010 NDPSC meeting.

EXPERT ADVISORY COMMITTEE RECOMMENDATION

The ACCS-ACMS joint meeting recommended that a new Schedule 4 entry be created for 5-ALA. The joint meeting further recommended an implementation date of at least nine months after the delegate's final decision.

BACKGROUND

Methylaminolevulinate (MAL) is used in photodynamic therapy (PDT) to treat cancerous and pre-cancerous cells. MAL is currently listed in Schedule 4, with no specified cut-offs or use limits. MAL is the methyl ester of 5-ALA.

As 5-ALA is the active principle of MAL, it is expected that it would normally be captured by the Schedule 4 entry of MAL, since a Schedule entry captures "every salt, active principle or derivative of the substance, including esters", as set out under Part 1(2)(c) of the SUSMP. However, the October 2003 NPDSC meeting determined that, until such time as a product was available in the Australian market, 5-ALA should remain unscheduled. There is no record of any subsequent reconsideration of this position.

In February 2010 the Cosmetic Physicians Society of Australia (CPSA) raised the following concerns with the TGA about the scheduling status of 5-ALA and its current use by beauty therapists for PDT:

- PDT was promoted for treatment of sun-damaged skin within the beauty profession without the relevant medical and clinical guidelines; and
- because 5-ALA was unscheduled, non-medical personnel can provide skin cancer treatment to the general public without the appropriate training, diagnostic skills, follow-up or monitoring.

The scheduling of 5-ALA was subsequently referred to the June 2010 NDPSC meeting for consideration. The NDPSC decided that it would be appropriate to include 5-ALA in

Schedule 4. Members noted, however, that a number of pre-meeting submissions opposed this decision and, in accordance with the transition arrangements for this final meeting of the NDPSC, agreed that this item could not be finalised at that meeting. The NDPSC therefore referred the matter to the delegate with the recommendation that a new Schedule 4 entry for 5-ALA be created.

SCHEDULING STATUS

As detailed above, not currently scheduled.

INITIAL SUBMISSIONS

December 2010 Pre-meeting Submissions

A single pre-meeting submission was received from the CPSA supporting that 5-ALA (and any of its derivatives and related compounds) used as photosensitising agents in PDT should be captured in Schedule 4.

The submission reiterated the following arguments, as presented in CPSA's February 2010 letter to TGA and subsequent pre-meeting submission to the June 2010 NDPSC meeting

- PDT is generally conducted by doctors to treat precancerous and some forms of cancerous skin lesions.
- Having 5-ALA unscheduled allows beauty therapists to access this substance at any strength (the medical strength 5-ALA was usually 20 per cent). This 5-ALA may also be a non-stabilised form which can lead to a variability of concentration and penetration with consequent unpredictability of results and potential side effects.
- One example of a beauty therapy training course for PDT claimed to use 5-ALA at a cosmetic strength of about 3 per cent.
- Beauty therapy training does not provide the individual with the ability to correctly examine, diagnose or treat advanced sun-damaged skin. The ability to biopsy for histopathological diagnosis of suspicious lesions before the appropriate treatment is prescribed is not within the beauty therapy skill base.
- Beauty therapists do not have professional indemnity insurance cover commensurate with that of a medical practitioner to safeguard potential clients.
- PDT is being promoted for the treatment of sun-damaged skin within the beauty therapy profession without the relevant medical and clinical guidelines. In Australia there is a distinct possibility of pre-cancerous and cancerous lesions being present.
- PDT is not a comfortable experience at therapeutic levels. The CPSA was concerned about aftercare, follow-up and pain management for those individuals who undergo this treatment.

- The application of PDT-type procedures may not be appropriate for the "skin condition" being treated due to inaccurate diagnosis.
- Treatment in a beauty therapy environment may lead the patient to believe they are adequately treated for their sun-damage, which in turn may lead to a false sense of security and delayed presentation to a medical practitioner. Correct diagnosis and treatment may then require a more involved medical intervention perhaps with now-necessary mutilation and increased overall health care costs.
- There are currently no advertising restrictions applying to beauty therapists which are equivalent to those imposed on the medical profession. This may lead to a series of false or exaggerated treatment claims, further enticing and confusing the individual considering such treatments.
- A Schedule 4 listing would increase public safety through increased likelihood of correct diagnosis and appropriate treatment and management of skin conditions.

Implementation

- A delayed implementation period was not recommended as this would leave potential clients of non-medically trained individuals open to harm by incorrect diagnosis and treatments of sun-damage.

June 2010 NDPSC discussion

Members noted the discussion of the June 2010 NDPSC meeting, including the following particular points.

- A Member asserted that the extent of non-medical use of 5-ALA was difficult to determine and the risks and benefits of use of this substance in this context should be considered in making a scheduling decision. The Member specifically noted the risk of potentially delaying diagnosis of cancer in relation to potential aesthetic benefits.
- A Member argued that a scheduling decision must be based on the inherent risk of the substance and not be used to restrict access in a particular setting without appropriate toxicological data to support that restriction. The Member also cautioned that there were different uses of the term "sun-damaged skin" which was contributing to the confusion in this debate. For the beauty profession, this often meant "signs of ageing" such as wrinkles, whereas for the medical profession, the term usually related to skin in a "pre-cancerous" condition.
- A Member stated that, given there are products containing 5-ALA currently available on the Australian market, the October 2003 NDPSC decision to leave 5-ALA unscheduled "until such time as a product was available in the Australian market" was no longer appropriate. The Member also noted that XXXXX supported a Schedule 4 listing.
- A Member asserted, and the NDPSC generally agreed, that 5-ALA should, by any objective determination, be captured by the Schedule 4 MAL entry. The NDPSC agreed to recommend a new Schedule 4 entry for 5-ALA.

June 2010 NDPSC submissions

Members noted the information submitted for consideration by the June 2010 NDPSC meeting, including the following particular points.

· Eleven pre-meeting submissions were considered, nine of which were in support of a Schedule 4 entry for 5-ALA. However, one of the opposing submissions included letters from seven beauty therapists/clinics also opposed to a Schedule 4 listing.

Submissions in favour of Schedule 4

· The CPSA reiterated a number of points raised in their initial letter to the TGA and further highlighted the lack of training of beauty therapists to adequately diagnose or treat sun-damaged skin. The submission also discussed the types of lesions that are able to be treated by PDT in order to highlight the need for professional intervention. This submission was endorsed by submissions from XXXXX.

· A number of medical specialists/clinics also supported Schedule 4, noting:

- concern over correct diagnosis of potential skin cancers before undertaking PDT;
- alarm that beauty therapists, who had minimal training in the treatment and recognition of skin cancer, have access to 5-ALA; and
- that interactions with medications, such as tetracycline antibiotics, griseofulvin and diuretics, were of particular concern as it was common for patients seeking PDT to be taking these medications.

Submissions opposed to Schedule 4

· XXXXX argued that there was no scientific basis for the restriction of PDT due to perceived threat to public safety. The following points were noted by Members.

- Beauty therapists are made aware of the potential for a client to present with skin cancers through training and will seek medical advice before treating any skin with abnormalities.
- 5-ALA enhances the effects of laser, intense pulse light (IPL) and light emitting diode (LED) treatments and these treatments have been used safely for years.
- XXXXX does not train in the removal of skin cancers with PDT. This is a different treatment protocol that is left strictly to the medical profession. Training stipulates that any pigmented skin be medically assessed for skin cancer and cleared before PDT skin rejuvenation treatments are offered.
- The vast majority of "non-medical" health practitioners freely and swiftly refer clients to doctors for assessment and treatment where there is even the slightest possibility of a skin cancer condition.
- XXXXX strongly opposed the scheduling of 5-ALA as it would severely limit public access to a safe and effective treatment offered by the wider aesthetic industry.

- XXXXX disputed the need for scheduling on the grounds of public safety for 5-ALA, arguing that the proposal was based on a business focus of some medical groups. Members noted that XXXXX had:
  - discussed clinical applications, methods of application, public benefits and risks and the commercial pressure that XXXXX asserted were influencing doctor statements;
  - included letters from seven beauty therapists with experience using PDT and 5-ALA, all supporting the position that 5-ALA should not be scheduled;
  - referred to a literature review of PDT (commissioned by XXXXX) and asserted that this located all known literature worldwide to identify any possible side effects and complications. Broadly speaking, there were few reports of significant adverse outcomes using 5-ALA in PDT. Two cases of skin cancer possibly related to PDT have been reported. The report also stated that PDT was generally considered to have a low risk of carcinogenicity;
  - asserted that there have been no serious adverse events reported to date by either beauty therapists or doctors in Australia or NZ using 5-ALA for PDT;
  - asserted that doctors were often uncertain as to the correct clinical parameters on the use of PDT and the "learning curve" was considered a lengthy one. However, with correct clinical training and access to TGA listed (or registered) light devices, a health practitioner could rapidly become competent and extremely safe in the patient assessment and use of PDT treatment;
  - advised that, based on some simple survey sampling, the total number of Australian clinics offering PDT to the public may be around 200 to 240 centres (primarily medical clinics). These clinics appear to prefer using 5-ALA rather than the more aggressive MAL, primarily used by a small number of dermatologists specifically for treatment of cancerous and pre-cancerous tissues identified in patients;
  - asserted that it is widely accepted by doctors, and others, that PDT has an extremely low risk profile and is an ideal tool for a variety of skin conditions and complaints, some medical and others not;
  - asserted that there was no scientific evidence to support the claim that an improvement in skin cancer prone tissue treated by a health professional other than that the treatment might "mask" or hide a skin cancer leading to serious adverse effects for the patient at a later date;
  - asserted that many clinics distribute cancer council literature and the vast majority appear to have appropriate arrangements for referring clients to local doctors for skin assessment and treatment;
  - asserted that the medical profession had been running campaigns to discredit other parties offering PDT, despite there being many thousands of PDT systems now safely in use in Australia and no evidence of widespread or serious

negligence or malpractice. Many dermal clinicians and beauty therapists have substantial clinical experience;

- asserted that there has been a concerted attempt by a small sector of the medical community to institutionalise a very simple, very safe and highly effective cosmetic treatment. The scheduling of 5-ALA will certainly lead to a severe future restriction of this excellent treatment without any corresponding benefit in terms of safety of the public; and
- the public already have adequate access to PDT treatments for serious sun damaged and marked (pigmented) skin and asserted that the average cosmetic doctor has little time to carefully consider the wider benefits of PDT and other reliable long lasting treatments.

EXPERT ADVISORY COMMITTEE DISCUSSION

Members agreed that the relevant matters under section 52E(1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of use and (b) purpose and extent of use.

A Member reiterated the argument from the June 2010 NDPSC meeting that 5-ALA, in the normal course of events, would have been captured by the Schedule 4 MAL entry and that use by beauticians had not been envisaged at the time of the October 2003 NDPSC determination on 5-ALA. Several Members also noted that a Schedule 4 listing was previously supported by XXXXX.

One Member noted that the hazard was from the PDT use pattern rather than the specific use of 5-ALA, although noting that MAL was already Schedule 4. Other Members noted that there was little actual data on the risks from cosmetic use of PDT generally, and 5-ALA specifically. One Member reiterated the CPSA point that PDT using 5-ALA was not a comfortable experience at therapeutic levels. The Member noted that there was significant impact on the skin that warranted medical supervision.

A Member queried whether there was a potential public health benefit from allowing access to 5-ALA. Other Members argued that there was such a benefit, but only where treatment using 5-ALA was appropriately supervised, noting the various concerns and issues raised through consideration at the June 2010 NDPSC meeting.

A Member asserted that the beauty industry was not intending to treat cancerous skin, but was seeking to treat certain visible signs of ageing (wrinkles). Other Members noted, however, that this was an unregulated industry. While some training courses recommended using low levels of 5-ALA, this was a voluntary guideline, and several Members advised of cases where some beauticians had been using higher concentrations of 5-ALA.

Several Members agreed that a Schedule 4 parent entry was appropriate and while there was still a question of allowing a low concentration cut-off, there was no tabled data to

justify such a cut-off. Members noted that the onus would be on an applicant to provide data to establish whether cosmetic use at a low concentration was legitimate.

Members noted that no non-human uses of 5-ALA, such as industrial use, had been identified through the public consultation on this matter. Members also noted that a Schedule 4 listing would not prohibit access for experimental and research purposes.

Implementation

Members noted that there was likely to be existing stock and that repackaging would take some time. A Member argued for no delay as the scheduling change was due to a safety concern and that jurisdictions could handle a relabelling delay separately from the scheduling decision.

Members generally supported a delayed implementation to minimise the regulatory impact of this decision and to allow time for the beauty industry to be educated about this decision.

DELEGATE'S INTERIM DISCUSSION

The delegate noted the Members' discussion and agreed with the ACCS-ACMS joint recommendation to create a new Schedule 4 entry for 5-ALA.

The delegate also noted the ACCS-ACMS joint recommendation that the implementation date be at least nine months after the delegate's final decision. The delegate noted that Amendment No.2 to SUSMP No.2 was expected to be implemented on 1 January 2012, and that this would be approximately nine months after the expected publication of the delegate's final decision.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of use and (b) purpose and extent of use.

DELEGATE'S INTERIM DECISION

The delegate decided to create a new Schedule 4 entry for 5-aminolevulinic acid. The delegate decided on an implementation date of 1 January 2012.

SUBMISSIONS ON INTERIM DECISION

No submissions were received on the interim decision.

DELEGATE'S FINAL DECISION

The delegate confirmed the interim decision to create a new Schedule 4 entry for 5-aminolevulinic acid. The delegate also confirmed an implementation date of 1 January 2012.

Schedule 4 – New entry

5-AMINOLEVULINIC ACID.

1.2 TRICLOSAN

DELEGATE'S REFERRAL TO EXPERT ADVISORY COMMITTEE

The delegate considered the scheduling of triclosan and decided to seek advice from the December 2010 ACCS-ACMS joint meeting on the following:

Triclosan – proposal to include in Schedule 6 with an exemption for:

- non-therapeutic human use (e.g. cosmetic use) containing 0.2 per cent or less; and
- all other preparations (e.g. therapeutic use and non-human use) containing 1 per cent or less of triclosan.

This proposal is a result of deliberations from the June 2010 NDPSC meeting, following consideration of recommendations from a NICNAS public report.

EXPERT ADVISORY COMMITTEE RECOMMENDATION

The ACCS-ACMS joint meeting recommended a Schedule 6 triclosan entry for cosmetic use in humans (including use in non-therapeutic mouthwashes) containing more than 0.3 per cent triclosan. The joint meeting confirmed that personal insecticides for human use would not be captured.

The joint meeting also recommended an implementation date of at least nine months after the delegate's final decision.

BACKGROUND

5-Chloro-2-(2,4-dichlorophenoxy)phenol, commonly known as triclosan, is used in the formulation of cosmetics and personal care products, cleaning agents, therapeutics, and agvet products as a preservative or anti-bacterial. It is also used to treat textiles and plastics due to its antimicrobial activity.

The August 1989 NDPSC meeting reconsidered the existing Appendix B listing for triclosan on the basis of new toxicology data, and re-affirmed the entry. Appendix B was subsequently removed from the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) in the mid 1990s. A new Appendix B was reintroduced in the early 2000s, but did not include a number of substances that had previously been in Appendix B, including triclosan, where the NDPSC was unable to locate data for these substances to continue justifying such listings.

In 2003, triclosan was declared a Priority Existing Chemical (PEC) for full chemical assessment under the *Industrial Chemicals (Notification and Assessment) Act 1989* (ICNA Act), because of environmental concerns.

The June 2005 NDPSC meeting noted that triclosan was not included in Appendix B when this Appendix was reinstated. The NDPSC agreed to defer any scheduling consideration until the ongoing NICNAS PEC review was completed.

The June 2010 NDPSC meeting considered the scheduling of triclosan, including the final PEC report. Noting that scheduling would need to be careful about unintended regulatory impact, the NDPSC agreed that the matter should be referred to the delegate for consideration under the new scheduling arrangements. The delegate was advised that while the June 2010 NDPSC meeting agreed that triclosan warranted a Schedule 6 parent entry, the NDPSC was unable to settle on an appropriate cut-off and that further public consultation may be necessary.

SCHEDULING STATUS

Triclosan is not currently scheduled.

INITIAL SUBMISSIONS

June 2010 NDPSC consideration

Members noted the consideration of triclosan at the June 2010 NDPSC meeting. In particular, Members noted the following points.

- The NDPSC agreed that a Schedule 6 parent entry was appropriate given the toxicological information provided in the NICNAS PEC Assessment Report (http://nicnas.gov.au/Publications/CAR/PEC/PEC30/PEC_30_Full_Report_PDF.pdf).
- A Member noted that the PEC report appeared to suggest a 0.3 per cent cut-off for cosmetic use, but that a subsequent NICNAS pre-meeting submission recommended a 0.2 per cent cut-off.
- A Member noted that the PEC review did not examine in detail the use of triclosan for therapeutic use. Also absent were any recommendations for other non-cosmetic use (such as cleaning products or as a preservative).
- A number of Members proposed a general cut-off at 0.3 per cent, given general support for this proposal in pre-meeting submissions and alignment with overseas regulatory systems. Other Members noted, however, that the use of 0.3 per cent formulations of triclosan was being reviewed by other regulatory systems, notably the US Food and Drug Administration (USFDA) (with a likely publication date of 2011). It was also noted that a recent EU Scientific Committee on Consumer Products (SCCP) opinion on triclosan (2009) considered the current concentration of 0.3 per cent in all cosmetic products as unsafe for the consumer, because of the magnitude of aggregate exposure.

- A Member suggested that triclosan be restricted to 0.3 per cent or more of cosmetic use only in Schedule 6. Other Members stated that parent entries should generally capture all uses, especially if concerns include an acute toxicity end point such as the inhalation toxicity of triclosan.
- Several Members noted in the NICNAS pre-meeting submission that the estimated Margin of Exposure (MOE) for 0.3 per cent cosmetic formulations was above 100 and therefore acceptable, and given that cosmetic products in Australia currently contain 0.3 per cent or less of triclosan, the risk to public health may be considered low. However, a Member noted concern that many registered non-cosmetic products contained triclosan at greater than 1 per cent. The Member also noted advice that in 2003, a quarter of triclosan products contained triclosan at levels greater than 0.2 per cent, but that more recent information was unavailable. The ACCS and ACMS Members noted new advice from the Secretariat summarising the current TGA and APVMA registered products.
- NICNAS responded to the observation that a 0.3 per cent cut-off resulted in an MOE only just above 100 by arguing that this marginally acceptable MOE had to be considered in light of human trials which showed evidence of significant plasma levels of triclosan in some volunteers after use of a single product containing 1 per cent triclosan over several months (sufficient to give MOEs as high as 175).
- NICNAS argued that these results were indicative of a sensitive subpopulation potentially at risk from widespread exposure to triclosan. It was asserted that this risk could be mitigated by restricting exposure through cosmetic use to 0.2 per cent or less.
- The NICNAS PEC Assessment Report used a No Observed Adverse Effect Level (NOAEL) of 40 mg/kg bw/d from a 2-year chronic dietary study in rats, based on hepatocyte hypertrophy and vacuolisation in males in the absence of necrosis, and slight changes in clinical chemistry in both males and females at 127/190 mg/kg bw/d (males/females). A Member suggested that the effects on hepatocytes were reversible and of questionable significance, and that the haematological effect was the true Lowest Observed Adverse Effect Level (LOAEL) in this study. The NICNAS representative maintained that the liver effects were toxicologically significant.
- Members noted that the New Zealand Cosmetic Product Group Standard listed the maximum allowable concentration for triclosan (as a preservative) as 0.3 per cent.

NICNAS PEC report & supplementary submission to June 2010 NDPSC

In addition to reviewing the triclosan discussion of the June 2010 NDPSC meeting, the ACCS and ACMS Members also noted that the NICNAS referred its 2009 Priority Existing Chemical (PEC) Assessment Report to the June 2010 NDPSC meeting with a recommendation, contained in a subsequent supplementary submission, that triclosan be included in Schedule 6 with an exemption for cosmetics and personal care leave-on, rinse-off and oral care preparations containing 0.2 per cent or less. This recommendation

was in contrast to the conclusions in the PEC report which could be interpreted as supporting a 0.3 per cent cut-off for non-therapeutic human use preparations.

In particular, Members noted the following points.

NICNAS PEC Report

- The EU maximum concentration level of 0.3 per cent or less for triclosan in cosmetic and personal care products was suggested as being protective to public health and also promoted international harmonisation. ACCS and ACMS Members noted that this conclusion was amended in the NICNAS supplementary submission in light of the EU SCCP (2009) report discussed below.
- Based on inhalation toxicity (2-hour LC_{50} less than 1300 mg/m^3) and respiratory irritation, undiluted triclosan appeared to meet the criteria for Schedule 6. Skin and eye irritation potential of triclosan meets criteria for Schedule 5, but with the low concentrations used in consumer products, the risk of an acute adverse health effect was low. However, the use patterns of triclosan-containing products vary greatly among individuals. Some studies in humans showed a high level of exposure following use of a single cosmetic or personal care product.
- Adverse health effects (liver) may result from repeated use of a single cosmetic or personal care product containing high concentrations of triclosan, or from aggregate exposure.

NICNAS supplementary submission

- The EU SCCP (2009) opinion on triclosan concluded that the current EU maximum concentration of 0.3 per cent in cosmetic products presented unacceptable risks to consumers, when total aggregate exposure was considered and using an NOAEL of 12 mg/kg bw/d. The NOAEL was based on haematotoxicity and decreased absolute and relative spleen weights at 40 mg/kg bw/day and above. The ACCS and ACMS Members noted that the final EU opinion on triclosan was adopted by the SCCP during the 7th plenary meeting of 22 June 2010. The SCCP concluded that on the basis of the available evidence, it was not possible to predict changes in the antibiotic resistance profiles of bacteria following exposure to triclosan or to any other of the biocides currently used in various applications. Overall, SCCP advised limiting the use of triclosan without proven benefit for human health but also accepted that where evidence exists that triclosan use is beneficial, e.g. in preventing disease in humans, it should be encouraged.
- At concentration cut-offs of 0.1 or 0.2 per cent, MOE values were well above 100, indicating low risk. However, at a concentration cut-off at 0.3 per cent, the MOE was as low as 112. NICNAS asserted that this raised concern that health effects may occur in individuals through combined use of multiple cosmetic products containing triclosan up to this concentration. Several Members at the June 2010 NDPSC meeting questioned this conclusion, given that the MOE was still above 100; the usually accepted standard for "low risk".

- Volunteer studies showed considerable variations in plasma steady state levels of triclosan following use of different products and high levels following repeated use of single products. The lowest MOE seen was 179 in males following the repeated use of a single hand wash product containing 1 per cent triclosan. Similarly, MOE values of 258 and 311 were seen in female and male volunteers following the repeated use of a toothpaste containing 0.3 per cent of triclosan.
- MOE values would be even lower than those observed in some individuals, through combined use of multiple products and/or products containing higher concentrations of triclosan.
- Human volunteers using a single personal care product containing 1 per cent triclosan for several months had triclosan levels in plasma equivalent to give a systemic MOE of 175, and therefore aggregate exposures would be of concern.
- To ensure an acceptable MOE for health effects from repeated exposure, it was recommended that leave-on, rinse-off and oral care preparations intended for cosmetic or personal care use contain a maximum allowable cut-off concentration of 0.2 per cent triclosan.

ACCS and ACMS Members additionally noted the following from the NICNAS PEC report.

Acute toxicity

- Low acute oral toxicity in rats and dogs (LD_{50} > 5000 mg/kg bw) and low acute dermal toxicity in rabbits (LD_{50} > 9300 mg/kg bw). It is a skin and eye irritant in rabbits, but not a skin sensitiser in guinea-pigs. No data were available on respiratory sensitisation potential for triclosan.
- Human volunteer studies show skin irritation in the absence of phototoxicity and indications of very weak skin sensitisation. There is very limited evidence of photo-sensitisation.
- On day 1 in a 21-day repeat dose nose-only inhalation study in rats, the 2-hour LC_{50} for triclosan aerosol was less than 1300 mg/m^3, and the test-substance caused severe respiratory tract irritation.

Repeat dose toxicity

- Overall, data from several animal species indicate that the principal effects following repeated oral exposure to triclosan are hepatic effects. Oral NOAEL values of 40 mg/kg bw/day (males) and 56 mg/kg bw/day (females) were established in a two year rat carcinogenicity study based on clinical chemistry (both males and females) and histological changes in the liver (males only).

Absorption and distribution

- Human data indicated that at least 97 per cent and 14 per cent of triclosan was absorbed by oral and dermal routes, respectively. Human oral and dermal data provided no evidence of bioaccumulation potential.

- There are no data to allow estimation of absorption of triclosan following inhalation exposure.

Public exposure

- Given the types of triclosan products available, the main route of exposure is dermal. However, oral exposure may occur through accidental ingestion of cosmetic and personal care products such as lip balm, toothpaste or mouthwash formulations. Inhalational exposure may occur through breathing aerosols from the use of cosmetic, personal care or cleaning products.
- A variety of cosmetic and personal care products contain triclosan. These include aerosols, rinse-off or leave-on products, oral care products and wipes. The concentration of triclosan in these products ranges considerably, from less than 0.01 up to 0.5 per cent. The highest concentration of triclosan was observed in rinse-off products (up to 0.5 per cent) whereas most other products contained less than 0.3 per cent of triclosan.
- Triclosan is present in a number of household cleaning products, at concentrations ranging from 0.04 per cent to 0.3 per cent. These include dishwashing detergents, laundry detergent, surface cleaners, and commercial and hospital grade cleaners. Currently the level of exposure from this source is relatively low with less than 1 tonne/year being used for these applications.
- Textiles containing triclosan include insulation batts, bedding, quilts and blankets, pillows, curtains and blinds and clothing. Triclosan is also used as an antimicrobial additive in plastics. No data are available on the leaching of triclosan from plastic and textile products and therefore the potential oral or dermal exposures and health risks from these products are uncertain.
- Triclosan is also used in certain industrial products such as antimicrobial treatments for air-conditioning heat exchange coils, tile grouts and tile and laminate paint.

June 2010 NDPSC pre-meeting submissions

Members noted that at the June 2010 NDPSC meeting, triclosan submissions were received from a number of stakeholders, with the main concern being the impact on different sectors of industry from a 0.2 vs 0.3 per cent cut-off. Other points included:

- general support for a 0.3 per cent cut-off for triclosan in cosmetics and personal care preparations. Several submissions highlighted that triclosan was used in some registered anti-bacterial soaps and anti-acne facial washes at levels up to 1 per cent;
- the majority of submissions raised concerns that they had not been consulted on the NICNAS final recommendation of 0.2 per cent, and that any such scheduling could have widespread commercial implications for industry;
- one submission suggested that for medicated soaps that contain 1 per cent triclosan, an entry in Schedule 5 or 6 or an entry in Appendix C (with appropriate exemptions) could be appropriate;

- other submissions asserted that a decision on scheduling should await publication of the outcomes of ongoing international reviews on triclosan; and
- another submission stated that any cut-off should be higher than 0.3 per cent, and that non-cosmetic preparations should be exempt from scheduling.

Submissions also questioned:

- the toxicological significance of the LOAEL established by NICNAS;
- the need for scheduling, given that the PEC report did not conclude that there were concerns to public health and the absence of adverse experiences reported for personal care products containing triclosan despite a long history of use; and
- the appropriateness of scheduling cleaning products containing triclosan.

December 2010 pre-meeting submissions

Seven pre-meeting submissions were received with the following major points noted by Members.

XXXXX

Restated its suggestion that any scheduling decision be deferred until completion of the ongoing international reviews on triclosan in 2011. Also stated that, as TGA had evaluated the safety of therapeutic products containing triclosan (whereas the NICNAS report had not assessed these), therapeutics should not be captured by any scheduling decisions. Restated that it would tentatively support a cut-off of 0.3 per cent for non-therapeutic products to support international harmonisation, although there was no scientific basis for this cut-off because:

- the MOE was above 100 even under the assumption that all products would contain the maximum cut-off concentration (0.3 per cent);
- the NOAEL of 75 mg/kg bw/d from a chronic dietary study in hamsters was more appropriate for assessing risks from daily use of cosmetic products, giving an MOE of 630 for a 0.3 per cent cut-off;
- data from a US Cosmetic Ingredient Review (CIR) 'Triclosan as used in Cosmetics - Tentative Report' (2010) (www.cir-safety.org/staff_files/triclo092010tentx.pdf) showed that triclosan was present in an average of 1.4 per cent of US products in the relevant categories (N=34397), with a maximum presence of 7.4 per cent of products in any one category (personal hygiene products). Thus it was unlikely that a user would be exposed to every product containing triclosan for every category of product. Noted that the CIR also reached this conclusion when recommending that the use of triclosan was safe.

XXXXX

- Agreed with a 1 per cent cut-off for therapeutic use, but was concerned that the June 2010 NDPSC meeting may not have considered the appropriateness of applying the cut-off to all products listed on the ARTG.

- Suggested that any scheduling decision could contain a transition period for reformulating products and amending product labels.

- Addressed specific items under section 52E(1) of the *Therapeutic Goods Act 1989*, with Members particularly noting the following.

  (b) purposes and extent of use

  - Argued that triclosan had a long history of safe use.

  (c) toxicity of a substance

  - The toxicological significance of the LOAEL from the chronic dietary study in rats relied on by NICNAS was unclear and in any case the estimated MOE was above 100.
  - Noted the US CIR (2010) conclusion that the use of triclosan was safe, and that a final report will be published in 2011.
  - Suggested that any scheduling decision be deferred until publication of the final outcomes of the EU SCCP and US CIR reviews.

  (d) dosage, formulation, labelling, packaging and presentation

  - XXXXX had advised that the maximum concentration: for leave-on topical and oral hygiene products was 0.3 per cent; wash-off or bath wash preparations was 1 per cent; and 0.3 per cent for cosmetics to satisfy major exports markets. ACCS and ACMS Members noted advice to the December 2010 meeting that there was a therapeutic bath wash product containing 2 per cent triclosan.
  - Reiterated the point made to the June 2010 NDPSC meeting that the EU SCCP (2009) concluded that the use of 0.3 per cent preparations was safe for all but leave-on products and mouthwashes, but that even this conclusion may be revised in a review by EC SCCP expected to be published in 2011.

XXXXX

- Only supported the use of triclosan in personal care and medical care preparations, and no longer supported its use in industrial preparations and household markets, i.e. household cleaning products.
- Noted the US CIR (2010) conclusion discussed above and suggested that any scheduling decision be deferred until its publication.
- Disagreed with the proposed 0.2 per cent cut-off in cosmetics, as the PEC report had recommended a 0.3 per cent cut-off, and in any case the estimated MOE was above 100 for formulations greater than 0.3 per cent.

- Stated that Australian products generally contained low levels of triclosan despite the lack of a maximum cut-off concentration.
- Maintained that a 0.3 per cent cut-off in cosmetics would be harmonised with other jurisdictions.

XXXXX

- Did not support a 0.2 per cent cut-off for non-therapeutic preparations. Additionally, scheduling therapeutic preparations would be incongruous with the conditions of their approval by TGA evaluators, and that it was not aware of triclosan in medicines being restricted by any controls overseas. To minimise trade impacts, suggested that any scheduling decision could await consideration of the final EU SCCP and US CIR reports.
- Requested discussion on the NICNAS exposure estimation methodology, particularly in light of more reliable population-based biomonitoring studies by the US EPA in 2008 and population data considered by US CIR (2010) showing that the use of triclosan was safe. Suggested that a similar population survey in Australia was appropriate and advised that plans were underway by industry to conduct such a survey.
- Stated that only the use of leave-on and mouthwash products containing 0.3 per cent were unsafe, resulting in formulators removing triclosan from leave-on products and reducing the concentration of triclosan in mouthwashes. Stated that exposure estimation in the revised EU SCCP report will reflect these changes.
- Noted that EU SCCP used a NOAEL approximately four times more conservative than the PEC (40 mg/kg bw/d) and US CIR (48 mg/kg bw/d) reports.
- Noted that NICNAS risk assessment guidelines advise that an MOE above 100 is acceptable to account for possible interspecies and intraspecies differences.

XXXXX

- Reconfirmed its views, put forth in a submission to the June 2010 NDPSC meeting, that a 0.3 per cent cut-off for cosmetics was appropriate. Also stated the need for harmonisation with international markets, and suggested that any scheduling change be delayed to allow reformulation and exhaustion of existing products and packaging. Proposed an implementation date no sooner than 1 January 2012.

XXXXX

- Disagreed with the proposed Schedule 6 cut-off at 0.2 per cent in cosmetics, because of a long-history of safe use and findings from the US CIR report which showed that triclosan did not meet criteria for a substance 'with a moderate potential for causing harm'. Stated that at both the 0.3 per cent and 1 per cent concentrations, the aggregate MOE calculated by NICNAS was above 100, and therefore acceptable.

- Stated that scheduling cosmetic preparations containing triclosan would require labels to carry statements alarming to consumers, and would be detrimental to Australian business without clear benefit to public health. Suggested that any scheduling decision for triclosan could entail a suitable transition period to allow reformulation and minimisation of regulatory impact.

XXXXX

- Advised that data from imported cosmetic preparations showed a maximum triclosan concentration of 0.87 per cent, and that this was also the maximum in locally manufactured cosmetics containing triclosan.

- Stated that neither a 0.2 nor 0.3 per cent cut-off for non-therapeutic preparations was justified. Agreed with a 1 per cent cut-off for scheduling triclosan in therapeutic and non-human use preparations given their long history of safe use, and proposed the same cut-off for non-therapeutic preparations on this same basis.

EXPERT ADVISORY COMMITTEE DISCUSSION

Members agreed that the relevant matters under section 52E(1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of use and (b) purpose and extent of use.

Members discussed the NICNAS concerns that the MOE was only just above 100 and that there were other data indicating that there may be a sub-population sensitive to triclosan, i.e. elevated plasma levels in some volunteers. Several Members disagreed with the sensitive population conclusion, arguing that the evidence was not strong enough to establish this. It was also argued that the MOE evidence, greater than 100 for 0.3 per cent, was appropriate. It was noted that NICNAS had used worst case scenarios, that the most sensitive species was used, as was the standard safety factor, and the MOE was still acceptable.

A Member noted that the end points of concern were liver and haematological effects which were relatively benign, although persistent across species so likely to be real effects. Several Members noted that while the inhalation hazard of triclosan, based on its LC_{50}, was indicative of a Schedule 6 entry, the actual inhalation exposure and risk was low for most uses of triclosan. One Member questioned whether triclosan should be scheduled at all. However, it was generally agreed that a parent entry for higher concentration triclosan in some uses was appropriate given that there was inhalation toxicity risk (if exposed) and the potential for aggregate exposure, particularly from cosmetic use.

Consequently there was support from a number of Members for a Schedule 6 parent entry for triclosan with a 0.3 per cent cut-off (rather than NICNAS's requested 0.2 per cent) for non-therapeutic leave-on and wash-off preparations. Another Member reiterated arguments made to the June 2010 NDPSC meeting that a 0.2 per cent cut-off for non-

therapeutic leave-on and wash-off preparations would have significant regulatory impact, particularly on cosmetics.

There was less support for the proposed 1 per cent cut-off for human or animal therapeutic use. A Member was concerned that this could be too restrictive, noting at least one therapeutic product contained 2 per cent triclosan. Several Members argued that if there were data to support a concern for therapeutic use then this should be addressed through a specific entry in Schedule 2, 3 or 4, not capture by a Schedule 6 parent entry. It was argued that there appeared to be no such basis for a Schedule 2, 3 or 4 entry. Members generally agreed that the current data did not support scheduling of triclosan for therapeutic use and that at present any risk would be sufficiently addressed through the TGA and APVMA product approval processes.

A Member noted that the NICNAS data appeared to indicate that the contribution of household cleaners and other products not intended for application to humans was low and recommended that the focus of scheduling should be on cosmetic and personal care products. Another Member noted that there appeared to have been no reports of safety concerns from use of products containing greater than 1 per cent triclosan that did not involve direct application to humans.

A Member raised concerns of possible impact on industrial use. However, it was recalled that there were already exemptions from Schedule 6 packaging and labelling requirements for products packed and sold solely for dispensary, industrial, laboratory or manufacturing purposes.

Several Members agreed that while there may be data to warrant a Schedule 6 parent entry, there should be many exemptions. Members discussed various possible exemptions and generally agreed that the current data did not warrant scheduling of triclosan containing products regulated by APVMA (including personal use insecticides) or TGA, those for industrial use, and products not intended for application to humans, such as cleaning products.

Several Members argued that the exemptions being discussed constituted pretty much all uses apart from cosmetic use and that consideration should be given to the possibility of a specific Schedule 6 entry just for cosmetic use. Members agreed that a positive Schedule 6 entry for cosmetic products containing more than 0.3 per cent triclosan was appropriate. It was noted that, as set out in the NICNAS Cosmetic Guidelines, therapeutic products cannot be classed as a cosmetic product.

Implementation date

A Member noted that most cosmetics already contained less than 0.3 per cent triclosan. As such, it appeared likely that an immediate implementation of the new triclosan scheduling would have low regulatory impact. However, other Members noted the support in various submissions for a deferred implementation date.

Members generally agreed that, as there was not a pressing public health issue, approaches which minimised the regulatory impact of the scheduling decision could be contemplated. A number of Members suggested either a six or nine month deferred implementation date, as formulation changes may be necessary. Members agreed to recommend an implementation date of at least nine months after the delegate's final decision.

DELEGATE'S INTERIM DISCUSSION

The delegate noted the Members' discussion and agreed with the ACCS-ACMS joint recommendation to create a new Schedule 6 entry for triclosan in cosmetic preparations containing more than 0.3 per cent triclosan.

The delegate also noted the ACCS-ACMS joint recommendation that the implementation date be at least nine months after the delegate's final decision. The delegate noted that there was potential for significant regulatory impact from this decision. The delegated also noted that Amendment No.3 to SUSMP No.2 was expected to be implemented on 1 May 2012, and that this would be approximately one year after the expected publication of the delegate's final decision. The delegate decided that an implementation of 1 May 2012 was appropriate.

The delegate agreed that the relevant matters under section 52E (1) of the Therapeutic *Goods Act 1989* included (a) risks and benefits of use and (b) purpose and extent of use.

DELEGATE'S INTERIM DECISION

The delegate decided to create a Schedule 6 entry for triclosan when for cosmetic use in humans containing more than 0.3 per cent triclosan. The delegate also decided on an implementation date of 1 May 2012 (approximately 1 year after expected publication of delegate's final decision).

SUBMISSIONS ON INTERIM DECISION

A single further submission was received from XXXXX supporting the interim decision. This further submission advised that, although the interim decision did not coincide exactly to its pre-meeting submission, XXXXX believed that the decision was pragmatic and acceptable to XXXXX.

DELEGATE'S FINAL DECISION

The delegate confirmed the creation of a Schedule 6 entry for triclosan when for cosmetic use in humans containing more than 0.3 per cent triclosan. The delegate also confirmed an implementation date of 1 May 2012.

Schedule 6 – New entry

TRICLOSAN in cosmetic preparations for human use containing more than 0.3 per cent triclosan.

1.3 LAURETH CARBOXYLIC ACIDS

DELEGATE'S REFERRAL TO EXPERT ADVISORY COMMITTEE

The delegate considered additional label requirements for laureth carboxylic acids and decided to seek advice from the December 2010 ACCS-ACMS joint meeting on the following:

Laureth carboxylic acids (LCA) – proposal to include LCA in Appendix E with appropriate labelling statements. Specifically, it is proposed that for preparations containing more than 5 per cent LCA:

- standard statement E1 "*if in eyes wash out immediately with water*" apply; and
- standard statement S1 "*if skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" apply to preparations which are not leave-on or wash-off.

The delegate additionally proposes labelling requirements for products to qualify for the current exemptions from the Schedule 6 LCA entry. Specifically, it is proposed:

- wash-off preparations, greater than 5 per cent up to 30 per cent or less are to be exempt only when labelled with "*if in eyes wash out immediately with water*";
- leave-on (1.5 per cent or less) no additional labelling required; and
- all other preparations, greater than 5 per cent up to 30 per cent or less are to be exempt only when labelled with "*if in eyes wash out immediately with water*" and "*if skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*".

The proposal is a result of deliberations at the June 2010 NDPSC meeting.

EXPERT ADVISORY COMMITTEE RECOMMENDATION

The ACCS-ACMS joint meeting recommended an Appendix E entry for preparations containing more than 5 per cent LCAwith the standard statements E1 "*If in eyes wash out immediately with water*" and S1 "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" also apply for preparations which are not leave-on or wash-off preparations.

The joint meeting additionally recommended that the Schedule 6 entry for LCA be amended to add the following labelling criteria for products to qualify for the current exemptions from the entry:

- leave-on preparations containing 1.5 per cent or less require no additional labelling;
- wash-off preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with a warning to the effect of "*If in eyes wash out immediately with water*"; and
- all other preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with warnings to the following effect "*If in eyes wash out immediately with water*" and "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*".

The joint meeting also recommended an implementation period of nine months after the delegate's final decision.

BACKGROUND

Laureth carboxylic acid is the INCI (International Nomenclature Cosmetic Ingredients) name for a set of polymers containing, among others, polyethylene glycol-5 lauryl ether carboxylic acid (PEG-5 lauryl ether carboxylic acid) and PEG-6 lauryl ether carboxylic acid; also known as laureth-5 carboxylic acid and laureth-6 carboxylic acid respectively. LCA is a member of the alkylethercarboxylic acid class of chemical which in turn is a member of the anionic surfactant group of chemicals.

The November 1999 NDPSC meeting noted the toxicity profile of a specific LCA salt, sodium laureth-6 carboxylate, in particular its severe eye irritancy potential, and agreed to list this specific LCA salt in Schedule 5 except for preparations containing 1 per cent or less.

The February 2010 NDPSC meeting considered a review of LCA prepared by NICNAS. The NDPSC proposed including LCA in Schedule 6 with a number of cut-offs. However, given the widespread use of LCA in cleaning and cosmetic products, there was significant potential for unintended regulatory impact from this decision. The NDPSC therefore agreed to foreshadow consideration of this decision at the June 2010 NDPSC meeting to allow time for additional public consultation.

The June 2010 NDPSC meeting considered a number of public submissions and decided to include LCA (excluding its salts and derivatives) in Schedule 6 with exemptions for:

- wash-off preparations, 30 per cent or less;
- leave-on preparations, 1.5 per cent or less; or
- in all remaining preparations, 30 per cent or less.

This decision was referred to the delegate who agreed to include this in SUSMP No.1 with a deferred implementation date of 1 January 2011.

The June 2010 NDPSC meeting also agreed that it would be appropriate to consider additional labelling for preparations containing greater than 5 per cent LCA. Therefore, the NDPSC agreed that the issue of additional labelling should be referred to the delegate as a new consideration to allow for further public consultation.

SCHEDULING STATUS

From 1 January 2011, LCA (excluding its salts and derivatives) has been captured in Schedule 6 with a number of exceptions.

INITIAL SUBMISSIONS

December 2010 Pre-meeting Submissions

XXXXX

- Asserted that there was an acknowledgement by the June 2010 NDPSC meeting that currently LCA is used safely without mandatory warning statements.
- Argued that, other than where they are now scheduled (Schedule 6), mandatory labelling should only be applied to scheduled products containing LCA at greater than 5 per cent.
- Requested that, if additional mandatory labelling is required for products to qualify for the scheduling exemptions, that time be allowed for industry to transition to the new labelling requirements.

June 2010 NDPSC Pre-meeting Submissions

A number of submissions argued that LCA should not be scheduled due to its long history of safe use and therefore did not warrant additional labelling restrictions through scheduling. One submission stated that the required label statements from a Schedule 6 listing would cause unnecessary alarm to consumers and would be inappropriate for cosmetic products.

June 2010 NDPSC Discussion

Members noted the following from the June 2010 NDPSC meeting.

- A Member noted the similarity of sodium lauryl sulfate (SLS) and LCA use patterns and risk profile and argued that similar scheduling should apply to both. It was noted that while LCA appeared to be more irritating than SLS, there was some uncertainty about this.

- A Member noted that the principle concern appeared to be human topical use and argued that scheduling should be limited to this use with appropriate cut-offs. Other Members argued, and the NDPSC generally agreed, that LCA's potential for serious eye irritation warranted a parent entry in Schedule 6 for all uses. A Member argued that this parent entry should be limited to LCA only, i.e. exclude salts and derivatives. The NDPSC agreed that this was appropriate to avoid unintended regulatory consequences.

The NDSPC also discussed potential cut-offs. A Member recalled that the intent of the February 2010 NDPSC meeting when it proposed cut-offs was to take a pragmatic approach that accommodated for the toxicity information tabled to date (especially the eye irritancy) while recognising the long history of safe use of many existing LCA products. Additionally, the similarity of SLS and LCA was again noted and it was argued that similar cut-offs should apply to both. It was noted that there was no significant opposition to this intent from the June 2010 pre-meeting submissions, only suggestions which would better align the cut-offs with this intent. In particular:

- *Use in leave-on products*. While one Member advocated limiting the leave-on limit to 1 per cent or less, Members generally agreed that there was little harm in extending the foreshadowed 1 per cent cut-off to 1.5 per cent to better reflect current usage of LCA.
- *Cleaning products not intended for skin contact*. A Member suggested a blanket exemption for cleaning products. Other Members were concerned about not having an upper limit when high concentrations of LCA had significant eye irritancy potential. It was noted that the risk from these products would be less than that from wash-off preparations and the foreshadowed cut-off for wash-off preparations was 30 per cent or less. Members agreed that it would be appropriate to increase the "other preparations" cut-off to 30 per cent or less.

Labelling Discussion

The June 2010 NDPSC meeting also discussed whether additional labelling was warranted (such as Appendix E entries). A Member suggested that the main eye irritancy concern for LCA was similar to that of SLS i.e. for preparations containing greater than 5 per cent. The Member suggested that any preparations above this threshold should comply with the Appendix E standard statement E1 "*If in eyes wash out immediately with water*" due to eye irritancy. The Member also suggested that perhaps the Appendix E standard statement S1 "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" would be appropriate for cleaning products containing greater than 5 per cent SLS.

Other Members suggested that this labelling need only apply as conditions for the exemptions from Schedule 6, and that anything captured by Schedule 6 would already adequately warn users as it would be labelled as "Poison". Therefore:

- wash-off preparations, greater than 5 per cent and 30 per cent or less should be exempt only when labelled with "*if in eyes wash out immediately with water*";

- leave-on preparations, 1.5 per cent or less should not require additional labelling; and
- all other preparations, greater than 5 per cent and 30 per cent or less should be exempt only when labelled with "*if in eyes wash out immediately with water*" and "*if skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*".

The NDPSC discussed these proposals and agreed that it would be appropriate to consider some additional labelling for preparations containing greater than 5 per cent LCA.

One Member expressed concern regarding the possibility that household products containing LCA that have significant potential to cause serious eye injury, as well as moderate acute oral toxicity, may be exempted from Schedule 6 without the mandatory requirement for appropriate warning statements and first aid instructions.

NICNAS Report

Members noted the following from the NICNAS report considered at the February and June 2010 NDPSC meetings of the NDPSC:

Public Health Standards

- When used in cosmetic and household products, LCA is not considered to pose an unacceptable risk to public health if used at less than 10 per cent with appropriate label statements regarding the potential for eye irritation.

Label statements

- Products should be labelled with a warning against eye contact, and directions on first aid measures if the product enters the eye, e.g. avoid contact with the eyes, in case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
- The following warning statements were recommended:
  - 10 per cent or more: Risk of serious damage to eyes; and
  - between 5 and 10 per cent: Irritating to eyes.

Toxicology

- LCA at 100 per cent concentration was found to be a severe irritant in an eye irritation test in rabbits, with corneal and iridial effects observed up to the end of the 20 day observation period. A test was conducted on a product containing less than 15 per cent LCA. The test substance was applied as a 10 per cent solution (therefore less than 1.5 per cent LCA). This diluted solution was found to be moderately irritating.
- LCA was also found to be slightly irritating to the skin of rabbits when applied undiluted with evidence of inflammation persisting for greater than 10 days.

Occupational health and safety

- Irritation is the primary risk presented by the notified chemical to workers in occupational settings. Eye, and to a lesser degree, skin irritation, are potential risks to reformulation and/or transportation workers because of their handling of LCA (80-90 per cent concentration) prior to and during reformulation. Appropriate handling techniques and the use of PPE should be in place to ensure the likelihood of exposure is very low so that the risk to workers would not be considered unacceptable.
- Hairdressers and beauty therapists will encounter repeated dermal exposure to cosmetic products, such as shampoos, containing LCA (15 per cent or less). The risk of eye exposure is not considered likely given the hairdresser will normally be standing up during application of the shampoo. While it is unknown whether skin irritation is likely after exposure at 15 per cent or less, it is assumed that significant irritation would be unlikely given the rinse-off nature of the products.

Public health

- Members of the public will experience widespread and frequent exposure to LCA through daily use of cosmetic and household products (15 per cent or less) which will involve direct contact with the skin and hair. There is potential for accidental eye exposure while using shampoo products containing the LCA and this could lead to eye irritation. This exposure could be to either a formulation of 15 per cent or less or a diluted shampoo solution.
- As severe eye irritancy was observed with LCA 100 per cent concentration, the potential for severe eye effects at concentrations greater than 10 per cent cannot be ruled out. At concentrations less than 10 per cent there is likely to be eye irritation, but this is less likely to be severe. Therefore, although LCA may cause some eye irritation when used in cosmetic and household products, the risk of serious eye damage may be minimised by restricting the concentration to less than 10 per cent and by clear and appropriate directions for use and safety precautions to avoid eye contact.
- First aid information should also be included on product packaging to minimise adverse effects if eye contact occurs. Extensive dermal exposure to LCA in cosmetic and household products at 15 per cent or less is not considered to present an unreasonable risk of skin irritation given that LCA was found to be only slightly irritating and was primarily intended for use in rinse-off products.
- A maximum systemic exposure of 0.79 mg/kg bw/day was estimated. As no repeat dose toxicity studies have been conducted, a NOAEL could not be established for LCA. Therefore a quantitative risk assessment could not be conducted. However, given the expected low systemic toxicity after repeated use and the current low introduction volume, LCA is not expected to pose an unacceptable risk of systemic toxicity to the public when used in cosmetic and household products at 15 per cent or less.

EXPERT ADVISORY COMMITTEE DISCUSSION

Members generally agreed that relevant matters under Section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits and (b) the purpose and extent of use.

While several Members had reservations about the delegate's scheduling decision for LCA, Members noted that they had only been asked by the delegate to provide advice on whether additional labelling was appropriate for LCA. The joint meeting had not been asked to reconsider the finalised scheduling decision i.e. Schedule 6 with various cut-offs.

Members generally agreed that, as LCA is a severe eye irritant, some additional labelling was appropriate. Members noted, however, that there were two distinct labelling issues to consider (and that these were not alternatives):

- additional labels for products captured by the Schedule 6 LCA entry; and
- additional labelling for products exempt from the Schedule 6 entry.

Members first discussed the need for additional labels for products captured by the Schedule 6 LCA entry. It was again noted that Schedule 6 products already had mandatory labelling, including "Poison". Members discussed whether this was sufficient to address the significant eye and skin irritation issues.

One Member noted that while such products were already likely to have some warning labels, it would be appropriate to ensure this through an Appendix E entry as proposed. Several Members supported the position of the June 2010 NDPSC meeting, and Members generally agreed, that this need only apply where the LCA concentration was greater than 5 per cent.

Members then discussed the need for additional labels for unscheduled LCA products. One Member argued that additional labels were not required as the decision to make these LCA products unscheduled implied that they were safe. Several other Members disagreed, noting that the LCA scheduling decision, including the exemptions, was made in conjunction with a recommendation for additional labelling.

A Member noted that while products like shampoos were likely to already have labels with an intent similar to the proposed labelling, there were other products which would not have such labelling. The Member asserted, and Members generally agreed, that the irritancy concerns when above 5 per cent LCA warranted the proposed label statements, even if otherwise exempt from scheduling. Such labels would communicate the irritancy concern and help mitigate the risks presented by these products.

Implementation

A Member highlighted that there were issues associated with communicating these labelling requirement changes. Several small industries use LCA and the regulation of these industries was often fragmented. The Member suggested that an implementation of

at least 12 months was required after the delegate's final decision. However, another Member asserted that most of these industries were proactive and compliant and six months would be sufficient. Members agreed that a more pragmatic period was nine months after the delegate's final decision.

DELEGATE'S INTERIM DISCUSSION

The delegate noted the ACMS-ACCS discussions and agreed that, as LCA is a severe eye and skin irritant, label warnings for products containing greater than 5 per cent LCA was appropriate.

The delegate noted the ACMS-ACCS joint meeting recommendation that the implementation period be at least nine months after the delegate's final decision. The delegate therefore decided that an implementation of 1 January 2012 was appropriate.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of the substance, and (b) purpose for which the substance is to be used.

DELEGATE'S INTERIM DECISION

The delegate decided to include preparations containing more than 5 per cent laureth carboxylic acids in Appendix E with the standard statements:

- E1 "*If in eyes wash out immediately with water*" and
- S1 "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" for preparations which are not leave-on or wash-off preparations.

The delegate also decided to amend the Schedule 6 entry for laureth carboxylic acids to add the following labelling criteria for products to qualify for the current exemptions from the entry:

- leave-on preparations containing 1.5 per cent or less – no additional labelling required;
- wash-off preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with a warning to the effect of "*If in eyes wash out immediately with water*"; and
- all other preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with warnings to the following effect "*If in eyes wash out immediately with water*" and "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*".

The delegate decided on an implementation date of 1 January 2012 (approximately nine months after expected publication of delegate's final decision).

SUBMISSIONS ON INTERIM DECISION

A single further submission was received from XXXXX supporting the interim decision. This further submission advised that, although the interim decision did not coincide exactly to its pre-meeting submission, XXXXX believed that the decision was pragmatic and acceptable to XXXXX.

DELEGATE'S FINAL DECISION

The delegate confirmed including preparations containing more than 5 per cent laureth carboxylic acids in Appendix E with the standard statements:

- E1 "*If in eyes wash out immediately with water*" and
- S1 "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" for preparations which are not leave-on or wash-off preparations.

The delegate also confirmed amending the Schedule 6 entry for laureth carboxylic acids to add the following labelling criteria for products to qualify for the current exemptions from the entry:

- leave-on preparations containing 1.5 per cent or less – no additional labelling required;
- wash-off preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with a warning to the effect of "*If in eyes wash out immediately with water*"; and
- all other preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with warnings to the following effect "*If in eyes wash out immediately with water*" and "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*".

The delegate additionally confirmed an implementation date of 1 January 2012.

Appendix E – Part 2 – New entry

POISON ..... STANDARD STATEMENTS

Laureth carboxylic acids
- leave-on or wash-off preparations above 5 per cent..... E1
- other preparations above 5 per cent..... E1,S1

Schedule 6 – Amendment

LAURETH CARBOXYLIC ACIDS – Amend entry to read:

LAURETH CARBOXYLIC ACIDS (excluding its salts and derivatives) **except**:

(a) in leave-on preparations containing 1.5 per cent or less of laureth carboxylic acids;

(b) in wash-off preparations containing 30 per cent or less of laureth carboxylic acids and, if containing more than 5 per cent laureth carboxylic acids, when labelled with a warning to the following effect:

IF IN EYES WASH OUT IMMEDIATELY WITH WATER;

(c) in other preparations containing 30 per cent or less of laureth carboxylic acids and, if containing more than 5 per cent laureth carboxylic acids, when labelled with warnings to the following effect:

IF IN EYES WASH OUT IMMEDIATELY WITH WATER; and

IF SKIN OR HAIR CONTACT OCCURS, REMOVE CONTAMINATED CLOTHING AND FLUSH SKIN AND HAIR WITH RUNNING WATER.

1.4 SODIUM LAURYL SULFATE

DELEGATE'S REFERRAL TO EXPERT ADVISORY COMMITTEE

The delegate considered additional labelling requirements for sodium lauryl sulfate and decided to seek advice from the December 2010 ACCS-ACMS joint meeting on the following:

Sodium lauryl sulfate (SLS) – proposal to include SLS in Appendix E with appropriate labelling statements. Specifically, it is proposed that for preparations containing more than 5 per cent SLS:

- Standard statement E1 "*if in eyes wash out immediately with water*" apply; and
- Standard statement S1 "*if skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" apply to preparations which are not leave-on or wash-off.

The delegate additionally proposes labelling requirements for products to qualify for the current exemptions from Schedule 6 SLS entry. Specifically, it is proposed:

- Wash-off preparations, greater than 5 per cent up to 30 per cent or less are to be exempt only when labelled with "*if in eyes wash out immediately with water*";
- Leave-on (1.5 per cent or less), toothpaste and oral hygiene preparations (5 per cent or less) and other animal use (2 per cent or less) – no additional labelling required; and
- All other preparations, greater than 5 per cent up to 30 per cent or less are likely to be exempt only when labelled with "*if in eyes wash out immediately with water*" and "*if skin or hair contact occurs, remove contaminated clothing and flush skin with running water*".

This proposal is a result of deliberations at the June 2010 NDPSC meeting.

EXPERT ADVISORY COMMITTEE RECOMMENDATION

The ACCS-ACMS joint meeting recommended an Appendix E entry for preparations containing more than 5 per cent SLS with the standard statements: E1 "*If in eyes wash out immediately with water*"; and S1 "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*", also apply for preparations which are not leave-on or wash-off preparations.

The joint meeting also recommended that the Schedule 6 entry for SLS be amended to add the following labelling criteria for products to qualify for the current exemptions from the entry:

- wash-off preparations containing 30 per cent or less of sodium lauryl sulfate and, if containing more than 5 per cent sodium lauryl sulfate, when labelled with a warning to the following effect of "*If in eyes wash out immediately with water*";
- leave-on preparations containing 1.5 per cent or less of sodium lauryl sulfate;
- toothpaste and oral hygiene preparations containing 5 per cent or less of sodium lauryl sulfate;
- other preparations for animal use containing 2 per cent or less; or
- other preparations containing 30 per cent or less of sodium lauryl sulfate and, if containing more than 5 per cent sodium lauryl sulfate, when labelled with warnings to the following effect of "If in eyes wash out immediately with water; and "*If skin or hair contact occur, remove contaminated clothing and flush skin and hair with running water"*.

The joint meeting further recommended an implementation period of nine months after the delegate's final decision.

BACKGROUND

Sodium lauryl sulfate is the approved International Organisation for Standardization (ISO) common name for sodium dodecyl sulfate (IUPAC). SLS has a tail of 12 carbon atoms attached to a sulfate group, giving it amphiphilic properties. SLS is therefore an anionic surfactant and has a long history of use in industry, personal care products, as a pharmaceutical excipient and as a food additive. SLS is currently listed on the Australian Inventory of Chemical Substances (AICS).

The February 2010 NDPSC meeting considered an evaluation report on an application submitted to the Australian Pesticides and Veterinary Medicines Authority (APVMA) for the approval of SLS as a new technical grade active constituent (TGAC). Registration had also been sought for a new product containing SLS at XXXXX. The NDPSC generally agreed that, based on the toxicological information provided (potential for serious eye and skin irritation), a general parent entry would be appropriate, i.e. broaden consideration from the proposed animal use to all use. The NDPSC proposed including SLS in Schedule 6 with exemptions for wash-off preparations (30 per cent or less); leave-on preparations (1 per cent or less); and in other preparations (2 per cent or less). However, given the potential for unintended regulatory impact, the NDPSC agreed to foreshadow this for consideration at the June 2010 NDPSC meeting to allow time for additional public consultation.

The June 2010 NDPSC meeting considered a number of public submissions and decided to include SLS (excluding salts and derivatives) in Schedule 6 with exemptions for:

- wash-off preparations, 30 per cent or less;
- leave-on preparations, 1.5 per cent or less;
- toothpaste and oral hygiene preparations, 5 per cent or less;
- in other preparations for animal use, 2 per cent or less; or
- in all remaining preparations, 30 per cent or less.

This decision was referred to the delegate, who agreed to include this in SUSMP No.1 with a deferred implementation date of 1 January 2011.

The June 2010 NDPSC meeting also discussed the merits of various proposals on additional labelling requirements for SLS. The NDPSC agreed that it would be appropriate to consider additional labelling for preparations containing greater than 5 per cent SLS. However, all the tabled suggestions diverged in some respect from the positions preferred by some stakeholders. Therefore, the NDPSC agreed that the issue of additional labelling should be referred to the delegate for a new consideration to allow for further public consultation.

SCHEDULING STATUS

From 1 January 2011, SLS (excluding its salts and derivatives) has been specifically captured in Schedule 6 with a number of exceptions.

INITIAL SUBMISSIONS

December 2010 Pre-meeting Submission

Two pre-meeting submissions were received with Members particularly noting the following.

XXXXX

- Asserted that there was an acknowledgement by the June 2010 NDPSC meeting that currently SLS is used safely without mandatory warning statements.
- Argued that, other than where they are now scheduled (Schedule 6), mandatory labelling should only be applied to scheduled products containing SLS at greater than 5 per cent.
- Also requested that, if additional mandatory labelling is required for products to qualify for the scheduling exemptions, time be allowed for industry to transition to the new labelling requirements.

XXXXX

- Reiterated that SLS has a long history of safe use.
- Requested an appropriate transition period should the proposed labelling requirements be introduced for products exempt from Schedule 6 containing more than 5 per cent SLS.
- Argued that this would allow a run out of stock and current printed packaging materials. This would also minimise the burden on industry given that no safety signal occurred to warrant the requirement.

June 2010 NDPSC Pre-meeting Submissions Regarding Labelling

Members noted that the pre-meeting submissions to the June 2010 NDPSC meeting included a number of comments regarding inclusion of SLS in Appendix E.

- For cosmetics and therapeutics, including toothpastes, shampoos, bath soaps, shaving cream, foundations and other make-up preparations, it was generally understood that these were for topical use and not for ingestion.
- Where SLS is used in food and ingestible therapeutics, warning statements for action in case of swallowing would be confusing to the consumer and commercially damaging to the product carrying such warnings. Appendix E basic and general

statements are not considered appropriate qualifying criteria for these products to be exempt from Schedule 6.

- The NDPSC noted, however, that Appendix E did not apply to medicines compliant with the Required Advisory Statements for Medicine Labels (RASML) and that there was a general exemption for food through an Appendix A entry.

· Standard statement E1 (*If in eyes wash out immediately with water*) is considered appropriate for wash-off preparations and words to the effect of standard statement E1 are already common place in industry for wash off products. However, the use of standard statement E1 on products such as toothpastes, dried egg foods or dentifrices would not be helpful and may be confusing to the customer.

· Standard statement E2 (*If in eyes, hold eyelids apart and flush the eye continuously with running water. Continue flushing until advised to stop by a Poisons Information Centre (e.g. phone Australia 131 126; New Zealand 0800 764 766) or a doctor, or for at least 15 minutes*) is not considered appropriate as under normal conditions a compliant product should not cause ocular damage if the eyes are rinsed immediately, i.e. standard statement E1 is sufficient.

· Products containing SLS are generally not at risk of being inhaled and as such respiratory warnings would be inappropriate.

· The majority of the products containing SLS, which qualify for the exemptions, are for use on the skin, thus skin statements are not appropriate.

· It would also not be appropriate to require special purpose standard statements on products that qualified for the Schedule 6 exemptions.

One submission argued, regarding possible inclusion in Appendix E, that at 2 per cent SLS was only a slight irritant, but with increasing concentration the irritancy increased. It was suggested that it may be beneficial to apply Appendix E standard statements to some of the exempt categories where appropriate for the use pattern. Standard statement E1 would be appropriate for higher concentration wash-off preparations where the product may accidentally contact the eyes and this would be appropriate for concentrations greater than 5 per cent.

June 2010 NDPSC Discussion

Members noted the following from the minutes of the June 2010 NDPSC meeting:

· A Member, reiterating that SLS had been used for a long time in a broad range of products with no evidence of adverse incidents, suggested limiting any scheduling to the new use identified by the evaluation report (animal use for injection). Several other Members agreed that the use examined in the evaluation report should be Schedule 6 but disagreed that this should be the only use scheduled. The NDPSC generally agreed that, based on the toxicological information provided, a Schedule 6 parent entry was appropriate for SLS given its potential for serious eye irritation.

- A Member argued that this parent entry should be limited to SLS only, i.e. excluding its salts and derivatives, noting a range of surfactant by-products and precursors which would otherwise potentially be scheduled. The NDPSC agreed that this was appropriate to avoid unintended regulatory consequences.

- A Member recalled that the intent of the cut-offs proposed at the February 2010 meeting was to take a pragmatic approach that incorporated the toxicity information tabled to date (especially the eye irritancy) while recognising the long history of safe use of many existing SLS products. Several Members noted no significant opposition to this intent in the pre-meeting submissions, but suggestions were made that would more closely align the cut-offs with this intent. In particular:

  - *Use in toothpaste up to 5 per cent*. Members generally agreed that a cut-off for this use was appropriate. Members also agreed that this should apply to all oral hygiene products.
  - *Use in leave-on products*. Members generally agreed that there was little harm in extending the foreshadowed 1 per cent cut-off to 1.5 per cent to accommodate existing use in some topical therapeutic products.
  - *Cleaning products not intended for skin contact*. One Member suggested a cut-off of 15 per cent might be appropriate, noting that there was very little data about this use pattern. Other Members noted that this would be somewhat incongruous given that the risk from these products would be less than that from wash-off preparations, and the foreshadowed cut-off for wash-off preparations was 30 per cent or less. The NDPSC agreed that it would be appropriate to increase the "other preparations" cut-off to 30 per cent or less.

Labelling Discussion

- Members discussed whether additional labelling was warranted (such as Appendix E entries). One Member expressed concern regarding the possibility that household products containing SLS that have significant potential to cause serious eye injury, as well as moderate acute oral toxicity, may be exempted from Schedule 6 without the mandatory requirement for appropriate warning statements and first aid instructions.
- A Member suggested that the main eye irritancy concern was for preparations containing greater than 5 per cent SLS. The Member suggested that any preparations above this threshold should comply with the Appendix E standard statement E1 "*if in eyes wash out immediately with water*" due to eye irritancy. The Member also suggested that the Appendix E standard statement S1 "*if skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" would be appropriate for cleaning products containing greater than 5 per cent SLS.
- Other Members suggested that this labelling need only apply as conditions for the exemptions from Schedule 6, and that anything captured by Schedule 6 would already adequately warn users as it would be labelled as "Poison". It was suggested that:

- wash-off preparations, greater than 5 per cent and 30 per cent or less, be exempt only when labelled with "*if in eyes wash out immediately with water*";
- leave-on (1.5 per cent or less), toothpaste and oral hygiene preparations (5 per cent or less) and other animal use (2 per cent or less) require no additional labelling;
- all other preparations greater than 5 per cent and 30 per cent or less be exempt only when labelled with "if in eyes wash out immediately with water" and "*if skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*".

The NDPSC generally agreed that it would be appropriate to consider some additional labelling for preparations containing greater than 5 per cent SLS. However, all the tabled suggestions diverged in some respect from the positions preferred by some stakeholders. Therefore, Members agreed that the issue of additional labelling should be referred to a delegate as a new consideration, noting the concerns of the NDPSC that preparations with greater than 5 per cent SLS may require some additional labelling.

Evaluation Report

Members noted the following key points from the XXXXX evaluation report which was considered at the February and June 2010 NDPSC meetings.

Public Health Standards

- The Acceptable Daily Intake for SLS was established at 0.1 mg/kg bw/d based on a NOEL of 100 mg/kg bw/d from a 28-day rat oral study and using a safety factor of 1000.
- No Acute Reference Dose (ARfD) for SLS has been established and no suitable data was available to enable an ARfD to be set.
- Based on its acute oral toxicity and severe eye and skin irritancy potential, SLS was recommended to be included in Schedule 6.

Recommended APVMA Label Statements

- New statements, including '*Will damage skin and eyes*' and '*Attacks skin and eyes*'.
- General Safety Precaution Statements also included '*Avoid contact with the eyes and skin*', '*If product on skin, immediately wash area with soap and water*' and '*If product in eyes, wash it out immediately with water*'.

TGAC Toxicology

Absorption, distribution, metabolism and excretion in mammals – no data available	
Acute toxicity	
Rat oral LD_{50} (mg/kg bw)	1200
Rat dermal LD_{50} (mg/kg bw)	No data
Rabbit dermal LD_{50} (mg/kg bw)	Approximately 600

Rat inhalation 4-hr LC_{50} (mg/m^3)	>3900 (one hour exposure)
Skin and eye irritation	Severe irritant
Skin sensitisation	Unknown, but unlikely to be sensitising
Short-term toxicity	
Target/critical effect	Liver toxicity
Lowest relevant oral NOEL (mg/kg bw/d)	100
Lowest relevant dermal NOEL (mg/kg bw/d)	No data
Genotoxicity	Unlikely to be genotoxic *in vitro* or *in vivo*
Long-term toxicity	No data available
Carcinogenicity	No evidence of a carcinogenic potential
Reproductive toxicity	Not a reproductive toxicant
Developmental toxicity	Not a developmental toxicant.

Human safety experience

- The US Cosmetic Ingredient Review of 1983 contained cosmetic experience submissions for shampoos containing SLS. The data are shown below:

Per cent SLS present in shampoo	Sales of shampoo per year in the USA	Total number of applications per year in the USA	Number of safety-related complaints
10	390,000 units	8,580,000	None in two years
14.5	Not reported	200,000	17 in 7 years
30	398,000 units	4,852,620	One in 2 years

- The US Food and Drug Administration (USFDA) lists SLS as a food additive exempt from the requirement for a food additive tolerance. The USFDA also considers SLS as Generally Recognized as Safe (GRAS).
- The Australia New Zealand Food Standards Code does not list all food additives approved for use in Australia, but instead states the acceptability of additives listed in the US GRAS list of flavouring substances (currently includes SLS). In Europe, SLS is listed in Annex II of Council Regulation (EEC) No.2377/90 meaning that no maximum residue limit (MRL) is required for a food product.
- The evaluator drew attention to the OECD SIDS (screening information dataset) Initial Assessment Report on Sodium Dodecyl Sulfate (1997) which concluded that, at present, SLS was of no concern for the general public and for workers. The evaluator also noted that a Cosmetic Ingredient Review of 1983 concluded that SLS appeared to be safe in cosmetic formulations designed for discontinuous, brief use followed by thorough rinsing from the surface of the skin. In products intended for prolonged contact with skin, concentrations should not exceed 1 per cent.
- The evaluator concluded that the amounts of SLS used in cosmetics, and hence the potential human exposure, are significantly smaller than those used in animal studies. Consequently, considering the human health effects associated with SLS together with data indicating potentially extensive use in both industrial and consumer areas, it appears that for consumers and workers, the hazard to human health is low.

EXPERT ADVISORY COMMITTEE DISCUSSION

Members generally agreed that relevant under Section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits (b) the purpose and extent of use.

Members noted that the use pattern and toxicity of SLS and laureth carboxylic acids (LCA) are similar, with similar risks which may need mitigation by labelling. Therefore, Members reiterated similar comments and concern over SLS as had been raised in the LCA discussion (Item 1.3).

While several Members had reservations about the delegate's scheduling decision for SLS, as they had for LCA, Members noted that they had only been asked by the delegate to provide advice on whether additional labelling was appropriate for SLS. The joint meeting had not been asked to reconsider the final scheduling decision, i.e. Schedule 6 with various cut-offs.

Members generally agreed that as SLS is a severe eye and skin irritant some additional labelling was appropriate. Members again noted that there were two distinct labelling issues to consider (and that these were not alternatives):

- additional labels for products captured by the Schedule 6 SLS entry; and
- additional labelling for products exempt from the Schedule 6 entry.

Members first discussed the need for additional labels for products captured by the Schedule 6 SLS entry. It was again noted that Schedule 6 products already had mandatory labelling, including "Poison". Members discussed whether this was sufficient to address the significant eye and skin irritation issues.

One Member noted that while such products were already likely to have some warning labels, it would be appropriate to ensure this through an Appendix E entry, as proposed. Several Members supported the position of the June 2010 NDPSC meeting, and Members generally agreed, that this need only apply where the SLS concentration was greater than 5 per cent.

Members discussed the need for additional labels for unscheduled SLS products. One Member argued that additional labels were not required as the decision to make these SLS products unscheduled implied that they were safe. Several Members disagreed, noting that the SLS scheduling decision, including the exemptions, was made in conjunction with a recommendation for additional labelling.

A Member noted that while products like shampoos were likely to already have labels with an intent similar to the proposed labelling, there were other products which would not have such labelling. The Member asserted, and Members generally agreed, that the irritancy concerns when above 5 per cent SLS warranted the proposed label statements, even if otherwise exempt from scheduling. Such labels would communicate the irritancy concern and help mitigate the risks presented by these products.

Additionally, several Members were concerned that although toothpaste had varying concentrations of SLS, toothpastes in general do not have label statements warning to rinse-out of eyes. A Member also asserted that paste preparations were more difficult to wash-off than liquid preparations. However, Members generally agreed that only toothpaste and other oral hygiene products with 5 or more per cent of SLS should have label statements.

Implementation

A Member again highlighted that there were issues associated with communicating these labelling requirements. Several small industries use SLS, and the regulation of these industries was often fragmented. Therefore, the Member suggested at least 12 months was required to implement these changes. Another Member asserted that most of the industries were proactive and compliant and six months would be sufficient. Members agreed that a more pragmatic period was nine months after the delegate's final decision.

DELEGATE'S INTERIM DISCUSSION

The delegate noted the ACMS-ACCS joint meeting discussion and agreed that, as SLS is a severe eye and skin irritant, label warning, (for products containing greater than 5 per cent SLS), was appropriate.

The delegate noted the ACMS-ACCS joint meeting recommendation that the implementation period be at least nine months after the delegate's final decision. The delegate therefore decided that an implementation of 1 January 2012 was appropriate.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of the substance, and (b) purpose for which the substance is to be used.

DELEGATE'S INTERIM DECISION

The delegate decided to include preparations containing more than 5 per cent sodium lauryl sulfate in Appendix E with standard statements:

- E1 "*If in eyes wash out immediately with water*"; and
- S1 "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" for preparations which are not leave-on or wash-off preparations.

The delegate also decided to amend the Schedule 6 entry for sodium lauryl sulfate to add the following labelling criteria for products to qualify for the current exemptions from the entry:

- wash-off preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with a warning to the effect of "*If in eyes wash out immediately with water*";
- leave-on (1.5 per cent or less), toothpaste and oral hygiene preparations (5 per cent or less) and other animal use (2 per cent or less) – no additional labelling required; and
- all other preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with warnings to the following effect "*If in eyes wash out immediately with water*" and "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*".

The delegate decided on an implementation date of 1 January 2012 (approximately nine months after expected publication of delegate's final decision).

SUBMISSIONS ON INTERIM DECISION

A single further submission was received from XXXXX supporting the interim decision. This further submission advised that, although the interim decision did not coincide exactly to its pre-meeting submission, XXXXX believed that the decision was pragmatic and acceptable to XXXXX.

DELEGATE'S FINAL DECISION

The delegate confirmed including preparations containing more than 5 per cent sodium lauryl sulfate in Appendix E with standard statements:

- E1 "*If in eyes wash out immediately with water*"; and
- S1 "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*" for preparations which are not leave-on or wash-off preparations.

The delegate also confirmed amending the Schedule 6 entry for sodium lauryl sulfate to add the following labelling criteria for products to qualify for the current exemptions from the entry:

- wash-off preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with a warning to the effect of "*If in eyes wash out immediately with water*";
- leave-on (1.5 per cent or less), toothpaste and oral hygiene preparations (5 per cent or less) and other animal use (2 per cent or less) – no additional labelling required; and
- all other preparations, greater than 5 per cent up to 30 per cent or less, are to be exempt only when labelled with warnings to the following effect "*If in eyes wash out immediately with water*" and "*If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water*".

The delegate additionally confirmed an implementation date of 1 January 2012.

Appendix E – Part 2 – New entry

POISON ..... STANDARD STATEMENTS
Sodium lauryl sulfate
· leave-on or wash-off preparations
above 5 per cent..... E1
· other preparations above 5 per cent..... E1,S1

Schedule 6 – Amendment

SODIUM LAURYL SULFATE – Amend entry to read:

SODIUM LAURYL SULFATE (excluding its salts and derivatives) **except**:

(a) in wash-off preparations containing 30 per cent or less of sodium lauryl sulfate and, if containing more than 5 per cent sodium lauryl sulfate, when labelled with a warning to the following effect:

IF IN EYES WASH OUT IMMEDIATELY WITH WATER;

(b) in leave-on preparations containing 1.5 per cent or less of sodium lauryl sulfate;

(c) in toothpaste and oral hygiene preparations containing 5 per cent or less of sodium lauryl sulfate;

(d) in other preparations for animal use containing 2 per cent or less; or

(e) in other preparations containing 30 per cent or less of sodium lauryl sulfate and, if containing more than 5 per cent sodium lauryl sulfate, when labelled with warnings to the following effect:

IF IN EYES WASH OUT IMMEDIATELY WITH WATER; and

IF SKIN OR HAIR CONTACT OCCURS, REMOVE CONTAMINATED CLOTHING AND FLUSH SKIN AND HAIR WITH RUNNING WATER.

2. MATTERS INITIALLY REFERRED TO ACMS#1

2.1 COUGH AND COLD

DELEGATE'S REFERRAL TO EXPERT ADVISORY COMMITTEE

The delegate considered the scheduling of cough and cold medicines and decided to seek advice from the ACMS on the following:

Cough and cold medicines – proposal to reschedule 19 substances used in over-the-counter cough and cold medicines to:

- Schedule 4 for use in children less than 2 years of age.
- Schedule 3 for use in children aged from 2 to 6 years of age.
- Schedule 2 for use in children and adults above 6 years of age.

The delegate proposes that this rescheduling apply to the following substances for use in cough and cold products (only where it will not result in less restrictive scheduling):

Brompheniramine	Oxymetazoline (excluding for nasal spray use)
Carbetapentane	Pheniramine
Chlorpheniramine	Phenylephrine
Codeine	Pholcodine
Dexchlorpheniramine	Promethazine
Dextromethorphan	Pseudoephedrine
Dihydrocodeine	Senega
Diphenhydramine	Triprolidine
Doxylamine	Xylometazoline (excluding for nasal spray use)
Ipecacuanha	

This proposal is a result of recommendations from the June 2010 meeting of the NDPSC following consideration of a review of cough and cold medicines by the TGA.

NOTE:

This matter is still under consideration and no interim decision was made. The delegate is considering the Committee's recommendations and discussion in context of the current regulatory framework and has requested further advice from the ACMS prior to making an interim decision.

A revised delegate's proposal inviting public comment will be published in the pre-meeting public notice for matters referred to the June 2011 ACMS meeting.

2.2 DICLOFENAC

DELEGATE'S REFERRAL TO EXPERT ADVISORY COMMITTEE

The delegate considered the scheduling of diclofenac and decided to seek advice from the ACMS on the following:

Diclofenac – proposal to include preparations containing 3 per cent or more of diclofenac for the treatment of solar keratoses in Schedule 4.

EXPERT ADVISORY COMMITTEE RECOMMENDATION

The ACMS recommended that diclofenac dermal preparations containing more than 1 per cent of diclofenac or preparations for the treatment of solar keratosis be included in Schedule 4.

The ACMS recommended an implementation date of not more than six months following the delegate's final decision.

BACKGROUND

Diclofenac, a phenylacetic acid derivative, is a nonsteroidal anti-inflammatory drug (NSAID). Diclofenac exhibits anti-inflammatory, analgesic and anti-pyretic properties by inhibiting prostaglandin synthesis through inhibition of cyclo-oxygenase-1 (COX-1) and COX-2. Its sodium salt is predominantly used for the relief of pain and inflammation in various conditions including musculoskeletal and joint disorders. Diclofenac sodium is also used in the management of actinic keratoses and fever.

Diclofenac was included in Schedule 4 in March 1981, following consideration of a product containing diclofenac sodium for the treatment of inflammatory and degenerative forms of arthritis and rheumatism.

In February 1997, the NDPSC agreed to reschedule diclofenac dermal preparations containing 1 per cent or less of diclofenac from Schedule 4 to Schedule 2. The NDPSC agreed that a Schedule 2 classification was appropriate for these products on the basis of the safety profile and approved indications for use in readily recognised conditions (minor pain relief). The NDPSC noted that, as it was only in possession of safety data relating to a 1 per cent formulation, consideration at that meeting was therefore limited to this concentration and did not include products indicated for the treatment of actinic keratoses.

In August 1999, the NDPSC considered recommendations from the Trans-Tasman Harmonisation Working Party to exempt diclofenac for dermal use. The NDPSC agreed that the scheduling of diclofenac for dermal use remained appropriate.

In November 1999, following the provision of additional information, the NDPSC agreed to refer a reconsideration of the scheduling of diclofenac in dermal preparations to a later meeting. In February 2000, the NDPSC considered additional safety data and agreed that dermal preparations of diclofenac should be exempt from scheduling, thus harmonising with the NZ scheduling of diclofenac. The record of that meeting indicated that this consideration related to diclofenac products indicated for minor pain relief. The record did not specify any information in relation to specific concentrations of diclofenac products for dermal use or in relation to the use of diclofenac for the treatment of keratoses.

In June 2010, the NDPSC noted a query on the scheduling status of diclofenac preparations for dermal use. The NDPSC's discussion at that meeting is summarised below under the Submissions heading.

SCHEDULING STATUS

Diclofenac is currently listed in Schedules 2, 3 and 4. All diclofenac preparations for dermal use are currently exempt from scheduling.

INITIAL SUBMISSIONS

June 2010 NDPSC Discussion

At the June 2010 meeting, the NDPSC noted a query regarding the status of a dermal diclofenac 3 per cent w /w gel product, listed on the Australian Register of Therapeutic Goods (ARTG) as Schedule 4. According to the scheduling at that time, all diclofenac preparations for dermal use were exempt from scheduling.

The NDPSC noted that the product was specifically registered for the management of actinic keratoses for application only to solar keratosis/keratosis and was not for application to normal skin. Members noted the TGA's recommendation that it was in the public interest for diclofenac 3 per cent w/w to be included in Schedule 4.

The NDPSC agreed that this mismatch required resolution and recommended that the delegate refer the matter to the ACMS for consideration.

Pre-meeting Submission

XXXXX agreed that products for the treatment of solar (or actinic) keratoses should be prescription-only medicines by virtue of the medical condition they are used to treat, and noted that the current schedule entry for diclofenac is inadequate in this regard.

XXXXX noted that diclofenac products indicated for the treatment of keratoses contain 3 per cent w/w diclofenac sodium and queried whether the proposal advertised in the public notice would achieve the anticipated outcome. ACMS Members noted that dermal

preparations containing 3 per cent diclofenac sodium would equate to 2.79 per cent of diclofenac.

XXXXX suggested the following alternative amendment to exemption (b) of the Schedule 4 entry: "in preparations for dermal use containing 1 per cent or less of diclofenac", i.e. dermal use greater than 1 per cent would change from unscheduled to Schedule 4.

Other considerations

According to the Martindale monograph for diclofenac, available dermal/topical preparations containing diclofenac included:

- diclofenac diethylamine gels consisting of the equivalent of 1 per cent of diclofenac sodium for the local symptomatic relief of pain and inflammation;
- diclofenac epolamine used topically as a plaster containing the equivalent of 1 per cent of diclofenac sodium for local symptomatic pain relief in ankle sprain and epicondylitis;
- topical solutions of 1.6 per cent diclofenac sodium for the treatment of osteoarthritis in superficial joints; and
- gel containing 3 per cent diclofenac sodium used in the management of actinic keratosis.

The ARTG listed one dermal product containing 3 per cent diclofenac sodium for the management of actinic keratosis. The ARTG also listed several other dermal diclofenac products containing either 1 per cent diclofenac sodium (equivalent to 0.93 per cent diclofenac) or 1.16 per cent diclofenac diethylammonium (equivalent to 0.92 per cent diclofenac) for use in anti-inflammatory pain relief.

EXPERT ADVISORY COMMITTEE DISCUSSION

Members agreed that the relevant matters under section 52E(1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of use and (b) purpose and extent of use.

Members discussed the appropriateness of scheduling preparations for the management of actinic keratosis in Schedule 4. One Member argued that the public experiences significant inconvenience when required to consult with a doctor in the management of chronic conditions. However, other Members argued that solar keratosis requires medical supervision and that arrangements, such as the use of repeat prescriptions, are in place for the management of chronic conditions. Members generally agreed that preparations containing any amount of diclofenac for the treatment of solar keratosis should be classified as Schedule 4. Although it was noted that it was not common for schedule entries to specify an indication, Members agreed that a specific listing in Schedule 4 for dermal preparations for the treatment of solar keratosis was appropriate.

Members discussed whether this proposed amendment to the schedule entry should also include a low-concentration exemption cut-off. Members agreed that a 3 per cent cut-off would not appropriately capture currently available dermal preparations for the treatment of solar keratosis. A Member asserted that a cut-off of 1 per cent or less should be applied, where dermal preparations containing up to and including 1 per cent of diclofenac would remain exempt. Other Members queried the choice of 1 per cent as a cut-off and argued that there was no data presented on the risks of use of 1 per cent versus 2 per cent diclofenac dermal preparations. Another Member noted that there was evidence of the safety and efficacy of 1 per cent preparations when dermal diclofenac was originally scheduled. It was further noted that during the product approval process, the TGA undertakes individual product evaluations including the assessment of safety and efficacy data. A Member asserted that this data is currently only available for dermal preparations which are not indicated for the treatment of solar keratosis containing up to 1 per cent diclofenac.

A Member noted that although diclofenac may be safe when used for pain relief in higher strengths, there was a risk that new products containing high amounts of diclofenac may become available on the market as unscheduled. A Member argued that new products would be subject to the product approval process. However, another Member noted that preparations prepared by compounding pharmacies are not subject to the approval process and a cut-off of 1 per cent would ensure appropriate restrictions on such preparations.

The Committee generally agreed that a recommendation should be put to the delegate where preparations containing more than 1 per cent diclofenac should be restricted to Schedule 4. Members also generally agreed that any dermal diclofenac preparation for the treatment of solar keratosis should be restricted to Schedule 4.

Implementation date

Members noted that apart from products for the management of actinic keratosis the ARTG did not list any other diclofenac products for dermal use containing more than 1 per cent diclofenac. Therefore, the proposed amendment to the Schedule 4 entry was not expected to inadvertently capture any other diclofenac preparations for dermal use.

Members considered whether a delayed implementation date would be required. Members noted that 3 per cent diclofenac sodium preparations for the treatment of solar keratosis are currently marketed as Schedule 4 products. Members also noted that several jurisdictions' legislation prohibits the labelling of unscheduled products as prescription medicines. Members agreed that timely implementation of the proposed decision would be advisable.

Members noted that the timing of the delegate's decisions is at the discretion of the delegate. However, it was also noted that the earliest implementation of the proposed amendment would involve the inclusion of an interim decision in the next scheduled public notice, anticipated to be published in mid-February 2011. The earliest public

notice which could contain the delegate's final decision in this matter is expected to be published in late March 2011. The subsequent amendment to the SUSMP is expected to become effective from 1 June 2011.

DELEGATE'S INTERIM DISCUSSION

The delegate noted the ACMS Members' discussion and agreed with the Committee's recommendation to schedule diclofenac dermal preparations containing more than 1 per cent of diclofenac and diclofenac dermal preparations for the treatment of solar keratosis in Schedule 4.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of use and (b) purpose and extent of use.

DELEGATE'S INTERIM DECISION

The delegate decided that diclofenac dermal preparations containing more than 1 per cent of diclofenac or preparations for the treatment of solar keratosis be included in Schedule 4.

The delegate decided on an implementation date of 1 June 2011.

SUBMISSIONS ON INTERIM DECISION

Following publication of the delegate's interim decision in the February 2011 public notice a submission was received from XXXXX. The submission was not considered a further submission as this party did not provide an initial submission to the invitation for submissions on the delegate's proposal. It was at the delegate's discretion whether to consider this submission in making a final scheduling decision

XXXXX

The submitted comments supported the inclusion of diclofenac preparations for the treatment of solar keratosis in Schedule 4, however asserted that dermal preparations of diclofenac, at any strength, for the treatment of pain and inflammation, should remain exempt from scheduling.

The main points from the submission have been summarised below:

- Noted that the initial delegate's proposal sought comment on restrictions on preparations containing 3 per cent or more of diclofenac for the treatment of solar keratosis in Schedule 4. Stated that as this proposal had minimal impact on products for other indications it had not provided a pre-meeting submission.
- Stated that the interim decision on the matter would have significant impact on industry XXXXX.

- Agreed that products for the treatment of solar keratosis were appropriately included in Schedule 4 due to the nature of the condition to be treated.
- Disagreed that all dermal preparations containing greater than 1 per cent diclofenac should be classified as Schedule 4.
- Noted that although in Australia the highest concentration of unscheduled dermal diclofenac products was at 1 per cent, XXXXX.
- Asserted that minimal absorption is expected from a dermal preparation when used on intact skin. Stated that associated safety risks were low as systemic absorption from dermally applied diclofenac was around 7 per cent and is well below systemic strengths of diclofenac currently available as OTC medicines.
- Claimed that dermal preparations of diclofenac offer consumers an alternative treatment option when systemic preparations may not be appropriate or suitable. XXXXX.
- Stated that similar to all NSAIDs, use of dermal diclofenac was limited to short term treatment. Noted that the potential for abuse was low.
- Stated that new formulations of diclofenac would be appropriately evaluated by the TGA, at which time both safety and efficacy could also be evaluated.
- Suggested deferring the decision so that a formal submission from the sponsor could be considered by the Advisory Committee on Medicine Scheduling.

DELEGATE'S RECONSIDERATION OF INTERIM DECISION

The delegate noted that only one submission was received following the publication of the interim decision on diclofenac. The submission was not considered a further submission under Regulation 42ZCZP of the Therapeutic Goods Regulations 1990 (the Regulations) as the party did not provide a submission in response to the original invitation for the making of submissions under subregulation 42ZCZK(1) of the Regulations.

In this instance the delegate considered it appropriate to include this submission in the scheduling consideration. However, the future consideration of this kind of submission will be determined on a case by case basis.

The delegate reiterated a point previously mentioned by the ACMS regarding a lack of Australian safety data on dermal preparations of diclofenac in concentrations greater than 1 per cent. The delegate asserted that a new scheduling consideration could be commenced should sufficient evidence of safety and benefit to the public become available.

The delegate again noted that currently there were no dermal products registered in Australia containing more than one per cent diclofenac other than those for the treatment of solar keratosis. The delegate asserted that if a product containing higher

concentrations of dermal diclofenac became available on the Australian market the scheduling of such a preparation would be separately considered.

DELEGATE'S FINAL DECISION

The delegate confirmed that diclofenac dermal preparations containing more than 1 per cent of diclofenac or preparations for the treatment of solar keratosis be included in Schedule 4.

The delegate also confirmed an implementation date of 1 June 2011.

Schedule 4 – Amendment

DICLOFENAC – Amend entry to read:

DICLOFENAC **except**:

(a) when included in Schedule 2 or 3; or

(b) in preparations for dermal use unless:

(i) for the treatment of solar keratosis; or

(ii) containing more than 1 per cent of diclofenac.

2.3 MERCURY / MERCUROCHROME

DELEGATE'S REFERRAL TO EXPERT ADVISORY COMMITTEE

The delegate considered the scheduling of mercury and mercurochrome and decided to seek advice from the ACMS on the following:

Mercury – proposal to clarify the Schedule 2 mercury entry by extending the current exemption for preparations containing 0.5 per cent or less of mercury to 0.50 per cent or less. This proposal may be applicable to mercurochrome (merbromin) products for external use.

EXPERT ADVISORY COMMITTEE RECOMMENDATION

The ACMS recommended that a Schedule 2 entry be created for mercurochrome preparations containing 2 per cent or less of mercurochrome for external use. The Committee also recommended that a new Schedule 4 mercurochrome entry be created for all other preparations of mercurochrome, excluding those listed in Schedules 2 and 6.

The ACMS recommended an implementation date of not more than six months following the delegate's final decision.

BACKGROUND

Mercury is a component in many products for human and animal external use. Merbromin (known in Australia as mercurochrome solution) is a mercurial antiseptic that has been used for disinfection of skin and wounds. It is currently available for human use in 1, 2 and 10 per cent solutions.

In February 2010, the NDPSC noted a stakeholder query advising that several entries on the Australian Register of Therapeutic Goods (ARTG) containing 2 and 10 per cent mercurochrome (containing 0.534 and 2.67 per cent mercury respectively) were listed as Schedule 2 medicines. It was noted that the cut-off for the Schedule 2 mercury entry was 0.5 per cent mercury. The NDPSC agreed that the amount of mercury in a preparation should not be rounded down and clarified that preparations for human use containing 2 and 10 per cent mercurochrome are captured by the Schedule 4 entry for mercury.

The delegate agreed to accept this as a delegate initiated scheduling consideration and decided to refer the matter to the ACMS for advice.

SCHEDULING STATUS

Mercury is currently listed in Schedules 2, 4 and 7 in the SUSMP. Mercurochrome is also separately listed in Schedule 6 and Appendix E for the treatment of animals in preparations for topical use.

INITIAL SUBMISSIONS

Request

XXXXX requested a reconsideration of the February 2010 NDPSC determination that 2 per cent solutions of mercurochrome for human use were to be captured by the Schedule 4 mercury entry.

The request queried the fairness of the process in which the NDPSC made its decision. It stated that as there was no notice that the scheduling of mercurochrome was being considered, the sponsors of mercurochrome-containing products had been denied natural justice by not being given the opportunity to provide comment. As a result, the NDPSC's clarification of the status of 2 per cent mercurochrome products had serious financial consequences for industry.

The request stated that if the opportunity for comment had been allowed, industry would have provided the following input for consideration.

- In the absence of specific guidance on rounding in the SUSMP, the concentration of mercury in 2 per cent mercurochrome products would be interpreted as falling within the 0.5 per cent cut-off in Schedule 2. This was based on scientific principles and on

the TGA's guidelines on rounding in the Australian Regulatory Guidelines for Prescription Medicines (ARGPM, Appendix 18, Page 4):

In cases where a numerical limit is specified as the primary decision criterion, the calculated result of the test is first rounded to the number of significant figures given in the limit before the decision criterion is applied. Where the number of decimal places is greater than those specified in the limits, the data should be rounded in accordance with the BP. If the last figure is 0-4 it is rounded down, and if it is 5-9 it is rounded up. For example, a result of 0.14 per cent complies with a specified limit of not more than 0.1 per cent, but would not comply with a limit of 0.10 per cent.

· In that case, the following calculation would apply:

- 2 per cent mercurochrome - equates to 0.534444 per cent mercury;
- the limit for mercury in Schedule 2 is 0.5 per cent (not 0.500 per cent);
- because the second and subsequent decimal places are 0 - 4, the limit can be rounded down to 0.5 per cent.

Pre-meeting Submission

XXXXX stated there was little if any benefit to the public in having 2 per cent mercurochrome solutions available as an over-the counter medicine, as there were more efficacious and less toxic products widely available. The submission queried as to how the proposal to amend the current Schedule 2 entry by changing the reference from '0.5 per cent of mercury' to '0.50 per cent of mercury' would serve to clarify this issue.

EXPERT ADVISORY COMMITTEE DISCUSSION

Members agreed that the relevant matters under section 52E(1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of use and (d) the formulation of the substance.

A Member noted that the NDPSC's February 2010 consideration of the scheduling status of mercury and mercurochrome was not a scheduling decision. The Member reiterated that the consideration sought to clarify the existing status of mercurochrome products which were inaccurately listed on the ARTG.

The Committee debated the application of rounding to statements of quantity in the SUSMP. A Member noted that the SUSMP was silent on an approach to rounding. However, the Member asserted that there was precedent from previous scheduling decisions where a high level of accuracy had been added where required i.e. by the addition of extra digits after the decimal point. Another Member asserted that the interpretation by some jurisdictions when enforcing limits was that a specification of 1 per cent in the schedule entry implied 1.0 per cent. However, other Members also noted that there was a precedent where certain jurisdictions could allow for rounding and this was addressed on a case-by-case basis.

Members also noted that specific enforcement of schedule entry cut-offs is addressed by the regulator and individual jurisdictions on a case-by-case basis. A Member suggested that a clarification on rounding in the SUSMP may be warranted, however other Members argued that such a move may inadvertently affect numerous substances, i.e. scheduling compliance relies on the specific policies of enforcing authorities and any move to a single position may result in a clash with these policies. Members also noted that issues with uniform enforcement policy may be raised by the jurisdictions with the National Consultative Committee on Therapeutic Goods (NCCTG).

The Committee noted that the chemical identity of mercurochrome is not precise and there is variation in the amount of mercury present in mercurochrome solutions. According to a monograph from the British Pharmaceutical Codex, mercurochrome may contain between 24 to 27 per cent mercury. Therefore, the concentration of mercury in 2 per cent solutions of mercurochrome could range from 0.48 to 0.54 per cent. Members noted that a separate schedule entry for mercurochrome for external use would assist in providing clarity in the interpretation of the substance's scheduling status.

The Committee discussed the appropriate scheduling of 2 per cent solutions of mercurochrome. A Member asserted that 2 per cent mercurochrome is appropriately captured by the Schedule 4 entry for mercury due to the risks associated with the product's use. The Member argued that these risks included the product's lack of efficacy and potential to mask more serious ailments, i.e. cellulitis. The Member further noted that there were other products currently available for disinfection of skin and wounds with less associated risks.

Other Members asserted that 2 per cent mercurochrome solutions were intended to be available as Schedule 2 products and had been assessed as such by the regulator as part of the product registration process. It was argued that these products may have been inadvertently captured by the Schedule 4 entry due to varying concentrations of mercury. A Member further argued that prior to the February 2010 NDPSC clarification, 2 per cent mercurochrome solution had a long history of safe use as a Schedule 2 medicine.

Members noted the risks and benefits of mercurochrome and agreed that, on balance, 2 per cent solutions of mercurochrome should be available as Schedule 2.

Implementation date

Members noted that the NDPSC's February 2010 clarification of the scheduling of mercurochrome may have had an adverse impact on industry. The Committee agreed that to minimise any additional impact, an implementation date of not more than six months following the delegate's final decision would be appropriate.

Members noted that the timing of the delegate's decisions is at the discretion of the delegate. However, it was also noted that the earliest implementation of the proposed amendment would involve the inclusion of an interim decision in the next scheduled public notice, anticipated to be published in mid-February 2011. The earliest public

notice which could contain the delegate's final decision in this matter was expected to be published in late March 2011. The subsequent amendment to the SUSMP was expected to become effective from1 June 2011.

DELEGATE'S INTERIM DISCUSSION

The delegate noted the ACMS Members' discussion and agreed with the Committee's recommendation to specifically schedule mercurochrome preparations in Schedule 2 containing 2 per cent or less of mercurochrome for external use. The delegate also agreed to create a new Schedule 4 mercurochrome entry for all other preparations of mercurochrome, excluding those listed in Schedules 2 and 6.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of use and (d) the formulation of the substance.

DELEGATE'S INTERIM DECISION

The delegate decided that a Schedule 2 entry be created for mercurochrome preparations containing 2 per cent or less of mercurochrome for external use. The delegate also decided that a new Schedule 4 mercurochrome entry be created for all other preparations of mercurochrome, excluding those listed in Schedules 2 and 6.

The delegate decided on an implementation date of 1 June 2011.

SUBMISSIONS ON INTERIM DECISION

No submissions were received on the interim decision.

DELEGATE'S FINAL DECISION

The delegate confirmed that a Schedule 2 entry be created for mercurochrome preparations containing 2 per cent or less of mercurochrome for external use. The delegate also confirmed that a new Schedule 4 mercurochrome entry be created for all other preparations of mercurochrome, excluding those listed in Schedules 2 and 6.

The delegate confirmed an implementation date of 1 June 2011.

Schedule 2 – New entry

MERCUROCHROME in preparations for external use containing 2 per cent or less of mercurochrome.

Schedule 4 – New entry

MERCUROCHROME **except** when included in Schedule 2 or 6.

2.4 PSEUDOEPHEDRINE

DELEGATE'S REFERRAL TO EXPERT ADVISORY COMMITTEE

The delegate considered the scheduling of pseudoephedrine and decided to seek advice from the ACMS on the following:

Pseudoephedrine – proposal to delete the existing Appendix H entry. This proposal is a result of a recommendation from the June 2010 meeting of the NDPSC.

EXPERT ADVISORY COMMITTEE RECOMMENDATION

The ACMS recommended deletion of the pseudoephedrine entry from Appendix H. The ACMS also recommended an implementation date of not more than six months after the delegate's final decision.

BACKGROUND

Pseudoephedrine is an oral sympathomimetic nasal decongestant used for the symptomatic treatment of rhinitis associated with colds and flu or hayfever. Over recent years, moves to combat the criminal diversion of pseudoephedrine to methylamphetamine has resulted in preparations containing smaller quantities of pseudoephedrine being rescheduled from Schedule 2 to Schedule 3 and all other preparations from Schedule 3 to Schedule 4.

In June 2005, when the NDPSC agreed to reschedule the majority of pseudoephedrine products from Schedule 2 to Schedule 3, it also agreed to remove pseudoephedrine from Appendix H, considering that such action was in line with the rescheduling of pseudoephedrine, i.e. because of diversion.

In October 2005, the NDPSC agreed to vary the initial scheduling decision from the June 2005 meeting by implementing it in two stages: the first stage being the removal of all Schedule 2 products to Schedule 3 from 1 January 2006; and the second stage involving the rescheduling of liquid and other preparations from Schedule 3 to Schedule 4 from 1 April 2006. The NDPSC also agreed to set aside the June 2005 Appendix H decision, i.e. pseudoephedrine was to remain in Appendix H, on the grounds that it was reasonable for the advertising status quo to remain, at least initially, to allow consumers to be informed of the impact of the scheduling changes.

In February 2006, the NDPSC again reviewed the Appendix H status of pseudoephedrine and agreed to retain it in Appendix H "at this stage, to allow consumers to be informed through advertising of the impact of the scheduling changes and available Schedule 3 products".

In June 2010, the NDPSC considered a proposal by XXXXX to delete pseudoephedrine from Appendix H. The NDPSC agreed that the pseudoephedrine Appendix H entry

should be removed. That meeting noted, however, that a number of pre-meeting submissions opposed this and, in accordance with the transition arrangements for this final meeting of the NDPSC, agreed to refer the matter to the delegate with the recommendation that the pseudoephedrine Appendix H entry be removed.

SCHEDULING STATUS

Pseudoephedrine is currently included in Schedules 3 and 4. It is also listed in Appendix H.

INITIAL SUBMISSIONS

June 2010 NDPSC Discussion

Members noted the following from the June 2010 NDPSC discussion.

- A Member asserted that five years had passed since the NDPSC's decision to reschedule pseudoephedrine from Schedule 2 to Schedule 3 and the need for consumers to be informed of the changes was no longer relevant. The Member further stated that the original decision to keep the Appendix H entry was only intended as a means to inform the community of the transition arrangements and was not intended as a long term arrangement.
- A Member suggested that as there was no evidence of inappropriate advertising of pseudoephedrine, there was no real harm in maintaining the Appendix H entry.
- Another Member asserted that for an Appendix H entry to be maintained there would need to be evidence of a significant public health benefit from allowing the advertising of pseudoephedrine.
- The NDPSC generally agreed that the arguments for maintaining the Appendix H pseudoephedrine entry were not strong and recommended that it be deleted.

June 2010 Pre-meeting Submissions

Members noted that a number of submissions had been made to the June 2010 NDPSC meeting on this issue.

- XXXXX was not opposed to deleting the Appendix H entry for pseudoephedrine. XXXXX believed, however, that the deletion would have little effect on illicit use and diversion.
- XXXXX did not support the removal of pseudoephedrine from Appendix H. These submissions argued that advertising materials were well regulated and that there had not been any case of inappropriate advertising of pseudoephedrine.
- XXXXX argued that the status quo on advertising pseudoephedrine should remain to assist legitimate users in accessing pseudoephedrine products.

- XXXXX also:
  - noted that the Advertising Code was available to provide guidance on how medicines could be advertised;
  - argued that it would be inappropriate for the Appendix H entry to be removed unless there were demonstrable, significant clinical or social reasons to do so;
  - asserted that pharmacists have been acquainted for many years with the supply of pseudoephedrine products to treat the symptoms of rhinitis. They were also equipped to respond to those consumers who may find phenylephrine ineffective and were professionally capable of assessing whether pseudoephedrine products provide a more suitable alternative;
  - stated that pharmacists were aware of the risk for illicit diversion and asserted that the use of real-time monitoring tools such as Project Stop has had a significant impact on this issue. The criminal elements who want access to pseudoephedrine were aware of which products were needed, and advertising, or lack there of, would have little impact;
  - asserted that, as pseudoephedrine is contained in many Schedule 3 solid and liquid oral preparations, deletion of the Appendix H entry would have a significant regulatory impact.

December 2010 Pre-meeting Submissions

Members particularly noted the following from the three pre-meeting submissions received on this issue:

- XXXXX reiterated their June 2010 NDPSC pre-meeting submission;
- XXXXX did not object to the deletion of pseudoephedrine from Appendix H;
- XXXXX did object to the deletion of pseudoephedrine from Appendix H on the basis of:
  - an asserted public health benefit in making consumers aware of their therapeutic options; and
  - no evidence had been presented to demonstrate that permitting advertising of pseudoephedrine resulted in an increase in criminal diversion.

The Committee noted that XXXXX had submitted the following additional arguments in support of the above position.

Public health benefit

- Given the genetic/metabolic diversity that exists in Australia, there is an inherit public health benefit in having multiple therapeutic options available to patients, i.e. different responders. The efficacy and safety of pseudoephedrine as an orally dosed systemic nasal decongestant is well documented.

- Advertising is in the interest of public health and the continued promotion of the quality use of medicines. It allows consumers to be aware of their therapeutic options for the symptomatic treatment of rhinitis associated with colds and flu or hayfever.
- Pseudoephedrine was up-scheduled due to concerns with the criminal diversion to methylamphetamine rather than a specific safety concern with the correct/legitimate use of pseudoephedrine.
- The primary result of the up-scheduling of pseudoephedrine was the introduction of safeguards that have been built into Australian community pharmacy practice, i.e. pharmacist intervention prior to purchase of the product (including counselling) and pharmacists recording the purchase of pseudoephedrine containing products to deter "pharmacy shopping" or "pseudo running".
- XXXXX.
- Due to a decline in sales, reduction in the demand and fewer products being made available to the consumer as a result, it was argued that up-scheduling had achieved its objective in making diversion more difficult by way of reduced access.
- Advertising non-prescription medications assists in reducing the burden placed on doctors in general practice treating patients with common illnesses that could have been self-managed.
- The Pharmaceutical Society of Australia's position statement on advertising states:

  Where it is demonstrated that brand advertising of particular Schedule 3 "pharmacist only" products will lead to improved health outcomes, the Pharmaceutical Society of Australia believes such advertising should be permitted on a case by case basis.

  The objectives of such advertising are to:

  - inform consumers of the availability of these Schedule 3 treatments;
  - convey information of an educational, rather than a promotional nature,

  and as part of the advertisement script:

  - emphasize that such treatments may only be used on the recommendation of, or after consultation with, a pharmacist or medical practitioner;
  - refer consumers to their pharmacist or doctor for further information, thus promoting better communication between consumers and health professionals.

Likelihood of advertising leading to inappropriate patterns of medication use

- It was accepted by the June 2005 NDPSC meeting that "pseudo-runners" generally would have specific information on the product that they intend to purchase and were unlikely to be influenced by advertising. The role that the pharmacist plays since the up-scheduling of pseudoephedrine has added an element of difficulty for the "pseudo-runners".

- Studies (www.wsmi.org/pdf/wsmi_brochureadvertising.pdf) have demonstrated that people do not choose to buy medicines if they have no need for them. Advertising cannot force people to buy and use a medicine they do not want or need.
- There has been no evidence provided to indicate that the current advertising status has led to an increase in criminal diversion.

Advertising of an off-label indication

- In Australia, pseudoephedrine is primarily indicated for the symptomatic treatment of rhinitis associated with colds and flu or hayfever. Off-label indications for pseudoephedrine may also be used as a first-line therapy of priapism and treatment for urinary incontinence. It is believed that the treatment of priapism and urinary incontinence are the only potential off-label indications for pseudoephedrine.
- To date, there have been no instances of promotion of the off-label indications stated above.

The responsibility of pharmacists to be actively involved in the supply of substances

- There is a need for pseudoephedrine containing medicines to be made available to consumers as a viable therapeutic option for the symptomatic relief of rhinitis associated with colds and flu or hayfever.
- The pharmacist has played an important role in:
  - ensuring appropriate use of products containing pseudoephedrine;
  - counselling customers on potential side effects that may be experienced;
  - determining the impact of polypharmacy and any potential drug-drug interactions;
  - ensuring that any other medical conditions will not be exacerbated by the appropriate use of the pseudoephedrine containing medicines; and
  - recording of customer details that do purchase pseudoephedrine containing products.
- The Department of Health and Ageing has developed a national strategy for the quality use of medicines and that, from this perspective, it is ideal to have a pharmacist assess whether a product requested by a consumer is appropriate for their conditions.
- There is no reason to believe that continued advertising of pseudoephedrine products would result in an increased workload or responsibility for pharmacists.

The level of patient education necessary to ensure correct use

- The level of consumer education required for appropriate use of pseudoephedrine products is deemed relatively minimal.
- Products containing pseudoephedrine all have packaging and labelling that meets the TGA's requirements and is sufficient to ensure correct use of the product.

- The pharmacist, at time of purchase, will reiterate the dosage instructions, indications and contraindications to consumers.
- Patient education is required on the availability of other therapeutic options for this class of products.

Available consumer medicine information

- Pseudoephedrine has been available as a Schedule 3 medicine for some time and it is a regulatory requirement that companies should have a consumer medicine information (CMI) for these products and that the dispensing pharmacist offers the CMI to the customer at the time of dispensing or at the request of the customer.
- Many companies make their CMIs available through their website and the TGA has developed a database of Product Information (PIs) and CMIs for products where there is a regulatory requirement to maintain these documents.

The desire of consumers to manage their own medication

- There is a social trend of consumers wishing to self diagnose and self treat various self limiting ailments. Consumer awareness of the various therapeutic options will help ensure the quality use of medicines.

Advertising controls through ASMI

- There is a requirement for any advertising through main stream media to be pre-approved by the Australian Self Medication Industry (ASMI). As this pre-approval process helps to maintain an appropriate level of control, no additional advertising control should be required.

EXPERT ADVISORY COMMITTEE DISCUSSION

The Committee agreed that the relevant matters under section 52E(1) of the *Therapeutic Goods Act 1989* included (e) the potential for abuse of a substance and (f) any other matters necessary to protect public health.

A Member asserted that there appeared to have been no cases of inappropriately advertising pseudoephedrine, nor was it likely that advertising had any effect on illicit use and diversion of pseudoephedrine. The Committee generally agreed with this conclusion, noting the recent shift in pseudoephedrine diversion activities to direct illicit import.

Several Members noted, however, that general scheduling policy is that Schedule 3 medicines are not allowed to be advertised, unless there is a strong case for public benefit from advertising. It was further noted that listing in Appendix H rarely occurs. These Members maintained that the lack of an identified problem from advertising was not a sufficient argument to maintain an Appendix H listing.

A Member noted that the main public health benefit argument for allowing advertising of pseudoephedrine products was that this would assist in making consumers aware of their therapeutic options. It was agreed that, on occasion, this had been sufficient for an

Appendix H listing where the public had a low level of education about a substance. Several Members argued, however, that there was no such case for advertising pseudoephedrine as consumer awareness of these products was well established. The current restrictions on pseudoephedrine products, i.e. the implementation of Project Stop and the need to show identification, were also widely known.

A Member noted that the February 2006 NDPSC agreement to retain pseudoephedrine in Appendix H had been limited. The Member asserted that the intent at that time was clear, in that advertising was only to be allowed during the transition period for the change in pseudoephedrine scheduling arrangements. It was argued that this transition period had now passed and there was no longer a strong need to inform consumers through advertising of the impact of the scheduling changes and available Schedule 3 products. The Committee agreed that the Appendix H listing for pseudoephedrine should be deleted.

The Committee then discussed the implementation of this recommendation. A Member advised that advertising approvals normally had a two year duration and suggested that this might be a factor. Other Members argued that any such approval would require the ongoing Appendix H status of pseudoephedrine and was not a barrier to removing the Appendix H listing.

Members noted that the timing of the delegate's decisions is at the discretion of the delegate. However, it was also noted that the earliest implementation of the proposed amendment would involve the inclusion of an interim decision in the next scheduled public notice, anticipated to be published in mid-February 2011. The earliest public notice which could contain the delegate's final decision in this matter is expected to be published in late March 2011. The subsequent amendment to the SUSMP is expected to become effective from 1 June 2011. The Committee agreed that an implementation date of not more than six months following the delegate's final decision would be appropriate.

DELEGATE'S INTERIM DISCUSSION

The delegate noted the ACMS Members' discussion and agreed with the Committee's recommendation to delete the Appendix H entry for pseudoephedrine.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (e) the potential for abuse of a substance and (f) any other matters necessary to protect public health.

DELEGATE'S INTERIM DECISION

The delegate decided to delete the pseudoephedrine entry from Appendix H. The delegate decided on an implementation date of 1 June 2011.

SUBMISSIONS ON INTERIM DECISION

No submissions were received on the interim decision.

DELEGATE'S FINAL DECISION

The delegate confirmed that the pseudoephedrine entry be deleted from Appendix H. The delegate also confirmed an implementation date of 1 June 2011.

Appendix H - Amendment

Pseudoephedrine – Delete entry.

PART B – FINAL DECISIONS ON PROPOSALS NOT REFERRED TO AN ADVISORY COMMITTEE

3.1 ETHYL ALCOHOL

SUBSTANCE DETAILS

Ethyl alcohol (also commonly referred to as 'alcohol') has a wide range of uses and presentations including in the recreational form of alcoholic beverages, for its effects on the Central Nervous System. According to its Martindale monograph, ethyl alcohol has a number of pharmaceutical applications, including:

- in the disinfection of skin before injection, venepuncture, or surgical procedures;
- in the disinfection of hands and clean surfaces;
- for its anhidrotic, rubefacient, and astringent and haemostatic properties;
- for its skin-cooling properties and to harden the skin;
- as an ingredient of several topical preparations used for skin disorders.
- as a solvent and preservative in pharmaceutical preparations;
- as a neurolytic in the management of severe and chronic pain;
- given intravenously in the treatment of acute poisoning from ethylene glycol and methyl alcohol; and
- as a sclerosant in a variety of conditions including aldosterone-producing adenoma, parathyroid adenomas, thyroid nodules, advanced rectal cancer, hepatocellular carcinoma, dysphagia associated with oesophogastric cancer, hepatic or renal cysts, and gallbladder obstruction.

Ethanol for any use was included in the equivalent of the current Appendix B of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) in November 1974 due to its low toxicity. This entry was subsequently amended to ethyl alcohol and a cross reference between ethanol and ethyl alcohol was added to the index.

INITIAL SCHEDULING CONSIDERATION

The delegate noted the following:

Applicant's submission

- XXXXX requested a rescheduling of ethyl alcohol from Appendix B to Schedule 9 (Prohibited Substances) with the following proposed Schedule 9 entry:

ETHYL ALCOHOL for human consumption **except**:

(a) when used as a carrier and preservative in therapeutic tinctures or essences used in the preparation of food products.

· The application stated that a Schedule 9 listing was appropriate due to the potential for misuse and abuse of ethyl alcohol and associated adverse effects on health, lifestyle and the community. The applicant also addressed criteria under 52E (1) of the *Therapeutic Goods Act 1989* (the Act) as summarised below:

(a) Risks and benefits

- Ethyl alcohol could cause death if used incorrectly. Prolonged exposure could cause deterioration of general health (specifically liver health) and addiction could manifest in less than one month from the time of first exposure.
- Alcohol containing grapes may be a tonic for the cardiovascular system.

(b) Purpose of use

- Stated that alcohol should not to be used for human recreational consumption other than in tinctures and as a preservative for food essences. Some exemptions may need to exist for religious purposes.
- Claimed that use should be limited to controlled medical and scientific research.

(c) Toxicity and safety

- Claimed that ethyl alcohol had no currently established therapeutic value.
- Stated that ethyl alcohol caused skin and eye irritation and ingestion could cause nausea, vomiting and inebriation. Chronic use could cause liver damage. A Material Safety Data Sheet (MSDS) for ethyl alcohol 70 per cent was provided as supporting data.
- Noted that "absolute" alcohol (approximately 100 per cent ethanol) may contain traces of 2-propanol, methanol or benzene. Stated that the latter two were very toxic, while "denatured" alcohol had substances added to it which make it unpleasant and possibly hazardous to consume.
- Stated that the typical Occupational Exposure Limit (OEL) is 1000 mg / m^3. [According to the MSDS included in the application, the OEL for Australia is 1000 ppm (1900 mg / m^3)].

(e) Potential for abuse / misuse

- Stated that ethyl alcohol was abused and misused by the youth and maturity every weekend and sometimes on Wednesdays (*sic* weekdays) and that this issue was acknowledged by government advertising campaigns.

(f) Other matters

- Claimed that substances with less hazardous profiles (*cannabis sativa*, dimethyltryptamine [DMT]) were listed in Schedule 9. [The application did not

provide any details of data or studies to support the claim that these substances were less hazardous.]

Other relevant considerations

- Ethyl alcohol is currently listed in Appendix B for any use, due to its low toxicity. Appendix B lists substances which are considered not to require control by scheduling.
- Appendix A currently lists a general exemption for any substance when used as a food (which can include beverages), except for food additives before incorporation into food or when used as a means of administering a poison for therapeutic use. The SUSMP does not apply to a poison contained in any product listed in Appendix A.
- In November 1984, an exemption for food was included in the then Poisons Standard (now the SUSMP). This exemption was included in recognition of controls outside of scheduling which ensure appropriate access restrictions.
- Products containing ethyl alcohol for human consumption when presented as a food or beverage are subject to controls outside of scheduling. Restrictions and labelling requirements associated with these products are enforced via specific Commonwealth and State and Territory legislation and by regulatory bodies such as Food Standards Australia New Zealand.
- Specific restrictions on non-food preparations containing ethyl alcohol are enforced by the relevant regulatory bodies (i.e. the Therapeutic Goods Administration for human therapeutic products and the Australian Pesticides and Veterinary Medicines Authority for agricultural and veterinary products).

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* (the Act) included (a) risks and benefits of the substance, (b) purpose for which the substance is to be used, (c) toxicity, (d) presentation of the substance, (e) potential for abuse and (f) other matters considered necessary to protect public health.

DELEGATE'S INTERIM DECISION

The delegate agreed that the restrictions on substances for human consumption as a food or beverage are regulated by separate legislation and enforced by Commonwealth and State and Territory regulatory bodies and therefore do not require additional controls through scheduling.

Specifically, the delegate agreed that the matters under section 52E (1) of the Act relevant to the consideration of ethyl alcohol for human consumption were sufficiently controlled through separate legislation and regulatory bodies as to ensure the protection of public health.

The delegate therefore decided that the current scheduling of ethyl alcohol remained appropriate (i.e no change to the Poisons Standard).

SUBMISSIONS ON INTERIM DECISION

The applicant was notified of the delegate's interim decision and invited to comment. Comments on the interim decision were received as summarised below:

Applicant's response

- Asserted that the current mechanisms used to regulate the consumption of ethyl alcohol are insufficient and the TGA should impose further restrictions. Claimed that the responsibility for restricting ethyl alcohol for human consumption should rest on TGA and a lack of action by the TGA would imply negligence.
- Reiterated that the risks associated with ethyl alcohol were greater than those associated with cannabis and/or DMT. The applicant provided a one page graphical comparison of the addictive properties of six different substances (sourced from the Henningfield PhD, for the National Institute on Drug Abuse, reported in the 2 August 1994 edition of the New York Times). Specifically, the graph:
  - Compared the dependence, withdrawal, tolerance, reinforcement and intoxication characteristics of nicotine, heroin, cocaine, alcohol, caffeine and marijuana. [It was noted that the graph did not provide any information on the properties of DMT].
  - Presented these properties on a scale ranging from 0 (less serious) to 6 (more serious).
  - Rated the withdrawal and intoxication effects of alcohol as "more serious". [It was noted that the graph did not contain any information on the methodology or analysis used to reach its conclusions.]

Applicant's further comments

The applicant also provided additional comments which were received following the close of comment. [In accordance with the Therapeutic Goods Regulations 1990, consideration of any information that was not contained in a valid submission received before the closing date is at the delegate's discretion]. These comments have been summarised below:

- Requested a provision within their proposed Schedule 9 entry to exempt ethyl alcohol for medical and scientific use.
- Claimed that ethyl alcohol was not fit for human consumption except when used in a religious (entheogenic) context.
- Noted the increased restrictions on access to alcohol in indigenous and remote communities in Australia and stated that this was indicative of the understanding that ethyl-alcohol was a dangerous and poisonous substance requiring prohibition by scheduling. [The delegate noted that these restrictions were enforced through separate programs].

- Asserted that the prohibition of ethyl alcohol would result in severe withdrawal effects in the population and stated that this was an indication of the addictive qualities of the substance.
- Stated that ethyl alcohol and its associated culture was a major factor in the mistreatment of women.

The applicant provided an article from the Australian Domestic & Family Violence Clearinghouse (*Alcohol Issues in Domestic Violence*, 2005) which examined the relationship between alcohol misuse and domestic violence. In summary, the article concluded that although there are significant links between alcohol abuse and domestic violence, such violence occurs within a more complex context where alcohol is an indirect variable. The article noted that issues surrounding restrictions on alcohol were being addressed through different state and territory programs.

The applicant also provided a paper from the National Drug Research Institute, Curtin University of Technology (*Restrictions on the Sale and Supply of Alcohol: Evidence and Outcomes*, 2007) which examined the various approaches to restricting alcohol consumption in Australia, including controls on its economic and physical availability. In summary, the paper made several recommendations on reducing the levels of harms associated with alcohol including price increases, limitation of trading hours of licensed premises and outlet density, restricting access to specific alcoholic beverages and restrictions on legal drinking age. The paper also discussed the potential positive and negative outcomes of the implementation of "dry communities" through specific state and territory legislation. The paper provided detail of some of the Australian programs developed to address alcohol consumption and did not make any mention of additional restrictions to ethyl alcohol through scheduling.

DELEGATE'S RECONSIDERATION OF INTERIM DECISION

The delegate noted the applicant's submissions and further comments on the interim decision. The delegate agreed that although these further comments did not constitute a submission made by the closing date, in this instance they would be included as part of the delegate's scheduling consideration.

The delegate reiterated that the restrictions on substances for human consumption as a food or beverage are regulated by separate legislation and enforced by Commonwealth and State and Territory regulatory bodies and therefore do not require additional controls through scheduling.

The delegate again stated that matters under section 52E (1) of the Act relevant to the consideration of ethyl alcohol for human consumption as a food or beverage were sufficiently controlled through this separate legislation and regulatory bodies as to ensure the protection of public health.

The delegate agreed that additional controls through scheduling on ethyl alcohol for human consumption were not considered appropriate within the current regulatory system.

The delegate also confirmed that the current Appendix B listing for ethyl alcohol remained appropriate for uses other than as a food or beverage.

DELEGATE'S FINAL DECISION

The delegate confirmed that the current scheduling of ethyl alcohol remained appropriate.

3.2 OFATUMUMAB

SUBSTANCE DETAILS

Ofatumumab is a human monoclonal antibody which appears to inhibit early stage B lymphocyte activation.

Ofatumumab is being investigated for the treatment of patients with chronic lymphocytic leukemia who have received prior therapy. It is also under investigation for the treatment of non-Hodgkin's lymphoma, rheumatoid arthritis, and multiple sclerosis.

SCHEDULING CONSIDERATION

The delegate noted that:

- As ofatumumab is not specifically scheduled in Australia, this is a consideration of scheduling of a new chemical entity as outlined in section 4.2 of the Scheduling Policy Framework.
- Ofatumumab is captured by the Schedule 4 group entry for monoclonal antibodies.
- Other monoclonal antibodies are specifically scheduled (rituximab is listed in Schedule 4) and a specific entry for ofatumumab would ensure clarity in enforcement of restrictions.
- Ofatumumab is not currently scheduled in New Zealand.
- Ofatumumab has been approved as a prescription medicine by the US FDA and the European Medicines Agency.
- The seriousness of the indication mandates interaction with a medical professional.
- There is limited experience in the use of ofatumumab in the Australian environment.
- There is no available data suggesting abuse / misuse potential which would warrant a Schedule 8 entry.
- Ofatumumab is associated with significant toxicity issues, where 95 per cent of patients reported adverse effects, of which 64 per cent were treatment related. The

most common adverse reactions were neutropenia, pneumonia, pyrexia, cough, diarrhoea, anaemia, fatigue, dyspnoea, rash, nausea, bronchitis, and upper respiratory tract infections.

- Although there is some evidence of pregnancy effects associated with ofatumumab, given the proposed indication treatment would always occur under the direction of a medical specialist and an Appendix D entry would not be required.
- There was no evidence of sedation effects which would warrant an Appendix K entry.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of the substance, (b) purpose for which the substance is to be used and (c) toxicity.

DELEGATE'S FINAL DECISION

The delegate decided to list ofatumumab in Schedule 4, for inclusion into the *Standard for the Uniform Scheduling of Medicines and Poisons 1, Amendment 2*, effective 1 June 2011.

Schedule 4 – New Entry

OFATUMUMAB.

3.3 RILPIVIRINE

SUBSTANCE DETAILS

Rilpivirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) of the diarylpyrimidine class indicated for the treatment of HIV-1 infection.

SCHEDULING CONSIDERATION

The delegate noted that:

- As rilpivirine is not scheduled in Australia, this is a consideration of scheduling of a new chemical entity as outlined in section 4.2 of the Scheduling Policy Framework.
- Rilpivirine is not currently scheduled in overseas countries.
- The seriousness of the indication mandates interaction with a medical professional.
- There is limited experience in the use of rilpivirine in the Australian environment.
- There are no indications of abuse potential or dependency to warrant a Schedule 8 entry.
- Adverse effects associated with rilpivirine include nausea, dizziness, vertigo and rash.

- Rilpivirine is metabolised by CYP3A and is affected by substances that induce or inhibit CYP3A activity.
- There is currently no evidence of effects in pregnancy or sedation which would warrant an Appendix D or Appendix K entry.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of the substance, and (b) purpose for which the substance is to be used.

DELEGATE'S FINAL DECISION

The delegate decided to list rilpivirine in Schedule 4, for inclusion into the *Standard for the Uniform Scheduling of Medicines and Poisons 1, Amendment 2*, effective 1 June 2011.

Schedule 4 – New Entry

RILPIVIRINE.

3.4 TOLVAPTAN

SUBSTANCE DETAILS

Tolvaptan is a selective, competitive arginine vasopressin receptor 2 antagonist used to treat hyponatremia (low blood sodium levels) associated with congestive heart failure, cirrhosis, and the syndrome of inappropriate antidiuretic hormone (SIADH).

SCHEDULING CONSIDERATION

The delegate noted that:

- As tolvaptan is not specifically scheduled in Australia, this is a consideration of scheduling of a new chemical entity as outlined in section 4.2 of the Scheduling Policy Framework.
- Tolvaptan is not currently scheduled in New Zealand.
- Tolvaptan was approved by the U.S. Food and Drug Administration as a prescription medicine on May 19, 2009. In 2009 it was also approved for use as a prescription medicine in the European Union.
- The seriousness of the indication mandates interaction with a medical professional (dilutional hyponatraemia including patients with heart failure, cirrhosis and SIADH).
- There is limited experience in the use of tolvaptan in the Australian environment.

- Although tolvaptan is a member of a group of substances prohibited in certain sports (diuretics), there is no available data to suggest abuse / misuse potential which would warrant a Schedule 8 entry.
- According to the Martindale monograph, common adverse effects of tolvaptan are thirst, dry mouth, asthenia, constipation, hyperglycaemia, and pollakiuria or polyuria. Tolvaptan is contra-indicated in hypovolaemic hyponatraemia, in patients who require a rapid increase in serum-sodium concentrations, and in those who cannot sense or who respond inappropriately to thirst. Rapid correction of serum-sodium concentrations with tolvaptan could increase the risk of osmotic demyelination syndrome. Tolvaptan is ineffective in anuric patients. There is a risk of gastrointestinal bleeding associated with the use of tolvaptan in patients with cirrhosis.
- Tolvaptan is a Pregnancy Category C drug. Based on animal data, use of tolvaptan may cause foetal harm. Although tolvaptan is excreted into the milk of lactating rats it is not known whether tolvaptan is excreted into human milk. Normally, substances listed as Pregnancy Category X are included in Appendix D or L, however Category C or D drugs have also been included. Pregnancy effects associated with the use of tolvaptan may warrant Appendix D and L considerations.
- There was no available data of sedation to warrant a need for an Appendix K entry.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of the substance, and (b) purpose for which the substance is to be used.

DELEGATE'S FINAL DECISION

The delegate decided to list tolvaptan in Schedule 4, for inclusion into the *Standard for the Uniform Scheduling of Medicines and Poisons 1, Amendment 2*, effective 1 June 2011. The delegate also decided to refer proposed Appendix D and Appendix L entries for advice from the Advisory Committee on Medicines Scheduling.

Schedule 4 – New Entry

TOLVAPTAN.

3.5 VINFLUNINE

SUBSTANCE DETAILS

Vinflunine is a fluorinated vinca alkaloid derived from vinorelbine that has a similar antineoplastic action to vinblastine. It binds to tubulin inhibiting polymerisation into microtubules and arresting mitosis.

Vinflunine has been investigated for the treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen.

SCHEDULING CONSIDERATION

The delegate noted that:

- As vinflunine is not specifically scheduled in Australia, this is a consideration of scheduling of a new chemical entity as outlined in section 4.2 of the Scheduling Policy Framework.
- Vinflunine is not currently scheduled in New Zealand.
- Related vinca alkaloids (vinorelbine and vinblastine) are currently listed in Schedule 4.
- The seriousness of the indication mandates interaction with a medical professional and adjunctive therapy.
- There is limited experience in the use of vinflunine in the Australian environment.
- There is no evidence to suggest abuse / misuse potential which would warrant a Schedule 8 entry.
- Toxic effects included myelosuppression, gastrointestinal, neuro-, cardiac and reproductive toxicity, consistent with other vinca alkaloids.
- The most common adverse reactions associated with vinflunine were anaemia, leukopenia, neutropenia, constipation, thrombocytopenia, fatigue, nausea, anorexia, alopecia, vomiting, stomatitis. These reactions are class effects of the vinca alkaloids.
- There was no evidence of effects in pregnancy or sedation which would warrant an Appendix D or Appendix K entry.

The delegate agreed that the relevant matters under section 52E (1) of the *Therapeutic Goods Act 1989* included (a) risks and benefits of the substance, (b) purpose for which the substance is to be used and (c) toxicity.

DELEGATE'S FINAL DECISION

The delegate decided to list vinflunine in Schedule 4, for inclusion into the *Standard for the Uniform Scheduling of Medicines and Poisons 1, Amendment 1*, effective 1 June 2011.

Schedule 4 – New Entry

VINFLUNINE.