Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

National Drugs and Poisons Schedule Committee

Record of Reasons

45th Meeting
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GLOSSARY

ABBREVIATION	*NAME*
AAN	Australian Approved Name
AC	Active Constituent
ACSPA	Australian Consumer and Specialty Products Association
ADEC	Australian Drug Evaluation Committee
ADI	Acceptable Daily Intake
ADRAC	Adverse Drug Reactions Advisory Committee
AGRD	Australian Guidelines for the Registration of Drugs
AHMAC	Australian Health Ministers' Advisory Council
APMF	Australian Paint Manufacturers Federation
APVMA	Australian Pesticides and Veterinary Medicines Authority
AQIS	Australian Quarantine and Inspection Service
ARfD	Acute Reference Dose
ASMI	Australian Self-Medication Industry
ARTG	Australian Register of Therapeutic Goods
BAN	British Approved Name
CAS	Chemical Abstract Service
CHC	Complementary Healthcare Council of Australia
CMEC	Complementary Medicine Evaluation Committee
CMI	Consumer Medicine Information
COAG	Councils Of Australian Governments

CPAS	Chemical Product Assessment Section
CRC	Child-Resistant Closure
CRIH	Chemical Review and International Harmonisation
CTFAA	Cosmetic, Toiletry & Fragrance Association of Australia
DAP	Drafting Advisory Panel
DSEB	Drug Safety and Evaluation Branch
EAGAR	Expert Advisory Group on Antimicrobial Resistance
ECRP	Existing Chemicals Review Program
EPA	Environment Protection Authority
ERMA	Environmental Risk Management Authority
FAISD	First Aid Instructions and Safety Directions
FDA	Food and Drug Administration (US)
FOI	Freedom of Information
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
JETACAR	Joint Expert Advisory Committee on Antibiotic Resistance

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
MCC	Medicines Classification Committee
MEC	Medicines Evaluation Committee
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
NOEL	No Observable Effect Level
NOHSC	National Occupational Health & Safety Commission
NPMB	Non-Prescription Medicines Branch
NZ	New Zealand
OCM	Office of Complementary Medicines
OCS	Office of Chemical Safety
ODBT	Office of Devices, Blood and Tissues
OOS	Out of Session
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
RFI	Restricted Flow Insert
SUSDP	Standard for the Uniform Scheduling of Drugs 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
UK	United Kingdom
USA	United States of America
WHO	World Health Organization
WP	Working Party
WS	Warning statement

1.8 NDPSC WORKING PARTIES

1.8.1 TRANS-TASMAN HARMONISATION WORKING PARTY

1.8.1.1 HARMONISATION OF MEDICINES AND THE OZNZ SCHEDULING DATABASE

PURPOSE

The Committee considered recommendations from the 14th (0ctober 2005) Meeting of the Trans Tasman Harmonisation Working Party (TTHWP) in relation to the harmonisation of a number of substances.

BACKGROUND

An updated version of the OZNZ Scheduling database became available to the Secretariat for editing on 19 August 2005. A scheduling standard database is planned to become available electronically to the general public when the new joint agency commences operation in July 2006.

As at 16 September 2005, 736 database records (out of an original 3834 records) were reviewed and processed by the Secretariat and a number of substances were identified as being unharmonised. The focus of the work on the database to date had been on medicine records. It is intended that the remaining records (ag/vet and industrial/domestic chemicals) will be processed after medicines.

DISCUSSION

The Committee considered the harmonisation recommendations which were the outcomes of TTHWP Meeting 14, held on 10 October 2005. The Committee discussed the following items which led to foreshadowed decisions for consideration at the February 2006 NDPSC Meeting:

- Aconitum spp: The members noted that while aconitum spp was Schedule 4 (S4) in Australia, in New Zealand it was Pharmacy Only for oral and dermal use (≤0.2 mg packs and >0.02 mg alkaloids); General Sale for oral and dermal use (≤0.02 mg packs) and Prescription for all other uses and doses. The Committee further noted no products were registered on the SMARTI database and that the Secretariat would check for products on the Australian Register for Therapeutic Goods (ARTG) which may be affected.
- Amorolfine: The Committee noted that while amorolfine was S2 for topical use (≤0.25%); S3 for topical use (>0.25%); and S4 for other uses and doses in Australia, in New Zealand it was General Sale for external use in medicines for tinea pedis; Pharmacy Only (≤0.25% except in medicines for tinea pedis); Restricted (>0.25%); and Prescription except for external use. The Committee further noted that no products for the treatment of tinea pedis were located in the SMARTI and ARTG

databases and that harmonisation was supported by the basis of the history of safe use in New Zealand.

- Antimony organic compounds: The Committee noted that while antimony organic compounds were S4 for therapeutic use except when in Appendix G (1 mg/kg (L)) in Australia, in New Zealand the parent compound, antimony, was Prescription (except when ≤1 mg/kg (L)). The members agreed that the S4 entry would be amended to read 'Antimony for therapeutic use except when separately specified in these Schedules' and further agreed to consider the requirement for a policy on the incorporation of Appendix G exemptions into Schedules at the February 2006 NDPSC Meeting.

- Atropa belladonna: The members noted that the only disparity in the scheduling of *Atropa belladonna* between Australia (S2 and S4) and New Zealand (Pharmacy Only and Prescription) was the exemption in the New Zealand classification for medicines containing ≤300 µg total solanaceous alkaloids/kg (L). Additionally, it was noted that the cut-off for *Hyoscyamus niger* was also unharmonised with New Zealand and agreed to consider adopting the New Zealand cut-offs for exemption for *Atropa belladonna* and *Hyoscyamus niger* at the February 2006 meeting.

- Beclomethasone: The Committee noted that beclomethasone was currently unharmonised due to the inclusion of a pack size limit of '200 actuations or less' in the S2 entry, and agreed to consider removing the statement 'when packed in a primary pack containing 200 actuations or less' from the S2 entry.

- Cephacetrile, cephaloridine, cephamandole and cephapirin: The Committee noted the entries for the above substances did not include the recommended INN, and therefore, agreed to amend the entries to 'cefacetrile', 'cefaloridine', 'cefamandole' and 'cefapirin', respectively, to harmonise with New Zealand.

- Mercury: The members noted that in Australia while mercury organic compounds were S2 for topical human therapeutic use (≤ 0.5 mercury); and mercury was S4 for therapeutic or cosmetic use except when included in other Schedules or in sealed device which prevented access to the mercury, in New Zealand mercury was Pharmacy Only for external use (≤0.5%) and Prescription for all other uses and doses (except ≤1 mg/kg (L)). The Committee agreed to consider removing the reference to 'organic compounds' in the S2 entry at the February 2006 NDPSC meeting to harmonise with New Zealand.

- Dibrompropamidine and propamidine: The Committee noted that propamidine or dibrompropamidine (a structurally-similar analogue) eye products (Brolene) were on the market in either Australia or New Zealand but that these substances were scheduled differently in both countries. Specifically, dibrompropamidine was unscheduled in Australia while propamidine for human therapeutic use was included in SUSDP Appendix B. In contrast, preparations for ophthalmic use were classified

as Pharmacy Only medicines in New Zealand while all other preparations were classified as Prescription medicines. It was unclear to the Committee as to why propamidine was listed for 'industrial use only' in SUSDP Appendix B. As a way forward, a member proposed that Australia consider harmonising with New Zealand and the Committee agreed to consider this item at the February 2006 meeting.

The Committee agreed to consider the items below at the February 2006 NDPSC Meeting following further investigation of certain issues:

- Boric acid: The Committee noted that while in Australia boric acid was S4 in glycerines and honeys and S5 except when containing ≤1% boron and in hand cleaners, in New Zealand it was General Sale (≤2%) and Pharmacy Only (>2%). The members noted that the New Zealand scheduling for boron evolved from the need to provide guidance to industry in terms of acceptable product strengths and indications when the issue of toxicity emerged from use of high strength boron products for the treatment of nappy rash in babies under occlusive conditions. The members further noted that there were no adverse reports associated with boron in Australia since the year 2000. However, it was also observed that harmonising with New Zealand would involve rescheduling the primary entry for boric acid from S4 to S3 and agreed that it would be appropriate to review the scheduling history of the substance and assess whether the historical safety issues considered significant by the NDPSC would still be relevant. The members requested that the Secretariat assess the potential regulatory impact of Australia harmonising the scheduling of boron with New Zealand and agreed that the issue would be gazetted for the February 2006 NDPSC Meeting when it could be further deliberated.
- Dimenhydrinate: The members noted that while dimenhydrinate was S2 (in packs ≤ 10 doses) for motion sickness, except for the treatment of children under 2 years of age; S3 in oral preparations except when in S2; and S4 for all other uses and doses, in New Zealand it was Pharmacy Only for oral use (packs ≤ 10 tablets/capsules) for motion sickness except when sold at transport terminals or aboard ships and planes; Restricted for oral use except when included in other schedules; and Prescription for all other uses and doses. The members also requested the Secretariat to investigate if the *Required Advisory Statement for Medicines Label* (RASML) included a warning statement against use in children under 2 years of age; if included, the Committee agreed that Australia would harmonise with New Zealand but if not included, members agreed to recommend to New Zealand to harmonise with Australia.
- Aspirin: The Committee noted that in Australia aspirin was S2 for certain preparations with an exemption for certain pack size and dose and mandatory label requirements; and S4 for preparations for injection or when combined with caffeine, paracetamol or salicylamides or their derivatives. In New Zealand, members noted that it was Restricted for slow release and enteric coated forms containing >300 mg/dose; and General Sale for all other formulations and doses not included in the Restricted medicine entry. A member indicated that New Zealand was prepared to consider harmonisation with the Australian OTC scheduling and that most products

on the New Zealand market were generally of similar pack size that it was unlikely for such products to be affected by harmonisation with Australia on OTC scheduling. It was pointed out that the main point of divergence in the scheduling of aspirin products in the two countries was the classification of aspirin combination products. The Committee noted that it was proposed at the TTHWP Meeting 14 that Australia consider rescheduling aspirin combination products currently in S4 to OTC availability to harmonise on the least restrictive scheduling which would also minimise the potential impact on New Zealand products. Members were informed that the TTHWP had already agreed to seek expert advice from XXXXXXXX with regard to the safety of combination aspirin products if rescheduled to over-the-counter (OTC) status particularly in relation to the historical issue associated with aspirin and renal disease. The Committee agreed to consider this matter at the February 2006 NDPSC Meeting subject to the availability of the expert advice.

- Camphorated oil: The Committee noted that in Australia camphorated oil for therapeutic use was S4 except in admixtures or exempt in essential oils packed and labelled as required. In New Zealand, it was Prescription Medicine for all preparations. The Committee was informed that the rationale behind the Australian exemption for admixtures containing camphorated oil could not be drawn from the old NDPSC minutes reviewed by the Secretariat. To progress the matter, members agreed that the potential regulatory impact of the proposal to harmonise with New Zealand should be assessed prior to consideration of this item at the February 2006 NDPSC Meeting and that a definition for "admixture" should be included in the agenda papers.

The Committee agreed to foreshadow decisions in relation to the substances listed below for consideration at the February 2006 meeting which were noted to achieve only partial harmonisation without further action from New Zealand. On this basis, the Committee also agreed to make recommendations to New Zealand which were aimed at achieving full harmonisation of scheduling.

- Budesonide: The Committee noted that budesonide was currently unharmonised due to the inclusion of a pack size limit of '200 actuations or less' in the S2 entry and because New Zealand did not include the condition 'for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over' in its Pharmacy Only entry. The Committee agreed to consider removing the statement 'when packed in a primary pack containing 200 actuations or less' in the S2 entry and further agreed to recommend that New Zealand include the above condition in its Pharmacy Only entry.
- Pirfenoxone sodium (catalin): The Committee noted that pirenoxine was currently unharmonised due a nomenclature difference between Australia (pirfenoxone sodium) and New Zealand (pirfenoxone) and a duplication of the substance entry in New Zealand. The members agreed to consider amending the S4 entry to pirenoxine (the rINN) and to recommend to New Zealand to delete the pirfenoxone and if appropriate catalin Part I entries and replace with a new entry for pirenoxine.

- Cephazolin: The Committee noted that cephazolin was currently unharmonised due to a duplication of the substance entry in New Zealand (cephazolin and cefazolin). The members agreed that Australia would amend the S4 entry to cefazolin (rINN) and recommend to New Zealand that it delete the duplicate entry (cephazolin).

- Cathine: The Committee noted that cathine, a psychoactive constituent of the Khat shrub, was S4 in Australia but cathine was not classified a medicine in New Zealand. Members were also advised that no product containing cathine was found on either the ARTG or SMARTI. The Committee noted that the TTHWP recommended that cathine be rescheduled to S9 based on abuse potential and on the grounds that cathine was not a recognised therapeutic ingredient. Members agreed to consider the proposal to reschedule cathine to S9 at the February 2006 NDPSC Meeting while noting that the TTHWP also made a recommendation to the MCC to consider recommending the inclusion of cathine in the Misuse of Drugs Act (MODA).

The Committee noted that acrivastine, amidopyrine and atosiban were all unscheduled in Australia but were classified as Prescription medicines in New Zealand. In order to harmonise with New Zealand the Committee agreed to include these substances in S4 of the SUSDP.

The Committee also noted that the general consideration of fractionated blood products was under item 13.6. Members agreed to include antithrombin and blood clotting factors as part of this consideration. It was noted that blood corpuscles and whole blood had been exempted in Australia through the establishment of an Appendix A entry for whole blood and blood components.

Members noted that cyclizine was to be considered separately under item 16.3 of the agenda and that the outcome of this consideration was expected to also address the harmonisation issue.

The New Zealand Member advised the Committee on the following issues:

- Amphotericin: The Committee noted that while amphotericin was S4 in Australia, in New Zealand it was Restricted for the treatment of oral candidiasis; and Prescription for all other uses. The member advised that the MCC would be reconsidering the scheduling of amphotericin at the November 2005 meeting. It was stated that XXXXXXXX in New Zealand objected to the MCC's recommendation to reclassify amphotericin in lozenges for the treatment of oral candidiasis from restricted medicine to prescription medicine on the basis that due process was not observed in the consultation process. The member undertook to advise the Committee of the outcome of the MCC consideration.

- Thenyldiamine: The Committee noted that while thenyldiamine was S4 in Australia, in New Zealand it was Pharmacy Only for nasal use or oral use (when in combination for coughs, colds or influenza or in day/night packs with thenyldiamine in the

bedtime dose and for use by adults or children of ≥2 years) and Restricted for oral use in solid form or liquid form (≤10 mg/ 5 mL). The members noted that the S2 and S3 entries were deleted at the June 2005 NDPSC Meeting as no products were marketed in either Australia or New Zealand but that whilst the MCC agreed to include thenyldiamine in Part I, the entries in Parts II and III were retained. A member noted that the retention in New Zealand of the entries in Parts II and III may have been an oversight and agreed to investigate the matter further and provide feedback at the next meeting.

The Committee noted that the following issues could not be resolved at the present time and that these matters should be reviewed again at a future meeting:

- It was indicated that New Zealand's position on the scheduling of vitamin A and beta carotene remained unchanged and that New Zealand would not support harmonisation with the Australian scheduling for these substances due to differences in the dietary intakes between the two countries.

- It was agreed that a broader policy approach was required to establish a process for dealing with medicines included in S5–S7 of the SUSDP. It was noted that under the new Joint Agency arrangement, only medicines listed in the medicine schedules, i.e. S2–S4, would be regulated. Ingredients in medicines currently listed in S5 and S6 of the SUSDP included anise oil, antimony, *Azadirachta indica* (neem), benzalkonium chloride, bioallethrin and camphor.

The Committee agreed to recommend that New Zealand harmonise with the Australian classification and nomenclature of the following medicines:

Acetylcysteine, *Acokanthera schimperi*, *Acokanthera ouabaio*, anabolic steroidal agents and androgenic steroidal agents, anagrelide, *Aspidosperma quebracho*, aspirin, benzphetamine, benzocaine, bismuth, bromides, *Brugmansia spp*, budesonide, *Calotropis procera*, *Calotropis gigante*a, carbaryl, cefazolin (delete cephazolin), pirenoxine (delete pirfenoxone) and thenyldiamine.

OUTCOME

The Committee noted and endorsed the TTHWP Meeting 14 recommendations and proposed actions for unharmonised substances and agreed to foreshadow consideration of the relevant substances and issues, including a number of foreshadowed decisions, at the February 2006 meeting.

FORESHADOWED DECISION (for consideration at the February 2006 Meeting)

Schedule 2 – New entries

ACONITUM spp:

(a) in preparations for oral use in packs each containing 0.2 milligrams or less of total alkaloids but more than 0.02 milligrams of total alkaloids; or

(b) in preparations for dermal use containing 0.02 per cent or less of total alkaloids in packs each containing 0.2 milligrams or less of total alkaloids but more than 0.02 milligrams of total alkaloids.

DIBROMPROPAMIDINE for ophthalmic use.

PROPAMIDINE for ophthalmic use.

Schedule 2 - Amendments

AMOROLFINE – amend entry to read:

AMOROLFINE for topical use in preparations containing 0.25 per cent or less of amorolfine **except** in preparations for the treatment of tinea pedis.

BECLOMETHASONE – amend entry to read:

BECLOMETHASONE in aqueous nasal sprays delivering 50 micrograms or less of beclomethasone per actuation when the maximum recommended daily dose is no greater than 400 micrograms for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over.

BUDESONIDE – amend entry to read:

BUDESONIDE in aqueous nasal sprays delivering 50 micrograms or less of budesonide per actuation when the maximum recommended daily dose is no greater than 400 micrograms for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over.

MERCURY – amend entry to read:

MERCURY for topical human therapeutic use in preparations containing 0.5 per cent or less of mercury.

Schedule 3 - Amendment

AMOROLFINE – amend entry to read:

AMOROLFINE for topical use **except**:

(a) when included in Schedule 2; or

(b) in preparations for topical use for the treatment of tinea pedis.

Schedule 4 - New entries

ACRIVASTINE.

AMIDOPYRINE.

ATOSIBAN.

DIBROMPROPAMIDINE **except** when included in Schedule 2.

PROPAMIDINE **except** when included in Schedule 2.

PIRENOXINE (catalin).

Schedule 4 - Amendments

ACONITUM - amend entry to read:

ACONITUM spp **except**:

(a) when included in Schedule 2;

(b) in preparations for oral use in packs containing 0.02 milligrams or less of total alkaloids; or

(c) in preparations for dermal use containing 0.02 per cent or less of total alkaloids in packs each containing 0.02 milligrams or less of total alkaloids.

AMOROLFINE for topical use **except**:

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

(b) in preparations for topical use for the treatment of tinea pedis.

ANTIMONY - amend entry to read:

ANTIMONY for therapeutic use **except** when separately specified in these Schedules.

CAMPHORATED OIL – amend entry to read:

CAMPHORATED OIL for therapeutic use.

CATHINE – delete entry.

CEPHACETRILE – amend entry to read:

CEFACETRILE.

CEPHALORIDINE – amend entry to read:

CEFALORIDINE.

CEPHAMANDOLE – amend entry to read:

CEFAMANDOLE.

CEPHAPIRIN – amend entry to read:

CEFAPIRIN.

CEPHAZOLIN – amend entry to read:

CEFAZOLIN.

PIRFENOXONE – delete entry.

Schedule 9 – New entry

CATHINE.

Appendix G – New entries

ATROPA BELLADONNA (belladonna)	300 micrograms
HYOSCYAMUS NIGER	300 micrograms

2. PROPOSED CHANGES/ADDITIONS TO PARTS 1 TO 3 AND PART 5 OF THE STANDARD FOR THE UNIFORM SCHEDULING OF DRUGS AND POISONS.

2.1 SUSDP, PART 1

2.1.1 INTERPRETATION – "DERMAL USE"

PURPOSE

The Committee reviewed the definition of "Dermal Use" in relation to application to nail.

BACKGROUND

At the August 1999 NDPSC Meeting the Committee agreed to include the current definition of "Dermal Use" in the SUSDP following a recommendation by the trans-Tasman Harmonisation Working Party. The intent of adding the "Dermal Use" definition was to differentiate from trans-dermal use. It would appear that the issue of whether the definition included nails was not considered.

The current SUSDP definitions are:

- **"Dermal use"** means application to the skin primarily for localised effect.
- **"External"** in relation to the use of a poison means application in the ears, eyes or nose or to a body surface other than in the mouth, rectum, vagina, urethra or other body orifice.
- **"Topical use"** means application of a poison for the purpose of producing a localised effect on the surface of the organ or within the tissue to which it is applied.

At the February 2005 NDPSC Meeting the Committee considered the interpretation of "Dermal Use", "Topical Use" and "External" as applied to substances for use on nails. This issue was raised when a company sought clarification as to whether a proposed product containing up to XXXXXXXX when applied to the nails for the treatment of fungal infections would fall under the definition for "Dermal Use". Members agreed that there was a need to provide clarity to stakeholders in terms of which SUSDP definition covers substances for application to the nail. The Members also agreed that additional information and consultation with stakeholders was required to ensure that there would be no unintended regulatory impact on products.

The June 2005 NDPSC Meeting considered submissions from XXXXXXXX regarding its application to the Over-the-Counter (OTC) Medicines Section, TGA, regarding XXXXXXXX, an antifungal treatment tincture for fungal nail infections containing the active miconazole. The Committee noted the OTC Section's response that, as the current definition in the SUSDP of "Dermal Use" refers to skin with no reference to nails, products such as XXXXXXXX are captured by Schedule 4, an outcome which appeared unintended.

The Committee agreed to gazette the Committee's intent to review the definition of "Dermal Use" in relation to application to nail as this would provide stakeholders with an opportunity to comment on any possible ramifications. The Committee also agreed for clarity to foreshadow an amendment to the Schedule 2 miconazole entry to allow application to nail in the absence of any public health concerns (further discussed in item 13.2).

DISCUSSION

The Committee noted that the following was considered at the June 2005 NDPSC Meeting:

- The OTC Section had identified a range of Schedule 2 antifungals whose entries included the word dermal which could potentially be associated with nail products open to inadvertent Schedule 4 capture. A search of the Australian Register of Therapeutic Goods (ARTG) for products containing the substances identified by the OTC Section was undertaken.
- The Committee agreed that while the above search, as well as various other searches of the ARTG, did not exhaustively identified all products for use on nails these investigations had indicated that many Schedule 2 substances for nails currently have a dermal definition and a decision that nails are not dermal could revert many of these products to Schedule 4.

Members also noted that the following arguments against considering nail to be "Dermal Use" were considered at the June 2005 NDPSC Meeting:

- Pharmacokinetically there is a difference between skin and nail and that for infections of the nail, often deep within the tissue, there was a need for different treatment than would normally be used for skin infections.
- A member noted that there would be a risk of inadvertently allowing a number of potential nail products to be in Schedule 2 when the Committee had not considered the use pattern "application to nail" when creating the Schedule 2 entry for these substances.
- Some products on the market, such as XXXXXXXX (a ketoconazole cream), specifically indicated not for infections involving nail – implying that some manufacturers viewed nail and skin as distinct.
- A member noted that if nails were included in the "Dermal Use" definition then this in effect robs the Committee of a definition for skin only.

In addition to the above arguments, the following points were made at the June 2005 NDPSC Meeting for considering nail to be topical:

- Nails implicitly come under the current external and topical use definitions.
- Topical would be a better fit given the use pattern was usually penetration within the nail i.e. within the tissue to which it is applied.

Members further noted that the alternative had been discussed at the June 2005 NDPSC Meeting – broadening the definition of "Dermal Use" to include nail – and the following points considered:

- Changing a Schedule entry from dermal to topical or external may imply that the poison can be applied to the ears, eyes or nose etc. which may not be appropriate and

would also require amendments to many Schedule 2 entries. The Members were advised that adding a specific reference to nail in an individual entry (such as was done to resolve the miconazole issue – see item 13.2) could also require amendments to many Schedule 2 entries.

- The Committee noted that many of the current dermal entries are harmonised with New Zealand and that there appears to be an implication that nail products in New Zealand are currently considered to be dermal products by industry.
- The Committee noted that the OTC Section's interpretation that products such as XXXXXXXX are captured by Schedule 4 does not appear to have been widely disseminated to manufacturers who still largely appear to consider their nail products covered by the term dermal.
- A member noted that concerns over high strength dermal products would be addressed by the registration processes. In response to some of the Committee's concerns, it was also noted that the registration process assesses efficacy.
- A member asserted that if dermal does not include nail there would be further confusion caused by the issue of defining what "around the nail" would mean.

A Member advocated that substitution of external for dermal may solve the issue on the grounds that inappropriate use should be a registration issue. Another Member noted, however, that registered products are not the only products that the SUSDP covers. The Member advised that a pharmacist could compound a scheduled substance and would therefore only be guided by the SUSDP entry. The Committee generally agreed that expanding the entries from dermal to external, to cover application to nails, could send an inappropriate message about the appropriate use for these substances.

The Committee considered a submission from XXXXXXXX. XXXXXXXX did not support changing the definition of "Dermal Use" to include the nails, asserting that this was contrary to the widely known and accepted definition of "dermal" and may cause confusion if a product was intended for use only on the skin. XXXXXXXX noted that this may require some entries in Schedule 2 for substances for nails that currently have a dermal definition to be amended. The Members also noted:

- XXXXXXXX conceded that amending the SUSDP definition of "Dermal Use" to include the nails would not affect any current SUSDP entries. However, XXXXXXXX asserted that if the definition were amended in this way, products intended for use only on the nail (such as high strength antifungal preparations) would still require additional wording such as "for use in dermal preparations for application only to the nails".
- XXXXXXXX proposed that, for products intended for use only on the nail, the term "ungual use" or "for application to the nails" was acceptable. For other preparations that can be applied equally to the skin and nails, the current definitions are adequate and "External" or "Topical Use" should be used as appropriate.

The Committee also considered a submission from XXXXXXXX. XXXXXXXX asserted that application to the nail would better fit within the definition of 'Topical', but agreed with the Committee that this may be problematic in that it could imply broader use than intended if the term 'topical' was used on its own. XXXXXXXX also noted:

- Amending the "Dermal Use" definition to include the indication for use on the nails would not solve the problem as not all dermal products are intended for use in this manner.
- Although application to nail does not fit within the "Dermal Use" definition, there are several nail products that are applied in this way, or around the nail. Defining 'around the nail' may itself be confusing as this could involve application to skin and the base of the nail.
- The efficacy of the product, including the method of application, is fully considered during the registration process. The issue for scheduling was to identify that a substance can be used on the nails.
- Regardless of whether the definitions are amended, XXXXXXXX asserted that it will be necessary to clearly specify in the schedule entry that the substance was also indicated for use on nails. XXXXXXXX's preference was therefore to leave the definitions as they currently are, and to include the additional indication(s) in the schedule entry e.g. SUBSTANCE in dermal preparations and in preparations for application to the nail.

The Committee also noted a submission from XXXXXXXX which indicated that it did not have any matters to raise at this time in regards to a proposal to include nails in the definition of dermal. A submission was also received from XXXXXXXX indicating an interest in products intended for "Dermal Use".

OUTCOME

The Committee confirmed that while nails are covered by the current definitions of "External" and "Topical Use":

- nails are not covered by the definition of "Dermal Use".
- that in order to avoid confusion it was preferable for medicines applied to the nail to specify in the Schedule entry a statement to the effect of "for application to nail" on a case by case basis.

2.1.2 DEFINITION OF COMPOUNDED

PURPOSE

The Committee considered the definition of compounded and the proposal that compounded does not include bilayer/multilayer preparations.

BACKGROUND

At the February 1987 NDPSC Meeting the Committee first included a compounded definition in an SUSDP entry, in this case the Schedule 2 dextromethorphan entry, requiring "when compounded with one or more other therapeutically active substances in such a way that dextromethorphan contained therein cannot be readily extracted".

At the May 1987 Meeting, Members agreed that a general definition for compounded was necessary as there was a problem with compounded preparations on the market being illegally separated. This intention was further considered and confirmed at the July 1987 NDPSC Meeting. Introduction of a definition, however, was deferred following objections from industry on the grounds that the proposed wording "readily separated or extracted" was meaningless and impractical.

The February 1991 NDPSC Meeting, following legal advice, foreshadowed a new definition of compounded "*combined with one or more other therapeutically active substances in such a way that it cannot be separated from them by simple dissolution or by other physical means*". The August 1991 NDPSC Meeting further considered this definition, noting comments which asserted that the word "physical" was still open to interpretation. It was particularly noted that if by "physical" it was meant that a chemical reaction does not take place, then it may be possible that other separation techniques such as chromatography could be regarded as a means of physical separation. It was noted that most compounded drugs can be separated by chromatographic methods. The Committee agreed, as chromatographic methods were not simple physical means available to the ordinary householder, to vary the definition by including the word "simple" in front of "physical means" to give the current SUSDP definition:

"Compounded" in relation to a substance means combined with one or more other therapeutically active substances in such a way that it cannot be separated from them by dissolution or other simple physical means.

The October 2002 NDPSC Meeting, in considering the problem of pseudoephedrine diversion, agreed that combination products, including bilayer preparations, where pseudoephedrine could be readily separated or extracted from other components in the formulation by dissolution or other simple physical means were not included in the definition for 'compounded' in the SUSDP.

At the February 2005 NDPSC Meeting the Committee noted a public submission from XXXXXXXX, a moderator of an online information/support website for abusers of codeine. XXXXXXXX advised that, based on the addicts (over 500) that had visited the website, the most abused over-the-counter (OTC) codeine preparation in Australia was XXXXXXXX as separating the codeine from ibuprofen involved simple physical separation of the layers. XXXXXXXX requested the Committee consider rescheduling XXXXXXXX to Schedule 3 to reduce the rate of addiction. The Committee agreed that this may be a formulation issue for consideration at the June 2005 NDPSC Meeting.

At the June 2005 NDPSC Meeting the Committee discussed the appropriateness of the scheduling of bilayer/multilayer formulations. Following consideration of the current definition of compounded the Committee agreed that, while the bilayer formulation of XXXXXXXX remained in the ARTG, the correct scheduling for this product was Schedule 8. In addition, the Committee agreed to foreshadow consideration of a possible amendment to the SUSDP interpretation of 'compounded' at the October 2005 NDPSC Meeting to add a statement to the effect that 'compounded' does not include bilayer/multilayer preparations.

DISCUSSION

The Committee noted the definition of 'multilayer tablet' in the TGA's Australian approved terminology for medicines:

- "a compressed tablet comprising two or more layers of different composition and that the layers may be concentric (compressed coated) or parallel."

[Section deleted]

In response to the information provided by XXXXXXXX XXXXXXXX asserted that this does not appear to be evidence of a significant abuse issue. It was noted that the anonymous nature of website services limited the opportunity for thorough analysis of the extent of the issue. With regard to XXXXXXXX contacting XXXXXXXX several times without response, XXXXXXXX advised that this was an issue of concern. The only contact that XXXXXXXX had knowledge of was an email post the June 2005 NDPSC Meeting. XXXXXXXX indicated that it would be following up on this issue with XXXXXXXX.

[Section deleted]

The Committee noted a summary of all available bi- and multilayered products listed on the ARTG in which there appeared to be no products that would be affected [sentence deleted].

The Committee noted a submission from XXXXXXXX requesting that the Committee consider the role of film coats in the prevention of simple physical separation.

The Committee also noted a submission from XXXXXXXX supporting the existing definition of compounded. XXXXXXXX asserted that it should not matter how substances are combined and that the important factor is that the combination should not be able to be easily separated. XXXXXXXX argued that the current definition was clear and should not be amended. In addition, XXXXXXXX noted that making the definition too specific by including bilayer or multilayer could prove problematic for new technologies that are being developed. XXXXXXXX also raised a concern about the June Record of Reasons dealt with [sentence deleted].

The Committee further noted that a submission was received from XXXXXXXX registering an interest.

The Committee agreed that the definition of compounded should not explicitly exclude multilayer formulations as new technologies may allow multilayer formulations which cannot be separated by dissolution or other simple physical means. The issue really appears to be the result of an oversight by the regulator in not realising that where compounded appears in an SUSDP entry the test to be applied, as clearly stated in the definition, is whether the substance can be separated by dissolution or other simple physical means.

OUTCOME

The Committee confirmed the current "compounded" definition and agreed that this definition allows for future multilayer formulations which are not separable by simple physical means. The Committee further highlighted that current bilayer and multilayer formulations can not be considered to be "compounded" if the layers are separable by simple physical means.

AGRICULTURAL/VETERINARY, INDUSTRIAL AND DOMESTIC CHEMICALS

3. MATTERS ARISING FROM THE MINUTES OF THE PREVIOUS MEETING (CONSIDERATION OF POST-MEETING SUBMISSIONS UNDER 42ZCZ)

3.1 STORAGE STATEMENT FOR SCHEDULE 5 AND SCHEDULE 6 PRODUCTS

PURPOSE

The Committee considered post-meeting comment regarding the June 2005 NDPSC decision to include a new paragraph in Part 3 of the SUSDP setting out the requirements for retail storage of Schedule 5 and 6 poisons.

BACKGROUND

At the June 2004 NDPSC Meeting the Committee agreed to replace the definitions for Child-resistant Closure (CRC) and Child-resistant Packaging (CRP) with the current definitions and included the current definition for "Non-access Packaging" in the SUSDP. Post-meeting comment from XXXXXXXX arising from the February 2004 NDPSC Meeting addressed issues including that there were differences between the Jurisdictions in the requirements for retail storage of Schedule 5 (and Schedule 6) poisons. The Committee agreed to refer this matter to the State, Territories and New Zealand Health Authorities (STANZHA) with a view to the development of a uniform approach to the retail storage of these substances.

At the June 2005 NDPSC Meeting the Committee considered a request for advice on the issue of child resistance for devices and products such as cockroach baits which comply with the definition of "Non-access Packaging" but do not comply with AS1928-2001. The Committee also considered a recommendation from STANZHA to include a paragraph in Part 3 of the SUSDP under the "storage" section relating to the retail storage of Schedule 5 and 6 poisons to enhance national consistency. STANZHA advised that should this proposition be accepted States and Territories would have the option to adopt the paragraph into their relevant poisons legislation, thus enhancing national consistency. STANZHA asserted that this would give a clear message to retailers as to the minimum standard that was acceptable for storage of these substances.

The Committee agreed to the STANZHA recommendation and further agreed that an additional exception be added to STANZHA's recommendation to reflect the existence of the definition for "Non-access Packaging" in the SUSDP. The new paragraph recommended for inclusion in Part 3 of the SUSDP under the "storage" section was:

44a. "A person who sells or supplies a Schedule 5 or Schedule 6 poison in a retail shop must keep those poisons in such a way that, when displayed for sale, they are positioned at least 1.2 metres above the floor **except** when-

- Packed in a container fitted with a child-resistant closure.
- In a container with a capacity of 5 litres/5 kilograms or more.
- Packed in child-resistant packaging.
- Packed in non-access packaging.
- A hair dye packed with a volume of 50 millilitres or less.

They should be displayed in such a way to prevent contamination of human or animal food, or beverages should a leak or breakage occur."

DISCUSSION

The Committee considered post-meeting comments from XXXXXXXX and XXXXXXXX.

XXXXXXXX supported the substance of the entry for retail storage for Schedule 5 and Schedule 6 poisons but made the following observations:

- The SUSDP and its individual provisions are not regulations and therefore should not be so described. The Secretariat advised that this appeared to refer to "..an additional exception "Packed in non-access packaging" to XXXXXXXX's recommendation would resolve the issue where some Schedule 5 and 6 storage regulations do not appear to account for packaging which.." from the June 2005 Record of Reasons. The context of this statement, however, was not that the SUSDP or its provisions were regulations but rather a discussion about State and Territory regulations controlling the storage of Schedule 5 and 6 poisons.
- The sentence "They should be displayed in such a way to prevent contamination of human or animal food, or beverages should a leak or breakage occur" should not form any part of a text that is intended to be adopted by reference into a law under which a person may be prosecuted for failure to comply.

XXXXXXXX submission further noted that in Victoria, section 27A of the *Drugs, Poisons and Controlled Substances Act 1981* creates an offence if a person sells or supplies a poison or controlled substance which the person has stored or packaged otherwise than in accordance with the Poisons Code.

XXXXXXXX therefore recommended that the last sentence of the storage entry be redrafted to impose an obligation on a person to store the poisons in a manner that prevents contamination of foods and beverages. XXXXXXXX asserted that normative

statements have no place in a document that is intended to be used for legal purposes. XXXXXXXX considered that the presence of the sentence in its present form could compromise the validity of the whole provision.

The Members noted the post-meeting submission from XXXXXXXX asserted the following:

- Industry could not have foreshadowed the detail of the decision and therefore could not have made an appropriate pre-meeting submission.
- XXXXXXXX supported the move towards national uniformity but questioned why such a regulatory response in some jurisdictions was not necessary in the past. XXXXXXXX questioned if there had been an articulation and quantification of 'the problem' at the retail level to warrant the decision.
- There had not been the opportunity for the ramifications of the change to be fully evaluated by industry for all Schedule 5 and 6 poisons in retail across the possible range of retail outlets; nor to identify specific products that may be forced into packaging changes.
- The proposal may have some significant cost implications to industry associated with "buying" shelving/display space in the region of 1.2 m or greater.

XXXXXXXX has recommended that the decision be deferred until there has been opportunity for XXXXXXXX to provide additional information through the XXXXXXXX Representative at the October 2005 NDPSC Meeting. The Committee was subsequently advised at the Meeting that, due to a delay in responses from stakeholders, this information would not be available until the February 2006 NDPSC Meeting.

Further advice has been received from XXXXXXXX in response to XXXXXXXX post-meeting comment. XXXXXXXX advised that:

- while Parts 1 to 3 and the Appendices are recommendations to the States and Territories and not regulations, jurisdictions do adopt some of this content and therefore the content needs to be written as regulations and in a "tight" legal language; and
- the final sentence in the proposed Part 3 entry for retail storage of Schedule 5 and 6 poisons be varied to replace the "should" with "must" to read "They must be displayed in such a way to prevent contamination of human or animal food, or beverages should a leak or breakage occur".

XXXXXXXX, in response to XXXXXXXX submission, has also noted that:

- all scheduled poisons carry the cautionary statement "KEEP OUT OF REACH OF CHILDREN" and that the Part 3 entry for storage of Schedule 5 and 6 poisons merely articulates the interpretation of what is considered to be out of children's reach.

- retailers in particular would be pleased to have some indication regarding this issue to assist with liability concerns if children manage to access poisons while in their stores.
- the new paragraph represents a significant advance so that retailers get uniform advice.
- QLD, NSW (for Schedule 6 only) and SA have similar existing requirements.
- a uniform approach will assist retailers and the regulators and that inclusion of the new paragraph is well overdue.

A XXXXXXXX member also noted that for clarity the Committee may wish to add "or" at the end of the "Packed in non-access packaging" provision to show that the requirements are all alternatives.

The Committee generally agreed that there was a strong desire by major retail chains to have a nationally consistent approach to the retail storage requirements for Schedule 5 and 6 products. A Member advised that he had been approached by XXXXXXXX who wished to encourage the NDPSC to implement a set of nationally uniform storage requirements for Schedule 5 and 6 products.

A Member also inquired whether the label statement "KEEP OUT OF REACH OF CHILDREN", the driver behind the development of a uniform storage statement, was more for the domestic rather than retail setting. However, another Member advised of a poisoning incident last year where an amount of a Schedule 5 aquarium liquid, displayed on a low shelf, was swallowed by a child. The Member advised that the retailer was informed that storage near the floor was not considered to be "out of reach of children". The Committee generally agreed that the label statement "KEEP OUT OF REACH OF CHILDREN" was appropriate in both retail and domestic settings.

A Member noted that the proposed storage statement could potentially see many more Schedule 5 products with CRCs or in CRP because sponsors would be seeking to avoid the additional cost of displaying their product above 1.2 metres from the ground, as set out in XXXXXXXX submission. The Committee was also advised of the wide range of retailers, not just large chains, which store Schedule 5 and 6 poisons. The Committee therefore agreed to a proposal to allow time for industry to present further information to the Members on the possible large ramifications of national storage requirements for Schedule 5 and 6 poisons.

OUTCOME

The Committee agreed to foreshadow consideration at the February 2006 NDPSC Meeting of a paragraph for inclusion in Part 3 of the SUSDP setting out the requirements for storage of Schedule 5 and 6 poisons in order to enhance national consistency, along the lines of the following draft:

44a. "A person who sells or supplies a Schedule 5 or Schedule 6 poison in a retail shop must keep those poisons in such a way that, when displayed for sale, they are positioned at least 1.2 metres above the floor **except**:

- when packed in a container fitted with a child-resistant closure;
- in a container with a capacity of 5 litres/5 kilograms or more;
- packed in child-resistant packaging;
- packed in non-access packaging; or
- a hair dye packed with a volume of 50 millilitres or less.

They must be displayed in such a way to prevent contamination of human or animal food, or beverages should a leak or breakage occur."

DECISION 2005/45-1 (Set Aside Decision 2005/44-6)

The Committee agreed to set aside DECISION 2005/44-6 made at the June 2005 NDPSC Meeting to include a new paragraph in Part 3 of the SUSDP setting out the requirements for retail storage of Schedule 5 and 6 poisons, based on post-meeting comment received, and to allow opportunity for further consultation with stakeholders.

4. OTHER OUTSTANDING MATTERS FROM PREVIOUS MEETINGS

4.1 PRAZIQUANTEL

PURPOSE

The Committee considered the scheduling of praziquantel.

BACKGROUND

Praziquantel is an anthelmintic drug used as an antiparasitic agent in humans and animals. It is in Schedule 4 for human therapeutic use and is unscheduled for animal use.

The Committee recalled that at its June 2005 meeting, the Committee noted advice from the Office of Chemical Safety in regard to an application from XXXXXXXX for approval of the new active ingredient emodepside, and registration of a product range called XXXXXXXX, containing XXXXXXXX emodepside and XXXXXXXX praziquantel. The products were topically applied liquids for the treatment and control of gastrointestinal parasites in cats and were to be made available in four different pack sizes (0.35, 0.7, 1.12 mL single dose packs and a 14 mL multi-dose pack for use in veterinary clinics). All packs contained the same concentration of constituents. The

XXXXXXXX range of products were, at the time, not registered in any overseas country, but an application had been approved by the European Medicines Agency for marketing in the European Community.

The June 2005 meeting also noted that data previously evaluated indicated that the acute oral toxicity of praziquantel was very low (LD_{50} 2840 mg/kg in rats). Toxic signs were indicative of central nervous system effects, mainly sedation. Praziquantel was not a skin irritant (after single and 3 week administration) or an eye irritant in rabbits. It was also not a skin sensitizer in guinea pigs.

The June 2005 NDPSC meeting considered the appropriateness of including praziquantel for veterinary use in Appendix B of the SUSDP. As there were a number of registered veterinary products containing praziquantel, the Committee agreed that it should first obtain from the Australian Pesticides and Veterinary Medicines Authority (APVMA) details of registered products, their approved use-patterns, overall label instructions and details of whether there had been any adverse effects arising from use. The results of a literature review of possible adverse effects arising from the use of praziquantel in veterinary use was also requested. The Committee further requested that the Secretariat research the background to the existing Schedule 4 entry for praziquantel. Further consideration of the scheduling of praziquantel was therefore deferred until the October 2005 meeting.

DISCUSSION

The Committee noted the historical background to the existing Schedule 4 entry for praziquantel:

- At the June 1976 NDPSC meeting praziquantel had been included in Schedule 4. The May 1977 NDPSC Meeting subsequently considered and agreed to a request for an exemption to scheduling for praziquantel.
- The February 1989 NDPSC meeting noted that praziquantel was a trematocide which had been used for eight years on an individual patient usage basis in migrants and returning travellers for the treatment of schistosomiasis. Animal and human data supplied by XXXXXXXX supported efficacy and safety of praziquantel in the treatment of schistosomiasis. It was also noted that praziquantel was an orphan drug in the USA and that ADEC had no objection to XXXXXXXX marketing of praziquantel for the treatment of schistosomiasis. The Committee recommended that the Appendix B entry be deleted and that praziquantel for human therapeutic use be included in Schedule 4.
- At the May 1995 NDPSC meeting the Committee considered a submission for registration of a new product containing 37.5 g/L levamisole and 18.8 g/L praziquantel intended as a specific anthelmintic for sheep and lambs administered as an oral drench. At that time praziquantel was in Schedule 4 for human therapeutic use but was not scheduled for animal use although it had widespread use as a veterinary drug. The Committee also noted that while no toxicology studies were

submitted on the formulation, a previous assessment by the TGA for the general marketing of praziquantel for human therapeutic use was made available for review. This assessment showed praziquantel to have low acute toxicity with a rat oral LD_{50} of 2250 mg/kg bw, a mouse LD_{50} of 2450 mg/kg bw, to be non-irritant and to be non-genotoxic. Repeat dose studies in rats and dogs showed increased liver and thyroid weights at relatively high doses, with no associated histopathological changes. Chronic studies, although performed in hamsters and rats, were not deemed to be of sufficient standard for carcinogenicity assessment. Developmental studies in the rabbit did not show foetal toxicity, but maternotoxicity and postnatal mortality was seen in a two-generation rat reproduction study.

- On the basis of its longstanding widespread safe use in human therapeutics and its low toxicity, the Committee, in May 1995, recommended that praziquantel remain unscheduled for animal use. This situation had remained until the present.

The Committee received advice from XXXXXXXX indicating that there were a considerable number of registered products. Details of those registered products were provided, including use-patterns. The XXXXXXXX advice also included a summary of Adverse Event Reports which indicated that:

- vomiting was one of the most commonly observed side effects of oral preparations in small animals. It was noted that the labels for these products included a warning statement that such reactions may occur.
- based on the very low number of adverse experience reports for these products when compared to the total number of doses sold, no regulatory action was required other than continued ongoing monitoring for any future adverse experience reports.

XXXXXXXX also provided an article which reported a literature review of non-clinical toxicity and pharmacokinetics for praziquantel. The following points from the praziquantel section of the article were specifically noted:

- the acute oral LD50 data for mouse, rat and rabbit - 2560 mg/kg (mouse), 2840 mg/kg (rat) and 1050 mg/kg (rabbit).
- that no particular toxic effects were noted in rats treated with up to 1000 mg/kg/day for 4 weeks and dogs with up to 180 mg/kg/day for 13 weeks. The NOELs for these experiments were reported as – rat 22 mg/kg/day and dog 60 mg/kg/day.
- the conclusion that findings of the interpretable studies had convincingly shown that praziquantel lacked mutagenic potential for man.
- that praziquantel had not shown harmful effects in fertility and foetal and maternal toxicity and teratogenicity experiments at up to 300 mg/kg/day. A limited peri/post-natal toxicity test also showed no harmful effect of 300 mg/kg/day in the dams or their pups but the former were only dosed on days 15-21 of gestation and not throughout lactation to weaning.

- that praziquantel was not carcinogenic in rats or hamsters treated for 104 and 80 weeks, respectively.
- the British toxicological surveillance system for adverse actions of veterinary drug therapies did not contain any relevant reports of harmful effects during clinical use.

DECISION 2005/45-2

Based on low toxicity of praziquantel, the Committee agreed to an Appendix B entry for animal use.

Appendix B - New entry

	Date of Entry	Reason for Listing	Area of Use
PRAZIQUANTEL	Oct 2005	a	2.1

4.2 ALKALINE SALTS

PURPOSE

The Committee considered the scheduling of alkaline salts with regards to pH cut-offs and child-resistant closures (CRC) for dishwasher products.

BACKGROUND

The February 2004 NDPSC Meeting considered a review of alkaline salts by XXXXXXXX. The review addressed issues including the cut-off pH for scheduling, total alkalinity, the concentration at which the pH of a product should be measured, and the greater accessibility of dishwasher detergents compared with laundry detergents in the home. Among the review's proposals was changing the cut-off pH for inclusion in Schedule 5 to "more than 11.0". Members were of the view that there was insufficient information to consider amending the Schedule 5 entry for alkaline salts as per the options set out in the report. Accordingly, the Committee sought further information from NICNAS on the international control of similar substances.

At the June 2004 NDPSC Meeting the Committee noted a NICNAS review of the international regulation of alkaline salts. Members were of the view that to reduce the current pH cut-off for alkaline salts in Schedule 5 to pH 11 the Committee would need to know the number of products currently marketed with a pH between 11 and 11.5 and the number of harmful exposures attributed to the use of these products.

At the October 2004 NDPSC Meeting, the Committee noted information regarding poisonings involving alkaline detergents from the XXXXXXXX Poison Information Centre (PIC). The XXXXXXXX PIC services XXXXXXXX. The Committee noted that the XXXXXXXX PIC information did not include any outcome data and agreed that this was potentially a deficiency when interpreting the true toxicity of the products. Members

also noted that the information did not characterise products that caused a poisoning into those with a pH between 11 and 11.5 and those with a pH above 11.5. The Committee agreed that there was not sufficient evidence to justify a change to the cut-off pH for inclusion in Schedule 5 for alkaline salts at this time. The Committee further agreed that the Secretariat investigate the possibility of data collection from the State and Territory PICs.

At the June 2005 NDPSC Meeting the Committee considered data from the XXXXXXXX, XXXXXXXX and XXXXXXXX PICs concerning alkaline salt exposures. The Committee agreed that while this data was useful, there was still a lack of outcome data and thus insufficient information to justify a change in the scheduling of alkaline salts. The Committee agreed to gazette for the October 2005 Meeting a consideration of scheduling of alkaline salts including CRC and labelling requirements for dishwasher products. The Committee also requested that XXXXXXXX be approached regarding the XXXXXXXX's capacity to contribute information on alkaline salt poisonings and whether alkaline salt poisonings are currently monitored by XXXXXXXX. The XXXXXXXX Member undertook to approach the manufacturers of the products mentioned in the PIC data seeking information on the pH strengths and market share of these products.

DISCUSSION

The Committee considered a submission from XXXXXXXX. XXXXXXXX gave details of an incident involving a child accessing an alkaline salt dishwasher powder (XXXXXXXX, pH 13.5), noting that:

- The child accessed the dishwasher powder from a cupboard under the sink. He was able to remove the CRC and swallow a large mouthful of powder, sustaining severe injuries.
- The cap of the bottle required 2 clicks to activate the CRC. When closed with only one click, the cap posed little resistance to opening. The Members noted that XXXXXXXX had raised this issue with Standards Australia and the manufacturer, recommending that where a CRC was required there should be no ambiguity about how the closure works or any potential for it to have different levels of functionality. The Committee agreed that the issue of CRC standards was a matter for Standards Australia.
- XXXXXXXX asserted that there was an inconsistency in scheduling of caustic dishwasher detergents in that powders are not scheduled whereas liquids, gels and tablets with a pH greater than 11.5 come under Schedule 5 and require a package with a CRC. XXXXXXXX noted that, under current scheduling, a CRC was not required for the powder dishwasher detergent ingested by the toddler.
- XXXXXXXX requested that the Committee address the inconsistency in the current scheduling of alkaline salt dishwashing detergents in powder forms. XXXXXXXX have also recommended that powder forms with a pH greater than 11.5 should come

under Schedule 5. The Committee's consideration of this issue is set out below under 'Powders Inconsistency'.

- Dishwasher detergents are common household products and are frequently stored in readily accessible places. Many products on the market are highly caustic. A review of the XXXXXXXX data revealed that in the last 6 years, 96 children under 4 years of age presented following ingestion of dishwasher detergent. Roughly one third of these children required admission for endoscopy and treatment following the ingestion.
- Both the acute and long term sequelae of caustic burns due to ingestion of dishwasher detergent could be minimised by reducing the pH of products on the market. Even a functional CRC is no guarantee that a child will not be able to access the contents. XXXXXXXX has requested that consideration be given by the Committee as to a safe upper limit for pH of caustic dishwasher detergents. The Committee's consideration of this issue is set out below under 'PH Cut-offs'.

The Committee also noted that the incident discussed by XXXXXXXX above formed the basis of a Choice article and a Sydney Morning Herald story addressing the dangers of alkaline salt dishwashing detergents.

The Committee considered a submission from XXXXXXXX which included:

- Reference to the case study discussed above by the XXXXXXXX submission, reiterating that this was a child who accessed a dangerous substance. [Paragraph deleted]
- An estimate that the risk of the powder involved in the case, on the basis of the pH, was similar to that of liquid sodium hydroxide. XXXXXXXX did note that a powder posed less of a risk than a liquid for causing severe burning upon ingestion, as most children will spit out a powder, but this was not always the case.
- Caustic oesophageal burns are a cause of severe morbidity in children that experience them and CRCs for very high pH products are not sufficient to prevent an incident such as happened to the toddler. XXXXXXXX recommended that the Committee consider a restriction of the pH for dishwashing powders to minimise the chance of a severe oesophageal burn. The Committee's consideration of this issue is set out below under 'PH Cut-offs'.

The Members also noted a submission from XXXXXXXX in New Zealand. The XXXXXXXX submission highlighted a cluster of severe injuries from ingestion of dishwasher powder in young children (5 within a period of 4 months: 4 were XXXXXXXX and one was XXXXXXXX). Details supplied included the ongoing treatment and extent of injuries for the children. The submission made a number of recommendations (some being New Zealand specific) including the following:

- Mandatory child-resistant packaging compliance needed to be urgently enforced.

- Enforcement of stringent safety standards on dispenser packaging with attention to CRC lid resistance. It was noted that only 1 of 9 staff members were able to secure detergent container caps properly in a test.
- Non-child-resistant refill packages should be discouraged, so as to also avert having containers with improper seal as a result of overuse.
- Advice to give water or milk following ingestion of the caustic substance was inappropriate. Swallowed powder mixed with water may intensify injury through exothermic reactions, induction of vomiting and extension of exposure area. A "scoop and wash-off" first aid advice may be more appropriate.
- Use of enzyme-based products with pH 11 or less should be required of the manufacturing source.
- Ongoing public education to heighten awareness should occur. This could take the form of prominent warning notices on containers, advice on storing products out of children's sight and reach, encourage attention to the dispenser and dishwasher prior and after its operation; and providing the first aid information in other commonly-spoken languages.

The Members also considered a submission from XXXXXXXX in response to the Committee's request that XXXXXXXX approach the manufacturers of dishwasher detergents seeking information on the pH strengths and market share of their products. The Committee particularly noted that:

- Data on the dishwasher detergent market indicated that XXXXXXXX had the largest market share [sentence deleted]. The other major players were XXXXXXXX.
- Dishwasher detergent brand data was supplied for the key products that represent more than XXXXXXXX of the sales in Australia. The data included poisons schedule, pH, presence of a CRC, recent changes to packaging and market share.
- This data showed the pH of XXXXXXXX and XXXXXXXX were 13.6 and 13-14 respectively.
- With regard to a coordinated response from industry about extra steps to reduce alkaline salt poisonings, XXXXXXXX advised that the vast majority of dishwasher products are used safely and effectively as intended. Additionally, two major brands have implemented product packaging changes for individual product lines in 2005 assist in reducing exposures (XXXXXXXX and XXXXXXXX). XXXXXXXX asserted that there were some consumer behaviours and other factors that may increase the risk of adverse exposures including:
    - Inappropriate storage, including easy access by children or with the CRC not engaged.
    - Older dishwashers or malfunctions that lead to sludge in machines post-wash.
    - Product being placed in machines before needed with the door left open.

- XXXXXXXX therefore considered that education and awareness are key issues and believes there was opportunity to work with KidSafe type programs to promote safe practices.
- XXXXXXXX recommended that the Committee consider adding the following to the entry under Part 2, 25 (1): "alkaline salts included in Schedule 5, when packed and labelled as dishwashing machine solids (including powders)". The Committee's consideration of this issue is set out below under 'Powders Inconsistency'.
- XXXXXXXX also recommended the Committee consider that provision be made for sharing the relevant PIC data with XXXXXXXX and that an NDPSC/ XXXXXXXX dialogue with PICs commence at the earliest opportunity with the objective of enhancing feedback loops for providing input to decision-making. The Committee agreed that the PIC data from the June 2005 NDPSC Meeting could be released to XXXXXXXX following PIC agreement. The Committee also agreed to explore further XXXXXXXX proposal that NDPSC and XXXXXXXX work cooperatively to provide further recommendations to the Committee regarding alkaline salts.

The Committee again noted the following from the June 2005 Meeting:

- XXXXXXXX New Zealand had released a position paper on dishwashing powder (Caustic Poison in Our Kitchens – January 2005) which stated there were 615 incidents in New Zealand between June 2003 and January 2005 with 15 admissions to hospital. The XXXXXXXX New Zealand paper noted that the provision of CRCs for alkaline dishwashing products in New Zealand was currently done on a voluntary basis.

The XXXXXXXX Member made the following points with regard to the issue of dishwasher detergents containing alkaline salts in New Zealand:

- There are basically two types of dishwasher products on the market:
  - older generation, higher pH, alkaline salt products; and
  - the newer, lower pH, enzyme/alkaline salt products.
- New Zealand had similar issues to Australia with regards to addressing alkaline salts poisonings. The XXXXXXXX Member asserted that this matter may even be worse in New Zealand given the lower market penetration of the low pH enzyme based products (about XXXXXXXX in Europe, over XXXXXXXX in Australia but only around XXXXXXXX in NZ). This probably reflects the relatively high level of local manufacture of the generic brands using the older (and cheaper), high pH formulations.
- All dishwasher detergents containing alkaline salts in New Zealand are still in the transitional part of the *Hazardous Substances and New Organisms Act* (HSNO) and as such are covered by the old toxic substances regulations which are largely in line with the Australian scheduling.

- New Zealand has, for some time, been recommending that industry put dishwasher detergents containing alkaline salts in child-resistant packaging (CRP) on a voluntary basis. There are no mandatory provisions currently in the New Zealand regulations.
- However, it has been proposed that these products move completely into the HSNO Act so that they will be covered by the new New Zealand packaging regulations. The default requirements for this are that all substances that are corrosive or irritant have to go into [sentence deleted].

The Committee identified three core issues from the above information for it to consider. These were pH cut-offs, child-resistant closures (CRC) for dishwasher products and an inconsistency regarding powders in the current scheduling. In discussing these issues the Members considered the following:

PH Cut-offs

The Committee again noted the information on dishwasher detergents from the XXXXXXXX, XXXXXXXX and XXXXXXXX PIC responses considered at the June 2005 NDPSC Meeting. The Members considered an analysis of this data by the XXXXXXXX Member showing both a table of individual exposures by brand and a summary of this table, highlighting referral to a doctor/hospital. The Committee generally agreed that, while this data had insufficient detail about the degree of morbidity or the clinical outcomes from the reported incidents to justify a change to the pH cut-off to 11, it did indicate that there were a number of exposures occurring in the home with infants.

The Committee also noted with respect to this issue that:

- Some products are based on global formulations and would require reformulation, at significant cost, should the Committee decide to reduce the pH cut-off to 11.
- The pH 11 cut-off was inconsistent with the criteria used in other countries reviewed by NICNAS and appeared to be arbitrary with little connection to human safety data. Identical products do not require mandatory labelling statements in New Zealand and Europe and a change to the pH cut-off would hinder pack harmonisation for exported products.

The Committee therefore agreed that there was, as yet, insufficient evidence that a lowering of the Schedule 5 cut-off from pH 11.5 to 11 would result in any significant reduction in morbidity. However, a Member noted that the reports of serious injury resulting from ingestion of alkaline salts had a strong correlation with the high pH dishwashing products. The Member therefore recommended that the Committee consider rescheduling those products with pH > 12.5 to Schedule 6 or 7.

The Committee generally agreed to the proposal to reschedule dishwasher products containing alkaline salts with a pH >12.5 to a more restrictive schedule to reduce harm and to encourage the ongoing industry move to lower pH formulations. However, following concerns about possible impact on important commercial use and noting that

this would affect at least two current domestic products, the Members agreed that it was appropriate to foreshadow this consideration. This would allow time for additional consultation, noting that there appeared to be no current issues arising from products for commercial business use and as such the Committee did not wish to interfere with such operations.

CRCs

The Committee recalled that at the June 2005 NDPSC Meeting it was suggested that the Committee consider the CRC requirements for alkaline salt dishwashing products in the SUSDP. In particular, it was advocated that there was a need to consider requiring all dishwashing products containing alkaline salts to be fitted with CRCs by:

- requiring all dishwashing products containing alkaline salts to have a CRC before qualifying for the current Schedule 5 exemption for a pH of < 11.5; and
- by expanding the current CRC requirements as set out in Part 2 of the SUSDP for alkaline salts labelled for use in dishwashers to include all forms, not just tablets, liquids or gels.

A Member asserted that if all dishwashing products containing alkaline salts were required to use CRCs then there would be a loss of incentive for companies to move to the less corrosive formulations. Additionally, it was noted that the use of CRC's on products where there may be little need for them could diminish the impact of CRCs as a safety measure.

The Members also noted that an added challenge of the dishwasher alkaline salts was that frequently children access the residue left in the dishwasher after use, an exposure route that would fail to be addressed by any CRC change. The Committee generally agreed with XXXXXXXX recommendation that this issue would need to be addressed by a broader education program to try to alert people of the dangers, noting the impending XXXXXXXX New Zealand (in collaboration with XXXXXXXX) proposed campaign on this issue. The XXXXXXXX New Zealand campaign was proposed to consist of a pamphlet, to be launched in November 2005, along with a fridge magnet and large posters for display in childcare centres etc. highlighting the dangers of dishwashing detergents to children in the home.

Powders Inconsistency

The Members noted that, while the Schedule 5 entry for alkaline salts does currently capture "solid preparations", Part 2, 25 (1) of the SUSDP does not provide CRC requirements for Schedule 5 alkaline salt solids which it does for liquids, gels and tablets, an anomaly that the Committee agreed to correct.

The Committee were also advised that the issue of confirming that an entry for solid preparations captures powders was raised by the Secretariat with XXXXXXXX

Members. The Committee particularly noted the following from the Member's responses:

- Agreement that "solid" includes "powders".
- General support for the inclusion of the wording "(b) in solid automatic dishwashing preparations (including powders)…" for clarification.
- A Member asserted that in drafting an amendment the Committee needs to also consider where 'solid' is used in other entries. Some of these entries where solid is used are also intended to cover powders. Amending the alkaline salt entry may lead to the assumption that solid does not include powder if it is not specified in the individual entry. The Member had recommended that the Committee consider an new entry in Part 1 Interpretation to either: define solid to include all forms of a substance that are not semi-solid, liquid or gas; or include a statement that a reference in the schedules to solid include powders. The Committee agreed to a new entry in Part 1 Interpretation to make it perfectly clear that powders are solids for the purposes of scheduling.

The Committee finally noted that laundry detergents should not be categorised with automatic dishwashing detergents for scheduling purposes as the former products were less likely to cause poisonings around the home due to reduced accessibility and as they were less alkaline, both in terms of alkaline reserve and pH.

OUTCOME

The Committee agreed

- there was insufficient information to justify a scheduling change at this time through reducing the pH cut-off for alkaline salts in Schedule 5 from a pH of 11.5 to 11.
- that there was sufficient data linking the high pH (>12.5) alkaline salt dishwasher products to a number of severe injuries to children to warrant foreshadowing of consideration of a scheduling change for these products to a more restrictive schedule at the February 2006 NDPSC Meeting, including the possibility of removing these products from the domestic market completely.

DECISION 2005/45-3

The Committee also agreed that all current Schedule 5 dishwashing products containing alkaline salts (i.e. with a pH > 11.5) are to have a CRC to reduce any potential for harm. The Committee further agreed to include a new entry in Part 1 Interpretation to explicitly identify powders as solids. In addition, Members agreed to a slight editorial change to the alkaline salts entry under Part 2, 25 (1) to clarify that a 5 kilogram capacity may substitute for the existing 5 litre capacity where appropriate.

Part 1, Interpretation - New entry

"Solid" is considered to include "powder" for the purposes of scheduling.

Part 2, Labels and Containers, Child-resistant Closures - Amendment

ALKALINE SALTS entries in the table in 25. (1) – Amend to read:

Column 1 **Name of the poison**	**Column 2** **Nominal Capacity**
Alkaline salts included in Schedule 5, when packed and labelled as dishwashing machine tablets.	All sizes
Alkaline salts included in Schedule 5, when packed and labelled as dishwashing machine liquids, solids or gels.	5 litres / kilograms or less

4.3 PARAQUAT

PURPOSE

The Committee considered a request for reconsideration of the scheduling of paraquat in XXXXXXXX.

BACKGROUND

The Committee recalled that at its June 2005 meeting, XXXXXXXX had applied for the registration of XXXXXXXX containing XXXXXXXX g/L paraquat dichloride as the active constituent. This new formulation was based on [sentence deleted].

The applicant requested a consideration of the scheduling of this formulation of paraquat. Paraquat was listed in Schedule 7 of the SUSDP with no cut-off to lower schedules and had only recently (2004) been the subject of a public health and safety review conducted by the Office of Chemical Safety (OCS) under the auspices of the Australian Pesticides and Veterinary Medicines Authority's (APVMA) chemical review program. The poisons schedule for paraquat was re-examined during this time and considered to be appropriate.

The Committee agreed that, because of its concern in respect to:

- the adequacy of the **[**XXXXXXXX**]**, (including the lack of follow up at lower doses),
- the absence of data [sentence deleted] and the likely effect on humans, and

- the absence of data comparing the XXXXXXXX formulation with the existing formulation,

the current scheduling of paraquat remained appropriate.

The Committee indicated that it would be prepared to reconsider the matter following the assessment of further information that addressed these concerns.

DISCUSSION

The Committee noted advice to XXXXXXXX from the Office of Chemical Safety that further data to address the Committee's concerns had been received. However, as this supplementary data had been received on 16th September 2005, there was insufficient time for the data to be reviewed by OCS, for the OCS draft report to be considered by XXXXXXXX and a final assessment report to be provided to the October 2005 NDPSC meeting for consideration. It was noted that the supplementary data would be assessed and the outcome referred to the February 2006 NDPSC meeting.

OUTCOME

The Committee agreed to defer further consideration of paraquat until the February 2006 meeting when the OCS assessment report was anticipated.

6. MATTERS REFERRED BY THE AUSTRALIAN PESTICIDES AND VETERINARY MEDICINES AUTHORITY.

6.1 METHYLEUGENOL

PURPOSE

The Committee considered the scheduling of methyleugenol.

BACKGROUND

XXXXXXXX, XXXXXXXX and XXXXXXXX, have applied to the APVMA for minor use permits for Fruit Fly Monitoring Traps, containing the insecticides dichlorvos or maldison plus the insect attractants methyleugenol, capilure or cue-lure. Various formulations in these permit applications have been previously assessed and hence did not require further assessment. Only the formulations containing methyleugenol required assessment by OCS and consideration of scheduling.

Methyleugenol belongs to the chemical class of alk–2–enylbenzenes (or allylbenzenes) comprising, among others, safrole, estragole, eugenol and myristicin. It is an insect parapheromone, which is attractive to male fruit flies.

Methyleugenol is also used internationally as a flavouring agent in foodstuffs such as jellies, baked goods, beverages and ice cream and as a fragrance in cosmetics (0.01–0.8%). It has also been used as an agent in sunscreens. Methyleugenol is a CNS depressant with anaesthetic, hypothermic, myorelaxant and anticonvulsant properties and has been used as an anaesthetic in rodents. It is a naturally occurring constituent of a number of plants such as rose, basil, hyacinth, lemongrass, citronella, fennel, tarragon, star anise, nutmeg, cinnamon leaves, clove oil, allspice and walnuts. It has also been found in blackberry essence, bananas and black pepper. Methyleugenol is a naturally occurring wood preservative responsible for the distinct odour and durability of Huon pine. The general population is exposed to methyleugenol through ingestion of food stuffs, or inhalation or dermal contact with fragrance products containing the compound.

DISCUSSION

The Committee noted the OCS assessment report and in particular that:

- no data were provided in support of methyleugenol as it was already an approved active ingredient. The evaluation was conducted using published data.
- methyleugenol is rapidly absorbed following oral administration to rats and mice. It is rapidly eliminated from the body mostly via urine after metabolism in the liver. There are three major metabolic pathways: hydroxylation, oxidation and *O*–demethylation. At low levels of exposure, there is increased hydroxylation; this pathway was not seen in rats treated with 10 mg/kg bw/d for five days. Only higher doses have been shown to cause toxicity in experimental animals.
- methyleugenol has an acute oral LD_{50} of 810–1560 mg/kg bw in rats and 540 mg/kg bw in mice. The acute dermal LD_{50} was > 5000 mg/kg bw in rabbits and the acute inhalation LC_{50} was >4800 mg/m^3 in rats. The substance was neither a skin nor an eye irritant in rats and mice, and although it caused some irritation to the skin of rabbits (occluded for 24 hours) it was not irritating to the skin in a human study. It was not a skin sensitiser at 8% in a human maximisation test.
- the liver and stomach were identified target organs in repeat-dose studies. In a sub-chronic study in rats, methyleugenol caused toxicity of the liver, testes, stomach, adrenals and uterus at doses of 100 mg/kg bw and above. In a similar study in mice, liver, stomach and testicular toxicity were seen at 30 mg/kg bw and above.
- methyleugenol is a multisite, multispecies carcinogen, inducing different types of liver tumours, as well as neuroendocrine tumours in the glandular stomach, in both mice and rats after oral administration (This was only seen at high doses of 37 mg/kg bw/d and above). Methyleugenol was genotoxic *in vitro* and *in vivo*.
- in view of the widespread use of methyleugenol in foods and the apparent absence of reports of any adverse effects on human pregnancy and foetal development, the

probability of adverse reproductive effects at expected exposure levels was considered low.

- eugenol and clove oil, which are structurally-similar to methyleugenol, are listed in S5 and S6, respectively, depending on the concentration and pack size. The structurally related compound, isoeugenol is also included in S6 except when in S5 (≥ 10% and ≤ 25 %) and is exempt from scheduling at ≤ 10 %.

Methyleugenol's primary use was that of a cosmetic fragrance and food flavouring agent. A search of the Australian Registry of Therapeutic Goods (ARTG) also revealed a large number of products containing methyleugenol as an ingredient.

The Committee noted that methyleugenol was not listed by FSANZs as a permitted food additive. However, the US Environmental Protection Agency (EPA) allows for exemption from normal tolerances when methyleugenol is used in Oriental fruit fly eradication programs. Methyleugenol had also been approved by the US Food and Drug Administration (FDA) for use as a synthetic flavouring substances and adjuvant for direct addition to food for human consumption.

The OCS report considered that, based on its acute oral toxicity, methyleugenol was a candidate for Schedule 6 of the SUSDP. Methyleugenol was associated with a risk of irreversible toxicity due to its hepatotoxic and carcinogenic properties following oral administration. However, considering these effects are likely to only occur at high doses, it was recommended that methyleugenol be placed in Schedule 6 with a cut-off to exempt considering the occurrence of this substance in natural foodstuffs. It was also considered that the scheduling could be similar to safrole which is in S6 except for internal use where it is in Appendix C (except if in preparations containing ≤ 1%).

The Committee also noted that the Council of Europe had listed an ADI of 5 mg/kg bw/day and estimated the intake of methyleugenol in the diet to be 0.19 and 0.53 mg/kg bw/day, for average intake and the 98.5^{th} percentile respectively, and the Research Institute for Fragrance Materials (RIFM) Expert Panel calculated the total human exposure from fragrance products to be 12.5 μ g/kg bw/day, which was considered very conservative. Methyleugenol is used primarily as a flavouring agent in foodstuffs and as a fragrance in cosmetics (0.01–0.8%).

A public submission had been received from XXXXXXXX expressing interest in the scheduling of methyleugenol.

The XXXXXXXX representative stressed that there were other non-agricultural uses of methyleugenol and was important that the Committee's decision should not inadvertently capture these. The Committee agreed that a 1% cut-off would ensure that only the agricultural uses before the Committee were covered by the scheduling decision. The Committee further agreed however, that should a post–meeting submission come forward noting non-agricultural products with a methyleugenol content of greater than 1% then

these should be referred for the February 2006 meeting of the Committee for further consideration.

DECISION 2005/45-4

The Committee agreed that the toxicology data justified the inclusion of methyleugenol in schedule 6 for all uses. The Committee further agreed that, on the basis of no observed adverse effects at low concentrations, to an exemption from schedule 6 for 1 percent or less.

Schedule 6 – New entry

METHYLEUGENOL **except** in preparations containing 1 per cent or less of methyl eugenol.

Appendix E – New Entry

POISON	STANDARD STATEMENTS
METHYLEUGENOL	A

Appendix F –New Entry

POISON	SAFETY DIRECTIONS
METHYLEUGENOL	1, 6

6.2 IODOMETHANE

PURPOSE

The Committee considered the scheduling of iodomethane.

BACKGROUND

XXXXXXXX had applied for the approval of iodomethane XXXXXXXX as a future constituent of a new soil fumigant for use in horticulture. This new active constituent has been proposed as a potential replacement for the currently used and structurally analogous methyl bromide which is categorised as a Class 1 ozone depleter and had been due to be phased out by January 2005 under the 1987 Montreal Protocol. The time limit for methyl bromide use had been extended until the end of 2005, to allow time to find alternatives. Iodomethane, which is photo-reactive at low altitudes and consequently has a short half-life in the troposphere, is one potential replacement.

The compound itself is a liquid, both volatile (boiling point 42.5C) and reactive, and has found use in industry as a methylating agent. It is only slightly polar and neither strongly acidic nor basic and as such does not dissociate in water.

No chronic studies were provided with the submission because the company claimed that planting of crops will be delayed until no more of the fumigant remains in the soil, thereby leaving no residues in food. The subchronic toxicity of iodomethane has been evaluated in a [sentence deleted].

Iodomethane is a volatile and reactive liquid and unlike methyl bromide, it is photoreactive at low altitudes and therefore will not persist in the troposphere.

Iodomethane is also used as a methylating agent in pharmaceutical and chemical synthesis, in microscopy, as a reagent, as a catalyst in production of organic lead compounds, as an etching agent, as a component in fire extinguishers, as a soil disinfectant for tobacco and formerly as a soil fumigant e.g. to control fungi in grain sorghum.

DISCUSSION

A search by the Secretariat of the ARTG and Pubcris databases did not reveal any pharmaceutical or AgVet products containing iodomethane as a constituent.

The Committee noted the following outcomes from the OCS evaluation Report:

[Section deleted].

Members agreed that iodomethane was a powerful methylating agent. Coupled with the potential for human exposure from anticipated use, the possible effects on metabolism, the neurotoxic consequences and possible effects on the central nervous system suggested that strict controls were essential. Inclusion in Schedule 7 and also Appendix J was considered to be appropriate.

The XXXXXXXX Representative indicated support for inclusion in Schedule 7 but noted that an Appendix J entry should be on a full understanding of, and guidance for the APVMA in respect to the Appendix J criteria viz, identification of the risks to be controlled, the nature of the required training and the support of appropriate enforcement mechanisms.

The XXXXXXXX Representative commented that iodomethane had been categorised as a potential carcinogen in the workplace and was required to be labelled with “may cause cancer” warnings. OH&S authorities had not seen the [section deleted] studies submitted with the application and it was noted that the OCS would bring these to the attention of the Australian Safety and Compensation Council. It was also commented that the XXXXXXXX data showed adverse effects at the same level of worker exposure levels. This strongly suggested that iodomethane should, in the workplace, be classified for

development toxicity accompanied by appropriate training and the need for specialist operators.

The XXXXXXXX Representative also noted that approval of the technical active was likely to be in anticipation of trials with the potential product in order to obtain data for the purposes of product registration. It was therefore essential, that in these circumstances, the technical material be accompanied by suitable warning statements and regulation. In this regard the XXXXXXXX Representative suggested that as it seemed likely that a Permit to undertake further trials might be sought, the APVMA should be advised of the need for warning statements on labels and stringent controls on the product and uses under investigation. The XXXXXXXX representative further suggested that APVMA should give consideration to the product being declared a "Restricted Chemical Product".

DECISION 2005/45-5

The Committee noted that the potential developmental, reproductive and neurotoxic effects of iodomethane warranted its inclusion in Schedule 7 as well as in Appendix J on the basis that users need to be appropriately trained to use this substance.

Schedule 7 - New entry

IODOMETHANE

Appendix J – New Entry

POISON	**CONDITIONS**
IODOMETHANE	1

6.3 FATTY ACIDS (OLEIC ACID, PALMITIC ACID, STERIC ACID, LINOLEIC ACID, LAURIC ACID, MYSTERIC ACID, PENTADECANOIC ACID, AZELAIC ACID, PIMELIC ACID) AND THEIR METHYL ESTERS

PURPOSE

The Committee considered the scheduling of the fatty acids (oleic acid, palmitic acid, steric acid, linoleic acid, lauric acid, myristic acid, pentadecanoic acid, azelaic acid and pimelic acid) and their methyl esters (methyl oleate, methyl palmitate, methyl linoleate, methyl stearate, methyl myristate, methyl laurate, methyl pentadeconate, dimethyl azelate, dimethyl pimelate).

BACKGROUND

XXXXXXXX applied for the registration of two products; XXXXXXXX containing XXXXXXXX g/L methyl oleate, XXXXXXXX g/L methyl palmitate, XXXXXXXX g/L dimethyl azelate and XXXXXXXX g/L dimethyl pimelate and XXXXXXXX containing XXXXXXXX g/L methyl oleate, XXXXXXXX g/L methyl palmitate, XXXXXXXX g/L methyl linoleate, XXXXXXXX g/L methyl stearate, XXXXXXXX g/L methyl pentadecanoate, XXXXXXXX g/L methyl myristate and XXXXXXXX g/L methyl laurate as active constituents in a formulation containing mineral oils. The products are synthetic analogues of the naturally-occurring appeasing pheromones secreted by cats and nursing bitches, respectively. These pheromones calm cats or dogs (including puppies) in stressful or unfamiliar environments and supposedly provide assurance when encountering novel experiences.

XXXXXXXX also applied for the registration of XXXXXXXX containing XXXXXXXX g/L oleic acid, XXXXXXXX g/L palmitic acid, XXXXXXXX g/L azelaic acid and XXXXXXXX g/L pimelic acid as active constituents in a formulation containing ethanol (XXXXXXXX %). The product is a synthetic analogue of the F3 fraction of the feline facial secretion. It is to be sprayed onto objects such as furniture to prevent urine marking or scratching by cats.

The active constituents for the three XXXXXXXX products have a range of existing uses including detergents, emulsifiers, wetting agents, waxes, plasticisers, adhesives, polyurethane resins and cosmetics. Some of them are also used as food flavouring substances and food additives.

The fatty acid methyl esters are made from their corresponding fatty acids by the esterification of the refined triglycerides with methanol in the presence of a base catalyst. During digestion, fatty acid methyl esters are readily hydrolysed by lipase enzymes and bile salts to their corresponding free fatty acids which are absorbed from the intestine. The free fatty acids are then metabolised by oxidative processes or reconstituted into triglyceride esters and stored in the fat depot in the body. The methanol formed from the methyl group is converted to formic acid.

The following fatty acids were not listed in the SUSDP: oleic acid, palmitic acid, linoleic acid, stearic acid, lauric acid, pentadecanoic acid, myristic acid and pimelic acid. Azelaic acid is listed Schedule 4 with an exception to Schedule 2 for dermal preparations. None of these compounds (including azelaic acid) were previously considered as an agricultural, or veterinary or home garden active ingredient by the NDPSC.

At the August 1995 NDPSC meeting the Committee included a Schedule 4 entry for azelaic acid following registration by the Australian Drug Evaluation Committee of an azelaic acid product. At the November 1996 NDPSC meeting the Committee considered a submission requesting the rescheduling of a cream containing 20% azelaic acid from Schedule 4 to Schedule 3. The Committee agreed that inclusion of azelaic acid in Schedule 2 for dermal use was appropriate in view of it toxicity and use for an easily

diagnosed condition (acne vulgaris). The February 1997 NDPSC Meeting considered post-meeting comment which asserted that Schedule 2 was not appropriate as lack of counselling could lead to inappropriate use resulting in severe skin reactions. The sponsor submitted a response which, the Committee agreed, adequately addressed the issues raised and therefore the Committee confirmed its November 1996 decision.

DISCUSSION

The Committee noted advice from the Office of Chemical Safety (OCS) which had undertaken an evaluation of the XXXXXXXX and XXXXXXXX. In particular, the Committee noted that:

- no toxicity studies were submitted on any of the active constituents in the XXXXXXXX and XXXXXXXX. There was a paucity of information on acute/short-term effects (oral, dermal, inhalational toxicity, skin and eye irritation, skin sensitisation), developmental toxicity and genotoxicity of each of the 9 methyl esters considered. However, since all the fatty acid methyl esters considered are readily metabolized to their parent fatty acids which are absorbed from the intestine, the available toxicity information for the fatty acids was used to prepare a hazard profile for each of the actives.
- the applicant provided toxicity information on the fatty acids in the form of MSDS or Registry of Toxic Effects of Chemical Substances (RTECS) summaries. This indicated that the acute oral toxicity of the fatty acids is low. They are slight to moderate skin and slight eye irritants and have been found, or are likely, to be irritating to the respiratory tract. Significant data gaps exist for palmitic acid, lauric acid, myristic acid, stearic acid, linoleic acid, azelaic acid and pimelic acid including data on carcinogenicity, genotoxicity, reproductive and developmental toxicity. No data was available for pentadecanoic acid. The following table summarises the toxicity data for specific fatty acids contained in the OCS evaluation:

Fatty Acid	**Acute Oral LD_{50} (g/kg bw)**	**Inhalation**	**Dermal Irritancy**	**Eye Irritancy**	**Carcinogenic(C) Genotoxic (G) Teratogenic (T)**
Azelaic	>5 (rat)	Irritant	Mild rabbit: 500mg/24h Possible Sensitiser	Mild rabbit: 3mg/24 h	
Lauric	12 (rat)	Irritant	Mild rabbit:500 mg	Mild rabbit:100 mg	Not G (by Ames)
Linoleic	10.8 (rat)	Irritant	Moderate rabbit:500mg/24h	Moderate rabbit: 100mg	
Myristic	10 (rat)	Irritant	Moderate (human: 75mg/3d)	Mild rabbit: 100mg	Not G
Oleic	25 (rat) and 28 (mice)	Irritant	Moderate human: 15mg	Mild rabbit: 100mg	Not C, G or T
Palmitic	10 (rat)	Irritant	Mild human: 75mg/3d	Possible Irritant	

Pimelic	7 (rat) and 4.8 (mice)	Irritant	Possible Irritant	Possible Irritant	
Steric	4.64 (rat) and >5 (rat)	Irritant	Mild human: 75mg/3d	Mild rabbit:500mg/24h	Not G (by Ames)

- [Paragraph deleted].
- [Paragraph deleted].
- as exposure under these circumstances is likely to be minimal and the acute toxicity of the products is low, no hazard based safety directions have been recommended by OCS.

The OCS had also undertaken an evaluation of the XXXXXXXX product. It was noted that:

- no toxicity studies were submitted on any of the active constituents. The applicant again provided toxicity information on the fatty acids in the form of MSDS or RTECS. This information was identical to that considered for the Feliway and DAP diffuser products which indicated that the acute oral toxicity of the 4 actives is low.
- based on a consideration of the toxicity profile and concentration of each product constituent XXXXXXXX was [section deleted].

In relation to the XXXXXXXX evaluation, the OCS had noted that the product was to be sold in XXXXXXXX mL glass bottles with a tamper-proof spray attachment (which can not be unscrewed). One XXXXXXXX mL bottle will deliver approximately XXXXXXXX single sprays.

Both OCS evaluations addressed the following with regard to the use of the fatty acids and fatty acid methyl esters as food additives:

- oleic acid, palmitic acid, lauric acid, myristic acid, stearic acid, linoleic acid, methyl linoleate, methyl myristate and methyl laurate are permitted food flavouring substances in the United States and Europe.
- there are approximately 2500 chemically–defined flavouring substances in use either in Europe or the United States. Of these substances, approximately 1500, including oleic acid, palmitic acid, methyl linoleate, methyl myristate and methyl laurate, have been evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and recognized as Generally Recognised As Safe (GRAS) substances. The JECFA has also considered the levels of daily intake of oleic acid, palmitic acid, lauric acid, myristic acid, stearic acid and linoleic acid in Europe and United States and concluded that their safety as flavouring substances was not of concern. In addition, JECFA considered that it was unnecessary to establish an ADI for these fatty acids based on the following considerations:
- due to their structural similarities, these fatty acids are classified in structural class I i.e. substances of simple chemical structure with known metabolic pathways and

where the substances are metabolized to innocuous end-products which would suggest a low order of oral toxicity.

- they have a current per capita intake equal or lower than the human intake threshold for class I substances (1800 μg/day).
- these fatty acids are normal constituents of coconut oil, butter and other edible oils that have a long history of use as foods or food component.
- the levels of daily intake in Europe and United States are:

Fatty Acid	Europe (μg/day)	United States (μg/day)
Lauric	590	1200
Linoleic	130	6
Myristic	160	72
Oleic	970	440
Palmitic	89	234
Steric	58	1800

- in the United States, the available quantitative data indicate that the dietary consumption of fatty acids from naturally-occurring sources exceeds the consumption from their use as flavouring substances.
- the JECFA has not evaluated pentadecanoic acid but it has been used as a biomarker for dairy fat intake in humans.
- Food Standards Australia New Zealand (FSANZ) advised the OCS that azelaic acid and pimelic acid are not approved food additives in Australia. Azelaic acid and pimelic acid are listed in the Australian Inventory of Chemical Substances (AICS), although they have not been assessed toxicologically.

The Committee noted that the OCS evaluations had recommended that, based on the low oral toxicity as well as on the use-pattern and presentation of the products [and additionally for XXXXXXXX "which appears to be suitable for domestic use"] the NDPSC consider it appropriate to include products containing the following fatty acids: oleic acid, palmitic acid, linoleic acid, stearic acid, lauric acid, pentadecanoic acid, myristic acid and pimelic acid in Appendix B of the SUSDP, when packed and labelled for veterinary use. It was also suggested that the NDPSC consider amending the Schedule 4 entry for azelaic acid to include an exception for preparations containing 1 percent or less of azelaic acid for the treatment of cats and dogs.

The Committee noted a submission from XXXXXXXX, in particular that:

- both methyl esters and ethyl esters of fatty acids will have the same metabolic pathway (rapid hydrolysis to fatty acid and alcohol) and are used to an equivalent extent for the same pattern of use. XXXXXXXX recommended that any consideration of scheduling of fatty acids should also include the relevant ethyl esters.

- according to PUBCRIS, products containing fatty acids and fatty esters used in agriculture fall into two main patterns of use: oils to assist the drying of vine fruits; and spray adjuvants to increase the lethal effect of pesticides on target organisms by increasing the transport of pesticide through the leaf cuticle.
- while this issue was referred by APVMA, XXXXXXXX suggested that the Committee consider the addition of fatty acid esters to the consideration of fatty acids and their methyl esters as this would capture and evaluate the family of fatty acids and not discriminate between products in the market place that have the same functionality and metabolic pathway.

A submission from XXXXXXXX expressing concern that the scheduling entry being considered was restricted to pesticides and veterinary medicines, drugs and poisons was also noted. The CTFA suggested that, since the SUSDP covers derivatives, a general entry could cover long chain fatty acids in common use in soaps and cosmetics.

A submission from XXXXXXXX requested further information on any proposed scheduling limits. XXXXXXXX and XXXXXXXX also made submissions registering an interest in this item.

The Committee was informed that the fatty acids would not be used for the treatment of cats and dogs *per-se*, but for application to their surroundings to control behaviour.

DECISION 2005/45-6

The Committee agreed:

- to include the fatty acids (lauric acid, linoleic acid, myristic acid, oleic acid, palmitic acid, pentadecanoic acid and pimelic acid) in Appendix B of the SUSDP based on their low toxicity.
- that the methyl esters of these fatty acids would meet the SUSDP definition of derivatives and do not need to be separately included in Appendix B. This would also hold for the current ethyl esters raised in a public submission.
- to amend the Schedule 4 entry for azelaic acid, based on the toxicity, to include an exception from the requirements of scheduling for preparations containing 1 percent or less of azelaic acid for the treatment of cats and dogs for behaviour modification.

Schedule 4 – Amend entry

AZELAIC ACID **except**:

(a) when included in Schedule 2; or

(b) in preparations containing 1 percent or less of azelaic acid for non-human use.

Appendix B – New entry

	Date of Entry	Reason for Listing	Area of Use
LAURIC ACID	Oct 2005	a	7.1
LINOLEIC ACID	Oct 2005	a	7.1
MYRISTIC ACID	Oct 2005	a	7.1
OLEIC ACID	Oct 2005	a	7.1
PALMITIC ACID	Oct 2005	a	7.1
PENTADECANOIC ACID	Oct 2005	a	7.1
PIMELIC ACID	Oct 2005	a	7.1
STERIC ACID	Oct 2005	a	7.1

6.4 CHLORHEXIDINE

PURPOSE

The Committee considered the scheduling of chlorhexidine.

BACKGROUND

Chlorhexidine is a chlorophenol biguanide with a broad antimicrobial spectrum. Because of chlorhexidine's cationic nature, its mode of action was thought to involve interaction with phosphates on the bacterial cell surface, then disruption of the cytoplasmic membrane with consequent leakage or precipitation of cytoplasmic components.

In Australia, there are around 40 products containing chlorhexidine that are registered for use in veterinary situations as disinfectants and antiseptics, such as in veterinary surgery, in teat dips and sprays, various other topical ointments, creams, sprays, lotions and medicated foams and shampoos, in oral rinses and sprays, and in pessaries. Concentrations of chlorhexidine in these products vary from up to 62 g/L chlorhexidine digluconate in concentrated teat dips/sprays to 0.1 g/kg chlorhexidine diacetate in an eye ointment for companion animals. Chlorhexidine is also available for human use as lotions, washes and creams for disinfection and cleaning skin wounds and as oral gels, sprays and mouthwashes for mouth infections.

At the November 1992 NDPSC meeting the Committee had been advised that chlorhexidine was one of a number of compounds, which at the 1974 May meeting had been exempted from scheduling but that no rationale was given in the Minutes. Chlorhexidine was removed from the SUSDP following the Committee's decision to delete Appendix B at the August 1995 NDPSC Meeting. At the February 2003 NDPSC meeting, chlorhexidine was one of the compounds that was returned to the SUSDP as part of the reinstatement of Appendix B on the grounds of low toxicity, limited data and the availability of registered or listed products (therapeutic goods).

As part of the Phase III Review of the FAISD Handbook, the Office of Chemical Safety (OCS) had reviewed the first aid instructions and established safety directions for an antiseptic/disinfectant product containing chlorhexidine gluconate that was not covered by existing entries. As a result of this exercise, it became evident to OCS that the eye irritancy properties of chlorhexidine were sufficient to warrant the reconsideration of its scheduling. The matter had therefore been referred to the Committee for consideration.

DISCUSSION

The Committee noted that chlorhexidine products are available as a number of salts. In interpreting the strengths of these products the Committee was advised that 1% chlorhexidine is equivalent to 1.14 % chlorhexidine dihydrochloride, 1.24% chlorhexidine diacetate and 1.8% chlorhexidine digluconate.

The OCS assessment report was provided to the Committee. The report noted that:

- Chlorhexidine has low acute oral and dermal toxicity as it binds strongly to the skin and mucosa and thus is poorly absorbed after ingestion or topical application. Oral bioavailability was estimated to be less than 1% in rats, dogs and monkeys. Results of studies using radiolabelled chlorhexidine in humans showed that little was absorbed from the GIT, and that no radioactivity was detectable in the blood after dermal exposure. On the basis of its mode of action and its irritant effects on the eye, accidental ingestion of chlorhexidine is likely to result in irritation of the GIT.
- Chlorhexidine is not a skin irritant in rabbits, but repeated daily dermal application to rats resulted in slight irritancy, and experience in humans suggested possible dermal discomfort at concentrations greater than 2%. Chlorhexidine was not a skin sensitizer in guinea pigs. Adverse allergic reactions in humans have been reported, but given the extensive use of chlorhexidine over a long period of time, these are considered rare occurrences. It has high inhalational toxicity, and is likely to be a respiratory irritant.
- Chlorhexidine is a severe eye irritant. In a primary eye irritation study of chlorhexidine acetate in rabbits, test animals suffered severe ocular irritation to the extent that they were sacrificed on humane grounds on day 7 of the study. A 20% aqueous solution of chlorhexidine gluconate also produced severe eye irritation in rabbits, irreversible after 7 days. Reversible corneal injury occurred in humans and rabbits after ocular exposure to commercial solutions containing 4% chlorhexidine gluconate (i.e. 2.3 % chlorhexidine). Permanent corneal opacities have been observed in humans and animals following prolonged exposure to such solutions. No corneal damage was observed in rabbit eyes exposed repeatedly to drops of 2% chlorhexidine, but conjunctival effects of note were documented in another study in which 2% or 4% chlorhexidine gluconate was applied to rabbit eyes, with slight conjunctival effects at 1% chlorhexidine gluconate, and no irritation at ≤0.5%.

- The acute toxicity of chlorhexidine is primarily related to its irritant or caustic effects, which increase with concentration. The acute oral LD_{50} of chlorhexidine gluconate has been reported as ~2500 mg/kg bw and 1800 mg/kg bw in mice, and 2000 mg/kg bw or >3000 mg/kg bw in two different strains of rat. Chlorhexidine acetate had a similar acute oral LD_{50} in rats of 2646 mg/kg bw, with an acute dermal LD_{50} in rabbits of >2000 mg/kg bw and an acute inhalation LC50 in rats of 300 mg/m3. Consistent with chlorhexidine acting as a mucous membrane irritant, animals that died in the inhalation study showed tracheas filled with mucous, corneal opacity, and discolouration and gaseous distention of the GI tract.
- In repeat dose studies, chlorhexidine was not carcinogenic in rats and mice, and while chlorhexidine produced some positive results in *in vitro* mutagenicity studies in bacteria, studies in mammalian cells *in vitro* were negative and are considered more predictive of the genotoxicity of an antimicrobial substance. Chlorhexidine did not produce any foetal malformations or significant developmental toxicity.

The OCS report noted that the inhalational LC_{50} for chlorhexidine acetate of 300 mg/m^3 was consistent with a Schedule 7 classification. The OCS evaluation also concluded that, on the basis of inhalational toxicity alone, 10% chlorhexidine would be an appropriate cut-off from Schedule 7 to Schedule 5 as the NDPSC guidelines indicate that an LC_{50} of >3000 mg/m^3 is consistent with Schedule 5.

However, the OCS report also noted that, according to the available information that has predictive value with respect to possible adverse effects arising from accidental ocular exposure to chlorhexidine, a concentration of 2 % chlorhexidine gluconate, equivalent to approximately 1.2 % chlorhexidine base, is sufficiently irritant to warrant inclusion in Schedule 5 of the SUSDP. Below this concentration, scheduling was not considered necessary. However, due to the paucity of data for intermediate concentrations of chlorhexidine, setting a cut-off from Schedule 5 to higher schedules was problematic. Chlorhexidine gluconate was likely to produce reversible eye injury at 4%, but effects were irreversible at 20%. Without specific data for intermediate concentrations, the maximum concentration of chlorhexidine that could be supported for inclusion in Schedule 5 was the equivalent of 4% chlorhexidine gluconate (i.e. 2.3 % of the chlorhexidine base), with higher concentrations to be included in Schedule 7.

The OCS evaluation therefore recommended that the Committee consider a Schedule 7 entry for chlorhexidine for the treatment of animals with a cut–off to Schedule 5 at 2.5 % chlorhexidine (expressed as base) and to unscheduled at 1 % or less of chlorhexidine (expressed as base).

The OCS also suggested that the Committee may also wish to consider the long history of chlorhexidine use in hospitals as a surgical scrub, for pre-operative skin disinfection and for the disinfection of inanimate objects, as well as in other antiseptic products. Given the toxicology concerns outlined in the OCS evaluation report the Committee considered broadening the OCS recommendation from animal use to all uses.

It was noted that a search of the Australian Registry of Therapeutic Goods (ARTG) revealed 97 products (fol 12-17) containing chlorhexidine at a variety of strengths. The ARTG entries were summarised in the following table:

ARTG entries for 97 products containing chlorhexidine and OCS proposed scheduling				
Unknown	≤ 1% (exempt)	≤ 2.5% (S5)	3% (S7)	> 3% (S7)
31	40	19	6	1 (11%)

The Committee also noted that chlorhexidine was not listed in the *Required Advisory Statements for Medicine Labels* (RASML). The Committee considered referring the issue of labelling of chlorhexidine for human use to the OTC Section.

The Committee further noted that, due to the lack of a Schedule 6 cut-off recommendation in the OCS evaluation (because of a lack of data on toxicology of intermediate strength chlorhexidine as set out above) many currently unscheduled human therapeutic products would become Schedule 7 if the OCS recommendations were adopted beyond the treatment of animals (i.e. 4% chlorhexidine gluconate products would be Schedule 5 as they have 2.24% chlorhexidine while 5% chlorhexidine products would be Schedule 7 as they have 2.8% chlorhexidine). The Committee therefore considered a 3% exemption to Schedule 5 to minimise regulatory impact.

A submission was received from XXXXXXXX which opposed any changes to the Appendix B status of chlorhexidine. The submission further asserted that if there existed good clinical reasons for restricting the availability of chlorhexidine for a specific veterinary application, any scheduling change should be restricted to that specified use of the substance. XXXXXXXX noted that it was not aware of any significant change in the usage or adverse effects of chlorhexidine that would warrant any change in scheduling.

A submission was also received from XXXXXXXX which expressed concern over the possibility of chlorhexidine and its derivatives being scheduled and covered by a general entry rather than a specific pesticide and veterinary medicine entry.

A submission was received from XXXXXXXX. XXXXXXXX identified chlorhexidine as an active constituent in 37 agvet products. XXXXXXXX noted that, while the current scheduling matter had been referred by the APVMA, chlorhexidine had wide application in a number of sectors – oral hygiene, therapeutic products, cleaning products etc. and therefore any scheduling outcomes may have specific product impacts.

A submission was also received from XXXXXXXX indicating an interest in chlorhexidine, noting a long history of supply of chlorhexidine for oral care. XXXXXXXX also registered an interest in this issue.

Concerns were raised by XXXXXXXX about the scheduling of chlorhexidine with respect to the possible considerable impact on the large number of existing registered

products. The XXXXXXXX Member suggested that the Committee consider foreshadowing a decision to allow consultation with industry, in particular the dairy industry.

OUTCOME

The Committee agreed to foreshadow the inclusion of chlorhexidine in Schedule 7 on the basis of severe eye irritancy. The Committee also agreed that the toxicology data justified an exception to Schedule 5 for 3 percent or less and an exemption to unscheduled for 1 percent or less. The Committee agreed that there were insufficient data to justify a Schedule 6 exception.

The Committee also requested the XXXXXXXX Representative to provide details of all registered products containing chlorhexidine.

The Secretariat was asked to gazette the proposals to allow for wide consultation and to encourage submission of information that would support further cut–off levels. The Secretariat was also asked to obtain any ADRAC reports involving chlorhexidine.

FORESHADOWED DECISION (To be considered at the February 2006 meeting.)

Schedule 7 – New entry

CHLORHEXIDINE **except**:

(a) when included in Schedule 5; or

(b) in preparations containing 1 per cent or less of chlorhexidine.

Schedule 5 – New entry

CHLORHEXIDINE in preparations containing 3 percent or less of chlorhexidine **except** in preparations containing 1 per cent or less of chlorhexidine.

Appendix B – Delete entry

CHLORHEXIDINE.

7. MATTERS REFERRED BY OFFICE OF CHEMICAL SAFETY (OCS) BRANCH

7.1 CHLORFLUAZURON

PURPOSE

The Committee considered the scheduling of chlorfluazuron.

BACKGROUND

Chlorfluazuron is a benzoyl phenyl urea insecticide which inhibits chitin formation, disrupting the insect cuticle at moulting.

Chlorfluazuron was first considered at the November 1987 NDPSC Meeting. Based on a review of toxicological data, the Committee exempted chlorfluazuron from the requirements of scheduling due to its low toxicity, and the chemical was entered into Appendix B. At the August 1995 NDPSC Meeting the Committee considered a review by the then Chemicals Policy and Review Section following concerns arising from the detection of chlorfluazuron residues in meat. The Committee confirmed that chlorfluazuron did not require scheduling. Chlorfluazuron remained in Appendix B until the Appendix was deleted from the SUSDP in March 1996.

The Office of Chemical Safety (OCS) advised that, during preparations to update its web publication on termite protection, it observed that, although chlorfluazuron was currently registered as a termiticide, it was neither scheduled nor included in Appendix B.

OCS had noted that examination of the NDPSC Secretariat's records revealed that chlorfluazuron appeared on a list, dated February 1998, of "Substances considered by NDPSC but not scheduled". However, the chemical was never placed on List 1 "Substances considered by NDPSC to be exempt from scheduling due to their low toxicity 1986-1996". Furthermore, chlorfluazuron appears not to have been reconsidered during preparations to reinstate Appendix B into the SUSDP. It is therefore possible that the chemical was omitted deliberately because at the time, there were no registered products containing it.

The OCS also observed that in January 2002 the Australian Pesticides and Veterinary Medicines Authority (APVMA) referred to OCS a submission seeking registration of a termiticide bait containing 0.1% chlorfluazuron. At that time, the evaluation noted that chlorfluazuron was not scheduled but the report was not referred to the NDPSC for consideration.

To remove ambiguity from the scheduling status of chlorfluazuron, OCS requested the Committee to consider and clarify the scheduling of chlorfluazuron.

DISCUSSION

The Committee noted advice from the OCS in regard to the scheduling of chlorfluazuron. OCS confirmed that:

- an extensive toxicology database of chlorfluazuron had been assessed by XXXXXXXX.
- three products were registered, all containing chlorfluazuron at 1 g/kg. They were used in subterranean termite baiting stations, into which they are added as a paste.
- [Section deleted].

The Committee also noted OCS advice that chlorfluazuron be placed in Appendix B of the SUSDP.

Scheduling on the basis of bioaccumulation would not be in accord with scheduling criteria and may lead to inconsistency with the scheduling of other substances of low acute toxicity but exhibiting persistence in components of the environment, for example, diuron, methoprene and simazine.

The Committee noted a submission from XXXXXXXX which, on behalf of XXXXXXXX, supported the listing of chlorfluazuron in Appendix B as a pesticide on the grounds of low toxicity and also as the use-pattern for application via a termite bait device restricted access to the material. It was asserted that chlorfluazuron was of much lower toxicity to humans and non–target species with less environmental impact than the persistent chemicals used for the establishment of sprayed termite barriers.

DECISION 2005/45-7

The Committee agreed that, based upon use-pattern and low acute toxicity, chlorfluazuron be included in Appendix B of the SUSDP.

It was further agreed that Part 2 (Areas of Use) of Appendix B be extended by adding "1.2.2 Termiticide" in order to more specifically reflect termiticide use as against insecticide use.

Appendix B, Part 2 - New entry

1.2.2 Termiticide

Appendix B - New Entry

	Date of Entry	**Reason for Listing**	**Area of Use**
CHLORFLUAZURON	Oct 2005	a	1.2.2

7.2 TERMITE BARRIERS

PURPOSE

The Committee considered the Appendix A entry for termite barriers.

BACKGROUND

At the February 2000 NDPSC Meeting the Committee considered an application by XXXXXXXX for an exemption from scheduling of a deltamethrin impregnated termite barrier – XXXXXXXX. This product was constructed from fibrous synthetic webbing sandwiched between two layers of plastic sheeting. The fibrous webbing was impregnated with deltamethrin at the rate of 1 g.a.i/m^2, equating to a concentration of 0.5% deltamethrin. The product was installed as a termite barrier around house perimeters and service penetrations as a combination moisture/termite barrier. Impregnation of the XXXXXXXX was an approved use of the deltamethrin concentrate (XXXXXXXX).

A Member advised the Committee that this consideration related to the presentation of the product rather than the toxicity of deltamethrin. As the poison is sandwiched between two sheets of plastic, it would be difficult for it to be ingested or for other contact with it to occur to any great extent. The Member supported a general exemption through Appendix A of the SUSDP for manufactured termite barriers which contain a poison laminated between impervious sheeting. A concentration cut-off was not considered necessary, as the lamination would make the poison virtually inaccessible. It was suggested however that exemption for this type of presentation should not be open to all poisons. Arsenic would be one poison in particular that should not be exempted in this way.

The NDPSC agreed that it would be appropriate to exempt the XXXXXXXX termite barrier from scheduling. The only concern raised in regard to this exemption related to the potential for subsequent exposure, for example on demolition of a property. The question was raised as to whether there should be some indication on the product that the material contains a poison. The Committee noted that labelling on the laminate would deteriorate over time and in any event the proposed product would be safer than other termiticides which are sprayed onto the soil. The Committee concluded that the concern with potential for subsequent exposure did not justify an alternative scheduling decision. The Committee therefore agreed to the following wording for the termite barriers entry in Appendix A:

> TERMITE BARRIERS consisting of a registered termiticide, other than arsenic, laminated between impervious sheeting.

The XXXXXXXX manufacturing concentrate and not the XXXXXXXX was the actual registered termiticide.

DISCUSSION

The Committee received advice from the Australian Pesticides and Veterinary Medicines Authority (APVMA) that it had determined that the registration of the XXXXXXXX manufacturing concentrate was inappropriate and that it was the termite barrier product itself that should attract registration. As such the registration of the manufacturing concentrate was soon expected to cease with the XXXXXXXX being registered.

The APVMA also noted inquiries from [Bayer, the Kordon registrant,] asking if the current Appendix A entry would apply once the product (the chemical toxicant laminated between impervious sheeting) was registered rather than the manufacturing concentrate thereby leading to the "registered termiticide" component of the product ceasing to be registered. This would mean the product would no longer fall into Appendix A as it would not contain a "registered termiticide". The APVMA indicated that the Committee may want to consider an amendment to the current Appendix A entry.

The Committee noted, that at the February 2000 NDPSC meeting, the Committee considered the following in framing the wording of an Appendix A entry:

- that, in the case of deltamethrin and the XXXXXXXX product, the manufacturing concentrate was registered through the APVMA (then the NRA) as a pesticide, although the treated product *per se* was not required to be registered. The Committee further noted that if a treated product were to be manufactured overseas and imported, there would be no registration requirement at all and no control over which poisons are used as termiticides.
- the alternative of including a specific exemption under the deltamethrin Schedule entries would necessitate the Committee considering specific exemptions for other termiticides on an individual basis each time a new product were proposed. For this reason the NDPSC agreed to proceed with an Appendix A exemption but to ensure that only poisons approved for this use in Australia could be used in the product and restricting the exemption to termite barriers containing a registered termiticide.

The OCS advised that currently, only deltamethrin was used in these termite barriers. Accordingly it was suggested that the term "registered pesticide" be replaced by "deltamethrin". Alternatively, and in line with the current entry, the Committee considered replacing "registered termiticide" with the words "an active constituent approved by the relevant registration authority".

DECISION 2005/45-8

The Committee agreed to confirm the exemption of termite barriers from the requirements of scheduling on the grounds of reduced risk associated with the poison being enclosed within laminated sheeting.

The Committee further agreed to amend the Appendix A entry for termite barriers to replace reference to "registered termiticide" with "an active constituent, other than arsenic, approved by the relevant registering authority".

Appendix A – Amendment

TERMITE BARRIERS – Amend the entry to read:

TERMITE BARRIERS consisting of an active ingredient, other than arsenic, approved by the relevant registration authority, and laminated between impervious sheeting.

7.3 FORMOTHION

PURPOSE

The Committee considered the scheduling of formothion.

BACKGROUND

Formothion is an organophosphate compound used as a systemic and contact insecticide. It has been used on tree fruits, vines, olives, hops, cereals, sugar cane and rice.

At the November 1974 NDPSC Meeting the Committee included formothion in Schedule 6. No rationale was given in the Minutes.

The Australian Acceptable Daily Intake (ADI) entry for formothion was reviewed in July 2003 by the Office of Chemical Safety (OCS). At that time, the OCS noted that:

- no toxicology evaluation for formothion was held by the OCS;
- there was no listing for formothion in the APVMA Active Constituent List or in the APVMA Minimum Composition Standards List; and
- there were no products containing formothion on the APVMA PubCRIS.

The OCS had therefore recommended the deletion of the Schedule 6 entry for formothion.

DISCUSSION

The Committee noted the OCS review which highlighted that:

- formothion had been registered as a Restricted Use Pesticide (RUP) in the USA, but according to the January 1998 Human Health Assessment Chapter of the

Reregistration Eligibility Document (RED), formothion was no longer registered in the USA.

- according to the Extoxnet summary the LD_{50} of formothion is 365-500 mg/kg for rats; 410-420 mg/kg for rabbits; 102 mg/kg for mice; and 210 mg/kg for cats. The dermal LD_{50} is > 1000 mg/kg for rats. The LC_{50} (4 hours) is 4.5 mg/L air for rats. Formothion is non-irritating to skin.

The Committee noted that, in considering previous decisions to retain SUSDP entries where there are no registered products, it had tended to approach this issue on a case by case basis. Some examples of where the Committee had decided to retain an entry were:

- The scheduling of vinclozolin, considered at the June 2004 NDPSC Meeting. Following a review, the APVMA had cancelled all vinclozolin registrations and as a consequence there were no products containing vinclozolin. The Committee agreed to include vinclozolin in Schedule 7 on the basis of its teratogenic potential and in order to maintain consistency with the scheduling of a closely related compound.
- The scheduling of carbaryl, considered at the October 2002 NDPSC Meeting. Removal of the Schedule 4 entry for carbaryl had been recommended by a TGA review on the basis that: it was carcinogenic; available data did not permit an adequate risk assessment; and that there were no human therapeutic products. The Committee agreed to retain the Schedule 4 entry to foster harmonisation with New Zealand and to maintain existing controls over imports and dispensing by pharmacists.
- The scheduling of demeton-s-methyl and demeton-o-methyl, considered at the August 2001 NDPSC Meeting. The Committee was advised that the registrant had not sought to continue registration of demeton-s-methyl and that there were no registered products for demeton-o-methyl. The Committee agreed that as registration of the products had lapsed, there was no longer a need to retain the Schedule 6 entries for demeton-s-methyl and demeton-o-methyl preparations (<10%). The Committee, however, agreed to retain the entries for demeton-s-methyl and demeton-o-methyl in Schedule 7.

The Committee considered establishing a policy for guiding its decisions about whether to retain SUSDP entries where there were no registered products. It suggested that there be a general policy of retaining parent entries for substances which no longer have registered products. This approach avoided the need to unnecessarily revisit the scheduling of substances should new products be subsequently registered.

OUTCOME

The Committee agreed:

- to retain the current Schedule 6 entry for formothion, and

- to the general policy of retaining in the SUSDP parent entries for substances which no longer have registered products based on them.

PHARMACEUTICALS

12. MATTERS ARISING FROM THE MINUTES OF THE PREVIOUS MEETING (CONSIDERATION OF POST-MEETING SUBMISSIONS UNDER 42ZCZ)

12.1 PSEUDOEPHEDRINE

PURPOSE

The Committee considered the post-meeting comment with regards to the decision to reschedule pseudoephedrine and remove it from Appendix H.

BACKGROUND

The June 2002 NDPSC Meeting rescheduled all OTC single-active immediate release pseudoephedrine (PSE) preparations from Schedule 2 (S2) to Schedule 3 (S3) of the SUSDP to help reduce the problem of diversion to the illicit drug trade while maintaining access for legitimate users. The October 2004 NDPSC Meeting considered rescheduling the remaining S2 PSE preparations to S3. The October 2004 NDPSC Meeting agreed to take no scheduling action at that time, in order to allow time for initiatives implemented by government, industry and pharmacy organisations to take full effect. The February 2005 NDPSC Meeting continued its consideration of illicit diversion of PSE and again noted the various initiatives in place through the NSW Poisons Advisory Committee, the Pharmacy Guild of Australia and the Australian Self-Medication Industry. Again, the Committee agreed to allow more time to determine the effectiveness of these initiatives and so expressed its intent to reconsider the scheduling of PSE at the June 2005 Meeting.

At the June 2005 Meeting, on the basis of the available information and in the interest of public health and safety, the Committee agreed to reschedule the majority of pseudoephedrine products to S3, with liquid preparations containing more than 800mg pseudoephedrine hydrochloride (or its equivalent) per pack or other preparations containing more than 720mg pseudoephedrine hydrochloride (or its equivalent) per pack becoming S4 medicines. This decision was based on the fact that PSE is the essential precursor for methamphetamine production, that the harm associated with methamphetamine is considerable and that rescheduling should reduce the illicit diversion from pharmacies while retaining accessibility to legitimate consumers. The Committee also agreed to remove pseudoephedrine from Appendix H of the SUSDP, considering that such action was in line with the decision to the re-scheduling of pseudoephedrine because of public health concerns with diversion.

DISCUSSION

A number of further public submissions concerning the June 2005 scheduling decision were received. Many opposed the implementation date of the scheduling change – 1 January 2001. XXXXXXXX pointed out that this implementation date demonstrates no

consideration of the impact on pharmacy practise: 1 January is in the middle of the Christmas break and the same logistical problems will be encountered as those that were encountered when levonorgestrel was rescheduled. XXXXXXXX supported the rescheduling but felt that 1 January 2006 was too onerous and instead suggested 1 June 2006. XXXXXXXX pointed out that the proposed implementation date does not allow enough time to allow for change in packaging etc and suggested 1 April 2007 instead. XXXXXXXX pointed out that pharmacists are already stretched with PBS requirements at this time of year and that staff re-training would have to occur during the busiest time of the year. XXXXXXXX suggested delaying the S4 scheduling change until April 2006 to allow pharmacists time for natural stock flow. XXXXXXXX asked that the Committee review or defer the decision regarding liquid preparations until there is robust data demonstrating the extent of diversion of liquid preparations is available.

A number of logistical concerns were mentioned in relation to the implementation date. XXXXXXXX pointed to the volume of products that will be affected: 100 products will become S4 and 200 products will become S3 (XXXXXXXX quote 52 presentations becoming S4 and 40 presentations becoming S3). XXXXXXXX was concerned that there will be stock run-out and write-off issues and Pfizer mentioned repackaging lag times. XXXXXXXX feared that old stock will be off-loaded or dumped. Other comments noted by the Committee included:

- XXXXXXXX and XXXXXXXX stated that there is no other effective nasal decongestant available: XXXXXXXX felt that phenylephrine provides a suboptimal product for legitimate consumers.
- XXXXXXXX strongly supported the re-scheduling decision. They pointed out that stock levels have been run down so there will be no problem with old stock. They further stated that phenylephrine products are now available so there will be little inconvenience to consumers.
- XXXXXXXX quoted various epidemiology data relating to increases in amphetamine-related arrests and amphetamine-related hospital admissions to illustrate their concerns regarding the adequacy of the proposed scheduling changes. They pointed out that pseudoephedrine is not an essential medical product and that there are no pseudoephedrine products in the United Kingdom. They felt that phenylephrine is an adequate alternative. After consultation with XXXXXXXX in the United Kingdom, the Secretariat noted that products containing pseudoephedrine are available in the UK as pharmacy medicines with a maximum recommended daily dose of 240mg in packs containing a maximum of a four day supply. The XXXXXXXX further stated that they do not feel that the Committee was adequately informed of the impact of methamphetamine on mental health services. They therefore recommended that all pseudoephedrine products be scheduled as S4 or higher or be banned all together.

The Committee was informed that a teleconference was conducted on 23 September 2005 with available jurisdictional Members to discuss issues in relation to the implementation of the pseudoephedrine decision. All participants agreed that there should be no delay in

moving all S2 pseudoephedrine products to S3 but were willing to delay the implementation of current S2/S3 pseudoephedrine-containing products to S4. It was noted that industry was keen for the S4 implementation to be delayed as long as possible, given their concerns about product becoming dead stock once it becomes S4. The consensus was that the implementation for S2 product to become S3 should remain 1 January 2006 and the implementation date for certain S3 product to become S4 should be, as per XXXXXXXX's recommendation, 1 April 2006. Participants also agreed that it would be reasonable for States and Territories to issue a general exemption to allow S3 pseudoephedrine product to be supplied with S2 signal headings. It was proposed that this exemption would be granted until the S4 implementation date i.e. 1 April 2006.

The Committee also considered a late submission from XXXXXXXX. XXXXXXXX was of the opinion that the rescheduling of those pseudoephedrine products which will eventually become S4 should be delayed. However, different Members put forward different suggestions as to how long this delay should be: XXXXXXXX representatives wanted to delay until 1 July 2006, XXXXXXXX representatives supported a 1 April 2006 implementation date and XXXXXXXX agreed with XXXXXXXX representatives that 1 July 2006 gave all stakeholders reasonable time to implement the changes.

A Committee Member raised the point that all S3 products require a CMI and some of these products do not yet have a CMI ready. Further to that, the protocol for S3 sales of pseudoephedrine was yet to be developed and the professional area of pharmacies would need to be re-organised to meet the new requirements. Another Member pointed out that, with initiatives such as "Project Pseudo" well in place, most pseudoephedrine product had already been moved into the dispensary area. Another Member brought it to the Committee's attention that, as far as cold and flu preparations go, January was a very quiet period for sales. In line with that, as the winter buys tend to happen around February/ March, it was expected that pharmacy stocks of these products should be low at the start of the year.

The Committee noted advice that had been received from the TGA regarding the variation of a decision which would involve implementing the decision over two separate dates. The Committee agreed that such action constitutes a variation of the original decision and was not a new decision.

The Committee considered a number of post-meeting submissions which argued strongly for the retention of pseudoephedrine in Appendix H. One of the most common arguments for this was the fact that there was no evidence that advertising would increase the risk of illicit diversion. [Sentence deleted]. They held the view that PSE was not rescheduled because of the harm that it causes per se but rather because of the public health harms caused by its diversion into illicit drug manufacture. The XXXXXXXX further highlighted that the edited Minutes of the NDPSC June 2005 Meeting noted that 'pseudo runners' are not likely to be influenced by advertising when attempting to divert PSE. XXXXXXXX, XXXXXXXX and XXXXXXXX and XXXXXXXX all made the same point.

XXXXXXXX and XXXXXXXX recommended that the issue of advertising of PSE be referred to the Therapeutic Goods Advertising Code Council (TGACC), as per the recommendations of XXXXXXXX. They further stated that the TGACC have mandatory statements and could thus ensure that any advertising include an agreed statement advising potential purchasers that they must discuss their purchase with a pharmacist. XXXXXXXX and XXXXXXXX agreed with this.

XXXXXXXX felt that banning advertising disadvantages genuine customers. This view was supported by XXXXXXXX, XXXXXXXX, XXXXXXXX and XXXXXXXX. XXXXXXXX made the further point that the Committee should have confidence in pharmacists to only allow supply of PSE to legitimate users. XXXXXXXX was of the view that advertising prohibition on pseudoephedrine may have a negative impact on public health through decreased public awareness of self-medication options. XXXXXXXX supported this view by putting forward that advertising is necessary to inform consumers that, while PSE has gone from S2 to S3, it does continue to be available. XXXXXXXX stated that communication of the changes (through advertising) would assist pharmacists' ability to implement the changes with the least amount of disruption. XXXXXXXX suggested that advertising could include advice or information regarding the illicit use problem and why pharmacists must ask questions, further ensuring a smooth transition.

XXXXXXXX suggested that the Appendix H entry includes the wording "... excluding in-store advertising". Both XXXXXXXX and XXXXXXXX agreed that it is only in-store promotions that potentially encourage illicit users. XXXXXXXX and XXXXXXXX also stated that there was no evidence that advertising increases the overall demand for cough and cold products. Rather, it increases market share for particular brands.

XXXXXXXX pointed out that legitimate commercial interests may be encroached upon if advertising was prohibited. XXXXXXXX stated that prohibition of advertising was anti-competitive because house brand cold and flu products could be implicitly advertised but branded products could not. XXXXXXXX pointed out that there are significant cost implications and mentions figures of between four and twenty million dollars for the Australian consumer.

A number of submissions pointed out that advertising of PSE was still permitted in New Zealand and thus, with trans-Tasman harmonisation in mind, PSE should remain in Appendix H here in Australia. XXXXXXXX, XXXXXXXX and XXXXXXXX all stated this point.

In a late submission, XXXXXXXX suggested that an additional complication for promotional and labelling material of alternative and/or replacement products might be that it would be an offence to make any reference to pseudoephedrine unless it was included in Appendix H. The Committee agreed that this is another issue that should be put to the TGACC for comment.

A Member raised the point that, while 'pseudo-runners' may not be influenced by advertising of pseudoephedrine product, the intention of removing the Appendix H entry for pseudoephedrine was to send a clear message that the Committee has serious public health concerns about the illicit diversion of pseudoephedrine to manufacture methylamphetamine and seeks to reduce the harm associated with this problem by reducing the amount of pseudoephedrine in the community. Another Committee Member suggested that, while there may be advantages in permitting the advertising of pseudoephedrine short-term to facilitate a smooth transition, there was little justification for permitting such advertising long-term. The Member suggested, therefore, that the issue of advertising be referred to the TGACC, as recommended by XXXXXXXX. This recommendation from XXXXXXXX also proposed that any advertising of pseudoephedrine include an agreed statement that advises potential purchasers that they will be required to discuss their purchase with the pharmacist. Thus the Committee agreed not to delete pseudoephedrine from Appendix H at this stage. It was agreed, however, to seek advice from the TGACC regarding the inclusion of an agreed statement on the need for pharmacists' involvement. The Committee will thus seek TGACC advice for consideration at the February 2006 Meeting.

DECISION 2005/ 45-9 (Variation to Decision 2005/ 44 – 23)

In accordance with sub-regulation 42ZCZ(3) of the *Therapeutic Goods Regulations 1990*, the Committee agreed to vary Decision 2005/ 44 23 to reschedule pseudoephedrine products to S4, with a cut-off to S3 for liquid preparations containing 800mg pseudoephedrine hydrochloride (or its equivalent) or less per pack or other preparations containing 720mg pseudoephedrine hydrochloride (or its equivalent) or less per pack. While the eventual scheduling outcome remains the same, the Committee agreed to implement the decision in two stages; the first stage being the removal of all remaining S2 (slow-release, combination and undivided preparations) products to S3 (implementation date 1 January 2006) and the second stage being to reschedule all liquid preparations containing more than 800mg of pseudoephedrine and all other preparations containing more than 720mg of pseudoephedrine to S4 (implementation date 1 April 2006).

The decision to reschedule pseudoephedrine was based, as per the June 2005 Meeting, on the following reasons:

- Pseudoephedrine is the essential precursor for methamphetamine production.
- The harm associated with the production and use of methamphetamine is considerable.
- Rescheduling all pseudoephedrine preparations to S4 with the S3 cut-off limits should reduce the amount of pseudoephedrine diverted from pharmacies into illicit methamphetamine manufacture and therefore the supply of methamphetamine to the community, while retaining accessibility to genuine consumers of an effective medicine.

The decision to implement the scheduling amendment over two dates was made so as to strike a balance between providing all stakeholders additional time to meet the requirements of the scheduling changes and ensuring that the serious public health concerns regarding the illicit diversion of pseudoephedrine are addressed as soon as is possible.

The Committee also agreed not to remove pseudoephedrine from Appendix H of the SUSDP. The Committee felt 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. Advice on advertising will be sought from the TGACC and this advice will be considered at the February 2006 Meeting.

For implementation on 1 January 2006:

Schedule 2– Amendment

PSEUDOEPHEDRINE – delete entry.

Schedule 3 – Amendment

PSEUDOEPHEDRINE – amend entry to read:

PSEUDOEPHEDRINE in preparations (other than preparations for stimulant, appetite suppression or weight-control purposes), in a primary pack with a recommended daily dose of 240 mg or less of pseudoephedrine:

(a) in undivided preparations containing 60 mg or less of pseudoephedrine per recommended dose;

(b) when in combination with other therapeutically active substances;

(c) in slow-release preparations; or

(d) in other divided preparations, where pseudoephedrine is the only therapeutically active substance, containing 60 mg or less of pseudoephedrine per recommended dose in a pack containing 30 or less dosage units.

Schedule 4 – Amendment

PSEUDOEPHEDRINE – amend entry to read:

PSEUDOEPHEDRINE **except** when included in Schedule 3.

For implementation on 1 April 2006:

Schedule 3 – Amendment

PSEUDOEPHEDRINE – amend entry to read:

PSEUDOEPHEDRINE (other than preparations for stimulant, appetite suppression or weight-control purposes) when supplied in a primary pack:

(a) in liquid preparations containing 800 mg or less of pseudoephedrine hydrochloride (or its equivalent); or

(b) in other preparations containing 720 mg or less of pseudoephedrine hydrochloride (or its equivalent).

12.2 POMEGRANATE (PUNICA GRANATUM)

PURPOSE

The Committee reconsidered its decision to include pomegranate in Schedule 4 of the *Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP).

BACKGROUND

Pomegranate has the botanical name of *Punica granatum*. Different parts of the *Punica granatum* plant have been used for different therapeutic purposes. The juice of the fruit contains antioxidants and has been used as a treatment for both atherosclerosis and for reducing cholesterol. The rind is an astringent and used as a treatment for diarrhoea. The seed oil contains fatty acids and polyphenols. The seed contains nonsteroidal oestrogenic substances. The dried barks of the stem and root have been used as an anthelmintic. These parts of the plant contain the toxic alkaloid pelletierine which, in overdose, can cause strychnine-like effects.

The February 2005 NDPSC meeting noted that the Trans-Tasman Harmonisation Working Party (TTHWP) had proposed a policy position that, where there were S2/ S3 entries but no products on the ARTG or on the New Zealand SMARTI, those scheduling entries should be deleted but the parent entry should be retained/ added in Schedule 4 of the SUSDP. While this proposal departed from the general principles of harmonising on the least restrictive schedule, it was only in relation to substances no longer marketed in either Australia or New Zealand. The February 2005 Committee Meeting was also advised that the TTHWP had recently been focusing on harmonisation in respect to Schedule 2 and Schedule 3 substances and had identified numerous substances which were not registered in either Australia or New Zealand.

At the June 2005 Meeting, the Committee agreed to amend the scheduling of the list of substances that the TTHWP had put forward to Schedule 4 poisons in the interests of trans-Tasman harmonisation. This list included pomegranate (*Punica granatum*).

DISCUSSION

The Committee noted that the New Zealand Medicines Classification Committee (MCC) considered pomegranate at its June 2005 Meeting, in the context of trans-Tasman harmonisation. Contrary to the policy decision that had been decided on by the TTHWP, the MCC agreed to reschedule pomegranate from pharmacy only to general sale. The MCC recommended that the NDPSC not include pomegranate in Schedule 4 of the SUSDP.

The Committee was informed that the NDPSC Secretariat was contacted by the OCM in regards to the addition of pomegranate to Schedule 4 of the SUSDP. The OCM stated that, in regards to scheduling of herbal substances, it is preferable to list the component or components contained within the plant, rather than the plant itself. In this way, it would not matter what genus, species or plant part contains the component as it would be relevant to all. When the component is not known, the correct botanical genus, species and plant part should be named. The OCM further stated that, as the entry for pomegranate is currently stated, it potentially captures products which are listed on the Australian Register of Therapeutic Goods (ARTG). Of course, this situation is exactly what the policy position of the TTHWP was attempting to avoid.

The information provided by the OCM revealed that there were six products currently listed on the ARTG which contain the fruit of *Punica granatum* and two products which contain the seed of *Punica granatum*.

The Committee noted advice obtained from the OCM that the Food Additives and Contaminants Committee have recommended that the root be prohibited for use in foods as a flavouring agent although pomegranate bark extract has a “Generally Recognised as Safe” status in the United States.

The potential toxicity of the bark and root of the plant was the main issue of concern discussed by the Committee. The Committee noted, however, that no product currently on the ARTG contains either root or bark of pomegranate.

DECISION 2005/45-10

As the scheduling of pomegranate would capture a number of products currently listed on the ARTG as an unintended outcome, the Committee decided to set aside the decision made at the June 2005 Meeting to include pomegranate in Schedule 4 of the SUSDP and to instead leave it unscheduled.

12.3 JALAP RESIN

PURPOSE

The Committee reconsidered its decision to include jalap resin in Schedule 4 of the *Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP).

BACKGROUND

Jalap is the common name for both *Ipomoea jalapa* and *Ipomoea purga*, (the approved Australian Herbal Names). Both of these herbs are allowable active ingredients on the Australian Register of Therapeutic Goods (ARTG), with no restrictions applied. Whilst these herbs are listed as two separate species, some references state that *Ipomoea jalapa* may in fact be a synonym for *Ipomoea purga*. The term "Jalap resin" most often refers to an extract of the root of *Ipomoea purga* but can also apply to other ipomea species.

The February 2005 NDPSC meeting noted that the Trans-Tasman Harmonisation Working Party (TTHWP) had proposed a policy position that, where there were S2/ S3 entries but no products on the ARTG or on the New Zealand SMARTI, those scheduling entries should be deleted but the parent entry should be retained/ added in Schedule 4 of the SUSDP. While this proposal departed from the general principles of harmonising on the least restrictive schedule, it was only in relation to substance no longer marketed in either Australia or New Zealand. The February 2005 Committee Meeting was also advised that the TTHWP had recently been focusing on harmonisation in respect to Schedule 2 and Schedule 3 substances and had identified numerous substances which were not registered in either Australia or New Zealand.

At the June 2005 Meeting, the Committee agreed to amend the scheduling of the list of substances that the TTHWP had put forward to Schedule 4 poisons in the interests of trans-Tasman harmonisation. This list included jalap resin.

DISCUSSION

The Committee was informed that the New Zealand Medicines Classification Committee (MCC) considered jalap resin at its June 2005 Meeting, in the context of trans-Tasman harmonisation. At that meeting, the MCC noted that this substance had never been scheduled in Australia and was a pharmacy-only medicine in New Zealand. The MCC could see little justification in making it a prescription medicine as it was a simulant laxative and so made no decision to reschedule at that time.

The Committee was further informed that the NDPSC Secretariat was contacted by the Office of Complementary Medicine (OCM) and a number of concerns were raised by them in regards to the addition of jalap resin to Schedule 4 of the SUSDP. Firstly, it was pointed out that, in regards to scheduling of herbal substances, it is preferable to list the component or components contained within the plant, rather than the plant itself. In this way, it would not matter what genus, species or plant part contains the component as it

would be relevant to all. When the component is not known, the correct botanical genus, species and plant part should be named. The term "jalap" is not a botanical term but rather a common name and as such may refer to a number of different species. The second concern raised by the OCM was that, as the entry for jalap resin is currently stated, it potentially captures products which are currently listed on the Australian Register of Therapeutic Goods (ARTG).

The information provided by the OCM revealed that of the two listable species, there are eight products currently listed on the ARTG which contain *Ipomoea jalapa* root and zero products which contain any part of *Ipomoea purga* root. The OCM also advised that "jalap resin" is a powerful purgative or stimulant laxative which can produce copious watery evacuations. It can produce considerable pain in large doses and, as its overuse may result in electrolyte depletion, it may therefore interact with cardiac glycosides such as digoxin.

A Member pointed out that the scheduling of stimulant laxatives remains unharmonised and that this issue will need to be addressed through the current processes in the near future.

DECISION 2005/45-11

As the scheduling of jalap resin would capture a number of products currently listed on the ARTG as an unintended outcome, the Committee decided to set aside the decision made at the June 2005 Meeting to include jalap resin in Schedule 4 of the SUSDP and to instead leave it unscheduled.

12.4 COPAIBA BALSAM

PURPOSE

The Committee reconsidered its decision to include copaiba balsam in Schedule 4 of the *Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP).

BACKGROUND

Copaiba balsam is the name of the oleo-resin obtained by incision from the trunk of various species of *Copaifera officinalis*; *Copaifera langsdorffii*; and *Copaifera reticulata*. Copaiba balsam is also known by other common names such as Balsam Copaiba, Copaiba Oleoresiin, Copaiva and Jesuit's Balsam. It is used therapeutically in both oral and topical forms, is also used as a flavouring in food and has a "Generally Recognised as Safe" (GRAS) status in the United States.

The February 2005 NDPSC meeting noted that the Trans-Tasman Harmonisation Working Party (TTHWP) had proposed a policy position that, where there were S2/S3 entries but no products on the ARTG or on the New Zealand SMARTI, those scheduling

entries should be deleted but the parent entry should be retained/added in Schedule 4 of the SUSDP. While this proposal departed from the general principles of harmonising on the least restrictive schedule, it was only in relation to substance no longer marketed in either Australia or New Zealand. The February 2005 Committee Meeting was also advised that the TTHWP had recently been focusing on harmonisation in respect to Schedule 2 and Schedule 3 substances and had identified numerous substances which were not registered in either Australia or New Zealand.

At the June 2005 Meeting, the Committee agreed to amend the scheduling of the list of substances that the TTHWP had put forward to Schedule 4 poisons in the interests of trans-Tasman harmonisation. This list included copaiba balsam.

DISCUSSION

The Committee noted that the New Zealand Medicines Classification Committee (MCC) considered copaiba balsam at its June 2005 Meeting, in the context of trans-Tasman harmonisation. At that meeting, the MCC noted that this substance had never been scheduled in Australia and was a pharmacy-only medicine in New Zealand. The MCC could find no reference to this substance in *Martindale* and so agreed that it was likely to be an obsolete item. Accordingly, the MCC agreed to reschedule copaiba balsam from pharmacy only to general sale. The MCC also asked the NDPSC consider removing copaiba balsam from the SUSDP.

The Committee was informed that the NDPSC Secretariat was contacted by the Office of Complementary Medicines (OCM) in regards to the addition of copaiba balsam to Schedule 4 of the SUSDP. Firstly, it was pointed out that, in regards to scheduling of herbal substances, it is preferable to list the component or components contained within the plant, rather than the plant itself. In this way, it would not matter what genus, species or plant part contains the component as it would be relevant to all. When the component is not known, the correct botanical genus, species and plant part should be named. Copaiba balsam is not a botanical term but rather a common name and as such may refer to a number of different species. The second concern raised by the OCM was that, as the entry for copaiba balsam is currently stated, it potentially captures products which are listed on the Australian Register of Therapeutic Goods (ARTG).

Further information provided by the OCM revealed that there are three products currently on the ARTG which contain the listable active Copaiba Oil (all topical products) and no products which contain the listable active *Copaifera langsdorfii*.

The Committee noted advice obtained from the OCM that when used orally for medicinal purposes, copaiba balsam can irritate mucous membranes and ingestion of five grams can cause stomach pains. Large doses can cause vomiting and diarrhoea.

A Member of the Committee pointed out that the substance was considered to be generally safe and that products on the ARTG are only used topically. For this reason, as

well as the fact that scheduling copaiba balsam would affect a number of ARTG listed products, scheduling of the substances was inappropriate.

DECISION 2005/45-12

As the scheduling of copaiba balsam would capture a number of products currently listed on the ARTG as an unintended outcome, the Committee decided to set aside the decision made at the June 2005 Meeting to include copaiba balsam in Schedule 4 of the SUSDP and to instead leave it unscheduled.

13. OTHER OUTSTANDING MATTERS FROM PREVIOUS MEETINGS

13.1 OSELTAMIVIR

PURPOSE

The Committee re-considered an application to reschedule oseltamivir from Schedule 4 to Schedule 3 with inclusion in Appendix H of the SUSDP.

BACKGROUND

The October 2004 NDPSC Meeting considered an application to reschedule oseltamivir from S4 to S3 for the treatment and prevention of infections due to influenza A and B viruses in adults and adolescents 13 years of age and over, with inclusion in Appendix H. At that time, the Committee considered the available data inadequate in providing a reassurance that widening the availability of oseltamivir for the treatment of influenza through inclusion in Schedule 3 would not facilitate the spread of resistance to neuraminidase inhibitor (NI) class of drugs. Furthermore, the Committee considered it important to its consideration if advice was received from authorities that deal with communicable diseases to gain an understanding of the implications an S3 availability of oseltamivir for the treatment of influenza would have on the national strategies for managing influenza epidemics or pandemics. Therefore, the Committee agreed to defer making a decision to the February 2005 meeting to allow input by the XXXXXXXX.

The February 2005 NDPSC Meeting noted comment from XXXXXXXX which focused on two critical issues concerning resistance potential, where there was a paucity of data, and depletion of stocks during an epidemic or pandemic. XXXXXXXX also advised that the Neuraminidase Inhibitor Susceptibility Network (NISN) was currently working with the WHO Collaborating Centre on Influenza in Japan to assess the likelihood of community transmission of resistant strains and that these trials were expected to be completed by middle of 2005. The Committee therefore agreed to defer further consideration of the rescheduling of oseltamivir until the NISN trials were completed to allow XXXXXXXX to consider further scientific data in order to make a final recommendation to the NDPSC on this matter.

At the June 2005 NDPSC Meeting, the Committee agreed to defer consideration of the rescheduling of oseltamivir from Schedule 4 to Schedule 3 until the final recommendation from XXXXXXXX had been received.

DISCUSSION

The Committee considered recent comment from XXXXXXXX where the following issues were highlighted:

- The NISN trials showed that there were inadequate data to assess the likelihood of the development of drug resistance in Influenza A virus, should oseltamivir be rescheduled to S3.
- While oseltamivir is available OTC in the UK, there are very stringent controls on such sales. Oseltamivir can only be sold to those who fit into an "at risk" demographic during influenza season and pharmacists must first undergo training, be formally accredited, undergo audits, have formal arrangements in place with local GPs and enter sales data on an NHS-maintained surveillance database before such sales can take place.
- While XXXXXXXX does concede the clinical benefits of oseltamivir when commenced within 48 hours of onset of symptoms during seasonal inter-pandemic outbreaks, there is potential for pharmacists to misdiagnose serious illnesses such as pneumonia. XXXXXXXX instead recommended that improved access to oseltamivir be considered through such avenues as primary care and/or through GPs during the seasonal inter-pandemic outbreaks.
- XXXXXXXX noted that lack of access to GPs results in lack of access to drug treatments for influenza and thus GP authorities should be allowed the opportunity to address this issue prior to any rescheduling decision being made.
- XXXXXXXX voiced concern regarding patients potentially being inappropriately treated with oseltamivir. While appropriately trained pharmacists would consistently apply the correct diagnostic algorithm, there are not the same systems in place in Australia to those that exist in the UK to enforce the application of such protocols. Furthermore, given that many people cannot distinguish between symptoms of the common cold and those of flu, pharmacists may be put under undue pressure to supply oseltamivir and this could increase overuse. Overuse may lead to a diminished public perception of the benefits of oseltamivir treatment; the adverse reactions such as nausea and vomiting may dissuade patients from using it when there is a genuine need.
- XXXXXXXX concluded by reiterating that oseltamivir should remain in Schedule 4, that alternate ways to increase access to oseltamivir during inter-pandemic influenza seasons should be looked into, that GP authorities be given the opportunity to address issues of prompt access to primary care physicians during the influenza season and that further research into the development of drug resistance be encouraged.

The Committee recalled that the June 2005 Meeting of the New Zealand Medicines Classification Committee (MCC) considered a submission for the reclassification of oseltamivir to restricted medicine but the decision was deferred pending further information, including the results of the NISN trial. The MCC also requested Medsafe to investigate the possibility of making oseltamivir available as a restricted medicine only when an influenza outbreak was declared in a particular area. The MCC will consider oseltamivir again at its next meeting (December 2005).

The Committee also recalled that, for the October 2004 Meeting, the evaluator of the XXXXXXXX submission did not support rescheduling and raised the following points:

- While XXXXXXXX asserted that the clinical diagnosis of influenza was reliable, the clinical experience and data did not support this assertion. Moreover, misdiagnosing conditions such as bacterial pneumonia is a potential risk.
- Point-of-care tests are available for diagnosing influenza but were not incorporated in the sponsor's suggested diagnosis algorithm.
- Current data on the potential for the development and spread of resistance to NIs is only preliminary and therefore insufficient to rule out a risk of widespread resistance developing.
- While XXXXXXXX did not support rescheduling, should the Committee decide to reschedule oseltamivir to S3, XXXXXXXX would support an Appendix H listing.
- XXXXXXXX supported XXXXXXXX's view (i.e. for oseltamivir to remain S4).

Overall, it was recalled that the October 2004 NDPSC Meeting considered the data available were inadequate in providing reassurance that rescheduling oseltamivir to S3 would not facilitate drug resistance. It was recognized that a conservative approach is required as reversing resistance rates may not be possible. The Committee also felt that it would be helpful to incorporate an optimized point-of-care diagnostic test into the supply algorithm.

The Committee was reminded that XXXXXXXX wrote to the NDPSC Chair in January 2005 asking for the Committee to defer its decision to allow input from XXXXXXXX. In this correspondence XXXXXXXX raised a number of points which were considered at the February 2005 Meeting. They were, in summary:

- The potential for resistance to develop is, as yet, not properly ascertained.
- The potential reduction of vaccine use in the inter-pandemic period.
- The potential for considerable wastage through inappropriate use.
- The likelihood of stock depletion during a pandemic.

The Committee considered a further submission from XXXXXXXX, provided in September 2005, in response to issues raised by XXXXXXXX. XXXXXXXX pointed out that a major focus for both XXXXXXXX and the NDPSC is the question of NI

resistance and the availability of data from the NISN. XXXXXXXX explained that the chairperson of the NISN would be making a presentation on as yet unpublished data on monitoring activities between 1999 and 2004 at a Roche symposium which was to be held at the European Scientific Working group on Influenza (ESWI). XXXXXXXX stated that they intended to provide this data to the NDPSC prior to the October Meeting.

The Committee considered the following arguments that XXXXXXXX offered on the subject of resistance:

- Resistance only occurs in people that actually have influenza. There is no risk of a resistant virus emerging in a patient given oseltamivir who is infected with any other respiratory virus. Furthermore, the likelihood of a person infected with a resistant strain of influenza virus being supplied oseltamivir is exactly the same whether that supply is through a doctor's prescription or through a pharmacist.
- There is already a significant body of data demonstrating the low incidence of resistance to oseltamivir. XXXXXXXX quotes an article from Ward et al, 2005 which states the cumulative incidence of resistance in adults and adolescents is 0.4%. Furthermore, monitoring studies from the NISN have shown that only 0.1% of 2691 isolates collected from 1999 to 2002 have shown resistance to NIs. Data from Japan shows that only 4 out of 1180 (0.4%) influenza A isolates from the 2003-2004 flu season showed oseltamivir resistance.
- Potentially, resistance to antivirals is more likely when there is a high viral turnover and high viral load. Earlier treatment reduces viral load and should therefore reduce incidence of resistance.
- There is no worsening of patient symptoms in resistant viral infections. Animal studies show that a virus resistant to neuraminidases is less "fit" and therefore compromised, preventing transmission and infectivity.
- Transfer of resistance from a seasonal strain to a pandemic strain could only occur via neuraminidase gene reassortment, requiring a person to be co-infected with both strains simultaneously. Add to this the fact that the resistant strain is less "fit" so there would be no selection advantage for the pandemic virus.

The Committee also considered these other points made by XXXXXXXX:

- In reply to XXXXXXXX's comment that OTC sales of oseltamivir will deplete supplies required for a pandemic stockpile, XXXXXXXX stated that the seasonal supply chain is separate to the pandemic supply chain and XXXXXXXX has an obligation to ensure that large pandemic orders do not compromise seasonal supply. XXXXXXXX's argument was that, as supply is driven by demand, rescheduling oseltamivir would increase demand and therefore ensure greater supply for both seasonal and pandemic requirements.
- XXXXXXXX also stated that, with the planned diagnosis algorithm, there would not be a greater likelihood of inappropriate treatment through S3 supply than there is now

through GPs. Furthermore, they stated that a point of care test is unnecessary because current tests do not have the required sensitivity or specificity.

- XXXXXXXX refuted the statement from XXXXXXXX that there isn't strong evidence to support claims of fewer deaths and lower hospitalization rates by quoting a retrospective cohort study using claims data from a US health insurer. They further stated that use of oseltamivir prophylactically is a TGA approved indication and would not increase likelihood of resistance. They believe that the UK experience (i.e. supply through trained pharmacists) is useful for basing the education and training requirements for pharmacists here in Australia. They also put forward that, by allowing advertising of oseltamivir should it become S3, there would be an increased awareness in the community of influenza and this in turn will increase vaccination rates.

The Committee noted comment received from XXXXXXXX where they raised the following points:

- That the profile of oseltamivir fits well with the NDPSC Guidelines for Schedule 3 medicines. The criteria which fitted within the guidelines included the fact that oseltamivir is substantially safe in use but requires professional advice or counselling by a pharmacist. Furthermore, the symptoms of influenza can be identified by the consumer and verified by the pharmacist and do not require medical diagnosis.
- The need for early treatment with oseltamivir and the low risk profile of the medicine makes it appropriate and in the public interest for the product to be advertised.

The supplementary XXXXXXXX submission, which summarized data presented at the European Scientific Working Group (ESWI) was received 7 October 2005. Briefly, this additional data addressed issues of resistance, through an abstract of a presentation made to XXXXXXXX by XXXXXXXX of the Neuraminidase Susceptibility Network (NISN) and also through findings from the Influenza Branch of the US Centre for Disease Control and Prevention. This submission also provided details of two new studies: Nordstrom et al (a retrospective cohort study) and McGeer et al. The Committee noted this new data presented by XXXXXXXX. One Member pointed out that the first study only used data from patients who had been supplied oseltamivir through a doctor's prescription while the second study looked at patients who required hospitalization as a result of influenza and then were treated with oseltamivir. Thus, neither study was completely relevant to oseltamivir being supplied as an S3 medicine.

One Committee Member raised their own concerns about resistance. The Member specifically quoted data from the article by Ward et al (previously mentioned). The covering letter from XXXXXXXX suggested that the overall resistance rate to oseltamivir is 0.4% (a figure which appears to have been garnered from the article by Ward et al). Apart from the higher figures in Japanese children, the only resistance rates the Member could find in this article were the incidence rates in clinical trial samples (0.33% in adults and adolescents, 4% in children and 1.26% overall). The Member stated that the article postulates on possible reasons for the higher incidence of resistance

described in children and goes on to suggest that this implies that the treatment of pandemic influenza in a totally naïve population may require higher exposures or longer treatment periods, or both, in order to reduce the potential for emergent resistant viruses. The Member also referred to another article supplied by XXXXXXXX (McKimm-Breschkin) which described results of recent animal studies that might raise concern. The article referred to a study in ferrets where, although mutant virus was not transmitted to contact animals, wild-type virus was isolated from contact animals, as though the mutant virus underwent reversion in the original infected animal. The article then put forward the theoretical possibility that oseltamivir treatment could generate a resistant mutant, which may result in continued spread of a wild type revertant virus after cessation of treatment. The article also quoted another study in ferrets which did show transmission of at least two different mutated viruses, despite compromised growth in vitro.

Another concern raised was that an S3 listing for oseltamivir would potentially mean that the capacity to obtain epidemiological data, including resistance patterns may be lost. Given that key stakeholders such as the NISN and XXXXXXXX have stressed the importance of ongoing monitoring, the Committee believed this to be a highly relevant issue.

Regarding the correct diagnosis of influenza, a Member raised the point that, as per the supply algorithm, the accuracy of diagnosis would increase as the prevalence of influenza increased. One Member pointed out the potential logistical issues of a patient's spouse/ carer presenting at a pharmacy rather than the patient themselves and such a situation would make correct diagnosis extremely difficult. The Committee was reminded that early stages of pneumonia can mimic early stages of influenza and this warrants physical examination prior to diagnosis. Several Members suggested that alternative channels of supply (other than via a doctor's prescription) would be appropriate, should a pandemic situation arise. The Committee was informed that pandemic treatment plans are not of the same paradigm as normal diagnosis and treatment. A Member suggested that making oseltamivir available now through pharmacists for seasonal treatment of influenza would guarantee that pharmacists are educated and ensure less confusion if or when a pandemic arrives. Regardless, one Member felt that it would be more reassuring for the community that pharmacists were fully educated for proper diagnosis before any rescheduling takes place.

The Committee further discussed seasonal vs. pandemic supply issues. Concern was raised about the perceived current worldwide shortage of oseltamivir. A Member pointed out that an increased demand in seasonal stock would ensure, through economies of scale, that pandemic stock availability would increase. While a number of Members agreed that the increased demand that would occur with an S3 listing might lead to an increased manufacturing capacity and therefore ensure adequate supplies should a pandemic occur, one Member felt that the logic of this statement was slightly at odds with XXXXXXXX's comment that the seasonal supply chain and the pandemic stockpile supply chain should be considered separate and XXXXXXXX's further statement that they had an obligation to ensure that pandemic stockpiles did not compromise seasonal supply. Another Member

stated that the situation that was currently being considered for rescheduling was seasonal influenza and not a pandemic so the Committee should only be concerned with issues relating to seasonal influenza. With that in mind, it was felt that it would be more appropriate that other avenues are explored to improve accessibility to oseltamivir for seasonal, rather than through down-scheduling. Such an approach would fit in with the recommendation from XXXXXXXX that GP authorities be given the opportunity to address the issue of prompt access to primary care physicians for those with respiratory symptoms during the influenza season prior to any decision for rescheduling being made.

OUTCOME

The Committee agreed that the current scheduling of oseltamivir remains appropriate for the following reasons:

- concerns regarding the likelihood of correct diagnosis by pharmacists without accurate point-of-care tests or physical examination during non-pandemic periods.
- concerns raised in regards to currently available inconclusive data relating to the likelihood of the development of resistance.

Further to and in line with these concerns, the Committee acknowledged the need for the continued gathering of epidemiological data in relation to prevalence/ resistance of influenza. Such data-gathering would be logistically difficult, should oseltamivir be down-scheduled. The Committee would also like to see possible arrangements explored for appropriate access to oseltamivir should a either a localised outbreak or an influenza pandemic occur.

13.2 MICONAZOLE

PURPOSE

The Committee considered the foreshadowed amendment to the Schedule 2 entry for miconazole from the June 2005 NDPSC Meeting.

BACKGROUND

Miconazole is an imidazole antifungal agent active against a wide variety of common fungi. Miconazole has been used for skin infections such as athlete's foot and ringworm, nail infections such as tinea pedis and for vaginal yeast infections. It has also been used orally for the treatment of oral and intestinal candidiasis. Intravenous infusion of miconazole has been used in the treatment of disseminated fungal infections although other azoles are now more commonly used.

The November 1988 NDPSC Meeting considered a proposal to reschedule miconazole from Schedule 3 to Schedule 2 for topical use. This request was supported due to a good safety record established over several years of use. However, there was objection to the

use of miconazole for the treatment of external vaginal irritation. The May 1989 Meeting considered the company's reply that the proposed uses of the XXXXXXXX range of topical products would include those minor fungal infections found in body skin folds and other areas such as the nails, but would not include external vaginal irritation caused by more serious vaginal infections which require clinical treatment and advice. The Committee confirmed a Schedule 2 miconazole entry "for human use in preparations containing 2 per cent or less of miconazole for treatment of fungal infections of the skin".

At the May 1990 NDPSC Meeting the Committee agreed to amend the Schedule 2 miconazole entry to "for human use in topical preparations containing 2 per cent or less of miconazole, for the treatment of fungal infections of the skin" to preclude the possible interpretation of the existing wording to include internal treatment.

At the November 1996 NDPSC Meeting the Committee agreed that the entries for the topical imidazoles, including miconazole, be amended in line with a new ketoconazole entry "for human use in dermal preparations" from the same meeting. The Members agreed that the inclusion of restrictions on concentration and a statement on the use of the preparations e.g. "for the treatment of fungal infections of the skin", would no longer be required as this was seen to be an issue of concern to the registration area. The Committee therefore agreed to amend the Schedule 2 miconazole entry to "for human use in dermal preparations". The Committee did not appear to consider any implications for the application of miconazole to nails in this shift from a topical to dermal definition.

At the June 2005 NDPSC Meeting the Committee considered foreshadowed amendments to topical antifungals which were the result of proposals from the TTHWP in relation to the harmonisation with New Zealand of scheduling for certain substances for the treatment of tinea pedis (bifonazole, clotrimazole, econazole, ketoconazole, miconazole, oxiconazole and tioconazole). In New Zealand, products containing these substances for the treatment of tinea pedis were exempt from scheduling. The Committee agreed that in order to harmonise with New Zealand, the Schedule 2 and Schedule 4 miconazole entries be amended to include an exception for the treatment of tinea pedis.

A separate but related issue – the interpretation of "Dermal Use", "Topical Use" and "External" as applied to substances for use on nails (see Item 2.1.1) – was also considered at the June 2005 NDPSC Meeting. An outcome of this consideration was that, although the Schedule 2 entry for miconazole uses dermal, the definition of "Dermal Use" in the SUSDP refers to skin with no reference to nails and as such products like XXXXXXXX could be considered to be captured by Schedule 4, an outcome which appeared unintended. The Committee therefore agreed for clarity to foreshadow an amendment to the Schedule 2 miconazole entry to allow application to nail in the absence of any public health concerns. The foreshadowed Schedule 2 amendment was:

MICONAZOLE for human use in dermal preparations and for application to the nails
except in preparations for the treatment of tinea pedis.

DISCUSSION

The Committee again noted two submissions from XXXXXXXX that were considered at the June 2005 NDPSC Meeting regarding its recent application to the Over-the-Counter (OTC) Medicines Section, TGA, to introduce several changes to the Product Information and label for XXXXXXXX, an antifungal treatment tincture for fungal nail infections containing the active miconazole. The OTC Section's response was that XXXXXXXX should be classified as a Schedule 4 product, citing the current definition of "Dermal Use" in the SUSDP.

The Committee reviewed XXXXXXXX request that Members consider two options:

- amend the miconazole entry to read "for human use in dermal preparations including fingernails and toenails; or
- amend the definition of dermal to include fingernails and toenails as well as the skin.

The Committee also again noted from the OTC Section's response the assertion that while the Schedule 2 entry for miconazole included dermal, this entry had been there for a long time and, at the time of the entry, there was no definition of "Dermal Use". The OTC Section had further noted that as "Dermal Use" referred to skin with no reference to nails, the OTC considered that products such as XXXXXXXX were captured by Schedule 4, an outcome which appeared unintended. The Committee also noted that the OTC Section's interpretation that products such as XXXXXXXX were captured by Schedule 4 did not appear to have been widely disseminated to manufacturers who still largely appeared to consider their nail products as dermal. The Committee considered the definition of "Dermal Use" in relation to the application to nail under Item 2.1.1. It was agreed that for medicines applied to the nail to specify this use in the schedule entry. Accordingly, Members agreed that amending the Schedule 2 entry for miconazole to explicitly state application to nail would resolve this issue.

The Committee also noted adverse reaction data in a Martindale monograph on miconazole. The Members particularly noted that local irritation and sensitivity reactions may occur when miconazole nitrate was used topically and that contact dermatitis had been reported.

The Committee considered a submission from XXXXXXXX supporting the separate identification in the miconazole entry for use on nails. The Members noted that XXXXXXXX supported this approach for other substances for use on nails (see Item 2.1.1).

DECISION 2005/45-13

The Committee agreed, in order to clarify the scheduling of miconazole products for use on nail and in the absence of any public health concerns, to confirm the foreshadowed decision from the June 2005 NDPSC Meeting and amend the Schedule 2 entry for miconazole to allow application to the nail.

Schedule 2 - Amendment

MICONAZOLE – Amend entry to read:

MICONAZOLE for human use in dermal preparations and for application to the nails **except** in preparations for the treatment of tinea pedis.

13.3 AMISULPRIDE

PURPOSE

The Committee considered the foreshadowed decision to include amisulpride in Appendix K of the SUSDP.

BACKGROUND

Amisulpride is an atypical antipsychotic of the benzamide class. It is indicated for the treatment of acute and chronic schizophrenic disorders in which positive symptoms (such as delusions, hallucinations, and thought disorders) and/or negative symptoms (such as blunted affect, emotional and social withdrawal) are prominent, including patients characterised by predominant negative symptoms.

Amisulpride was included in Schedule 4 at the November 2000 NDPSC Meeting on the grounds of harmonisation with New Zealand and that it was a new substance and the condition being treated required medical management.

The June 2005 NDPSC Meeting considered the foreshadowed decision to include amisulpride in Appendix K of the SUSDP. At the time, the Committee found it difficult to evaluate the sedation potential of amisulpride. A concern was expressed that inclusion of a substance in Appendix K that may not cause drowsiness would dilute the importance of the sedation warning label. Due to the conflicting information from the available data, PI and CMI documents for amisulpride relating to its sedating potential, the Committee agreed to defer consideration of this matter and seek expert advice from the ADEC.

DISCUSSION

The Committee was informed that the ADEC advice on the matter discussed was not yet received.

The pre-meeting submission from XXXXXXXX stated that they wish to reserve the right to comment once the advice from the ADEC had been received.

OUTCOME

The Committee agreed to defer further consideration on the inclusion of amisulpride in Appendix K of the SUSDP until advice from the ADEC is received.

13.4 PHENYLEPHRINE

PURPOSE

The Committee considered the scheduling of phenylephrine with a view to harmonising with New Zealand.

BACKGROUND

Phenylephrine hydrochloride is a sympathomimetic with mainly direct effects on adrenergic receptors. It has predominantly alpha-adrenergic activity and is without significant stimulating effects on the CNS at therapeutic doses. Its pressor activity is weaker than that of noradrenaline but of longer duration. After injection it produces peripheral vasoconstriction and increased arterial pressure; it also causes reflex bradycardia. It reduces blood flow to the skin and to the kidneys. Phenylephrine and its salts are most commonly used, either topically or by mouth, for the symptomatic relief of nasal congestion. They are frequently included in preparations intended for the relief of cough and cold symptoms. For nasal congestion, a 0.25 to 1% solution may be instilled as nasal drops or a spray into each nostril every 4 hours as required, or phenylephrine hydrochloride may be given by mouth in doses up to 20 mg every four hours. In ophthalmology, phenylephrine hydrochloride is used as a mydriatic.

Phenylephrine was first considered by the Committee in August 1967. At that stage, all substances containing phenylephrine and its salts were put into Schedule 3. In January 1969, an exemption from scheduling requirements was made to this entry for tablets or capsules containing 0.5% or less, for other preparations for internal use containing 0.1% or less and for substances, other than preparations for internal use, containing 0.5% or less. In May 1986, ophthalmic preparations containing 5% or more were made Schedule 4. In August 1991, parenteral forms of phenylephrine were added to the Schedule 4 entry. At the November 1999 Meeting, as a result of recommendations from the trans-Tasman Harmonisation Working Party (TTHWP), the Committee amended the Schedule 2 entry for phenylephrine. It was noted at the November 1999 Meeting that the amendment only obtained partial harmonisation with New Zealand but the Committee decided that there should be no variation to the scheduling decision taken by the Australian Health Ministers Advisory Council Committee. The wording from that amendment remained current at the time of the October 2005 Meeting.

At the June 2004 Meeting, the Committee considered the TTHWP Decision 10/4 to remove phenylephrine from the 2-year list of unharmonised substances. At this meeting, the Committee noted that harmonisation efforts were focused on scheduling provisions and that differences in supply arrangements within both countries could lead to an unharmonised approach in respect to supply. This is the case with phenylephrine because, despite consistency with scheduling provisions, nasal preparations containing phenylephrine will continue to be sold at airports in New Zealand. The Committee decided therefore to remove phenylephrine from the 2-year list.

DISCUSSION

It was highlighted that the November 2004 MCC Meeting considered a submission from XXXXXXXX which proposed to amend the current scheduling of phenylephrine, expressed as a percentage to accommodate liquid dose forms, to allow a cut-off point of 10 milligrams or less per oral dose form for general sale and a pharmacy-only classification for solid dose forms containing more than 10 milligrams. The MCC noted that the scheduling changes that were made in 1999 which moved products containing 0.5% of phenylephrine to general sale were made according to the principles of harmonisation and that, at the time of the scheduling change, there were no products marketed in New Zealand that would be affected.

The following points were raised during the discussion of this submission:

- A literature review revealed that phenylephrine has variable bioavailability (up to 30% was quoted) due to metabolism through the gut wall. The therapeutic index was referred to as good and effects on blood pressure occur at doses which were substantially higher than those used for nasal decongestion.
- Data from New Zealand's Centre for Adverse Reaction Monitoring (CARM) showed only 19 ADRs for phenylephrine since 1965, most of which could not be prevented by health professional intervention in the sale of the product. It was noted that phenylephrine had not been widely available in New Zealand for the last 10 years. A literature search on ADRs in the UK (where phenylephrine has been widely available for some time) revealed relatively few reports.
- Phenylephrine is not easily converted to methamphetamine.
- Possible drug interactions include monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants, selegine and methyldopa.
- Rescheduling with a total daily dose cut-off rather than a unit dose cut-off would allow for slow-release preparations as well, should companies choose to develop slow-release formulations.

The November 2004 MCC recommended that phenylephrine for oral use should be a general sale medicine in products containing 50 milligrams or less per recommended daily dose for consumers under 65 years of age and that products recommending higher doses or use by the elderly should be pharmacy-only medicines and that this classification should be reviewed by a joint committee in two years.

The Committee recalled that the TGA had approved an application from XXXXXXXX to register XXXXXXXX (containing phenylephrine XXXXXXXX mg per tablet) on XXXXXXXX. The approved indication was for blocked or runny nose in adults and children over 12 years of age. The recommended dose was one tablet every four hours, with a maximum of six tablets in twenty-four hours. The pack size was 24 tablets. This product was classified in New Zealand as General Sale, while Schedule 2 in Australia. The OTC Medicines Section had informed the NDPSC Secretariat in September that

XXXXXXXX had registered XXXXXXXX more products containing phenylephrine with chlorpheniramine and paracetamol for relief of sinus pain/congestion and relief of allergies. These were formulated to replace products containing pseudoephedrine and are named XXXXXXXX. These XXXXXXXX products are also available in New Zealand.

Members noted that a search of the ADRAC database had revealed a total of 37 reports of reactions relating to phenylephrine (14 of which where it was the sole suspected substance) and 33 reports for phenylephrine hydrochloride (12 of which where it was the sole suspected substance).

Public submissions were received from XXXXXXXX, XXXXXXXX, XXXXXXXX, XXXXXXXX, XXXXXXXX and XXXXXXXX.

- XXXXXXXX sent in a pre-meeting comment to support harmonisation with New Zealand. Their argument was that the current Schedule 2 phenylephrine entry is such that a large divided dose would be required.
- XXXXXXXX strongly recommended the retention of all solid dosage forms of phenylephrine to remain in Schedule 2. They argue that, because consumers might incorrectly assume that phenylephrine is an equivalent replacement for pseudoephedrine, solid dosage forms should only be available from an environment where there are opportunities for intervention and where professional advice is available.
- XXXXXXXX had also stated in their pre-meeting comment that phenylephrine solid dose forms should remain in Schedule 2. They state that the 'umbrella branding' of XXXXXXXX means that, if consumers self-select, they will assume it to be an equally effective product as that which contains pseudoephedrine. XXXXXXXX maintained that, because the FDA use identical warnings for pseudoephedrine and phenylephrine in regards to cardiac risks, effects on prostate and interaction with monoamine oxidase inhibitors (MAOIs), it is illogical to make phenylephrine a general sale product. XXXXXXXX also voiced concerns with the MCC's statement that labelling can address concerns regarding the risk of consumers doubling up on sympathomimetic ingredients. They further contested that labelling can ensure that consumers over 65 years of age will not purchase phenylephrine from supermarkets.
- XXXXXXXX's only concern was that any consideration of the scheduling of phenylephrine in Australia and New Zealand take into account that their products (containing XXXXXXXX % phenylephrine) are currently unscheduled in both countries and would prefer this situation to remain unchanged.
- XXXXXXXX's submission was substantial. In brief, the following points were made:
    - There is a considerable body of evidence to demonstrate that phenylephrine is a safe and effective substance at therapeutic doses. They support harmonisation with New Zealand and to not harmonise would be detrimental to industry viability.

- The ADRs reported to various regulatory agencies were quoted. Australia and New Zealand were mentioned, as was the United Kingdom. Figures from the UK Medicines Control Agency database showed a total of 166 reports involving 227 AE (39 for single ingredient products) from 1963 to June 2004.
- Phenylephrine oral doses (liquid or solid) containing 10mg are general sale items in the UK, Canada and the USA.
- Mention was made of phenylpropanolamine being withdrawn from the market and pseudoephedrine then becoming popular for cold and flu treatments. They state that as far as abuse potential goes, phenylephrine differs structurally to phenylpropylamines that have been abused/ used for illicit purposes. XXXXXXXX compared the chemical structure of phenylephrine to substances such as dexamphetamine, methamphetamine and methylenedioxymethylamphetamine (MDMA – ecstasy) and from this argued that it would be highly unlikely that phenylephrine would either be used as a precursor for any of the abusable amines or that phenylephrine itself would be abused.

One Committee Member highlighted that solid dose form phenylephrine products have been available as general sale products in the United Kingdom for over twenty years with minimal reports of adverse events. This Committee Member reiterated the point that, as phenylephrine is unlikely to be used as a precursor for methamphetamine, it is safer than pseudoephedrine from a public health safety point of view.

A Committee Member felt the argument provided in one of the submissions that, because phenylephrine is a less potent sympathomimetic than pseudoephedrine, it should remain a Schedule 2 substance was not convincing. Another Member was of the view that, while down-scheduling of phenylephrine will in all likelihood eventually occur, if this happens at the same time as pseudoephedrine being up-scheduled, it may potentially confuse some consumers.

A Member reminded the Committee of the issues surrounding the substance oxedrine. Oxedrine is a naturally occurring sympathomimetic amine which was scheduled S4 by the Committee in February 2003 due to public safety concerns after its use was being promoted as an appetite suppressant. The Member felt that, if phenylephrine were to be down-scheduled, companies may promote products containing phenylephrine for weight loss. It was pointed out that, such products would be deemed therapeutic goods and as such would need to go through the TGA process before they could be marketed.

DECISION 2005/45-14

The Committee agreed, on the grounds of the safety profile of oral phenylephrine (which is demonstrated in part by the lengthy market experience as a general sale item in the United Kingdom) and on the grounds of harmonisation with New Zealand, to amend the current Schedule 2 entry for phenylephrine to increase the exemption for oral use to include preparations containing 50mg or less per recommended daily dose. It was also

agreed that the labelling issues raised by the MCC should be referred to the MEC for consideration.

Schedule 2 – Amendment

PHENYLEPHRINE – Amend entry to read

PHENYLEPHRINE **except**:

(a) when included in Schedule 4;

(b) in oral preparations containing 50 mg or less of phenylephrine per recommended daily dose in packs containing 250 mg or less of phenylephrine; or

(c) in topical eye or nasal preparations containing 1 per cent or less of phenylephrine.

13.5 REQUIRED ADVISORY STATEMENTS FOR MEDICINE LABELS

PURPOSE

The Committee considered the foreshadowed proposal on consequential amendments to the SUSDP for consistency with the *Required Advisory Statements for Medicine Labels* (RASML). The Committee also considered an apparent inconsistency between the SUSDP definition of "primary pack" and "labels" than that used in the RASML.

BACKGROUND

The warning statements and safety directions related to human medicines in Appendix F, Part 3 of the SUSDP and the "reverse schedule" entries (substances required to carry mandatory warning statements as a condition of exemption from scheduling) were included in a new document, the RASML. The RASML was given legal effect in relation to medicines via *Therapeutic Goods Order 69* (TGO 69 as amended by TGO 69A – effective 1 July 2004), which required medicines to include statements in accordance with the provisions of the RASML. The RASML also provided a one-year transition period for existing products and took full effect on 1 July 2005.

The February 2005 NDPSC Meeting considered a paper prepared by TGA's Over-the-Counter (OTC) Medicines Section proposing consequential amendments to the SUSDP for consistency with RASML. The Committee agreed that there may be a need to retain the Appendix F, Part 3 entries for human therapeutic use until the Joint Agency commences operation, including certain 'reverse scheduling' provisions specified in the Schedules for substances that may have a dual purpose of use. The Committee also

agreed to foreshadow the proposed consequential amendments to the SUSDP for consideration at the June 2005 meeting.

However, the Committee did not proceed with the foreshadowed amendments to the SUSDP at the June 2005 NDPSC Meeting. The Committee instead agreed to reconsider the matter at the October 2005 NDPSC Meeting, following resolution of an apparent inconsistency between the SUSDP definition of "primary pack" and "labels" than that used in the RASML. The definitions were:

SUSDP

- "**Primary pack**" means the pack in which a poison and its immediate container or immediate wrapper or measure pack are presented for sale or supply.
- "**Label**" means a statement in writing on a container of a poison.
- "**Immediate container**" includes all forms of containers in which a poison is directly packed but does not include any such container intended for consumption or any immediate wrapper.

Therapeutic Goods Act 1989 (the Act)

- "**Primary Pack**", in relation to therapeutic goods, means the complete pack in which the goods, or the goods and their container, are to be supplied to consumers.
- "**Label**", in relation to therapeutic goods, means a display of printed information:

  (a) on or attached to the goods; or

  (b) on or attached to a container or primary pack in which the goods are supplied; or

  (c) supplied with such a container or pack.

TGO 69

- "**Label**" means a display of printed information upon, or securely affixed to, the container and any primary pack containing the goods.
- "**Main Label**" means:
  - where there are two or more labels or two or more portions of a single label - that label or portion of the label where the product name is more or most conspicuously shown; or
  - where the product name is equally conspicuous on two or more labels or portions of a label - each such label or portion;
- "**Primary Pack**" has the same meaning as in subsection 3(1) of the Act

RASML

- "**Label**" has the same meaning as defined in subclause 2(1) of TGO 69.
- "**Main Label**" has the same meaning as defined in subclause 2(1) of TGO 69.

- "**Primary Pack**" has the same meaning as defined in subsection 3(1) of the Act.

DISCUSSION

The Committee recalled that the OTC Medicines Section, in their pre-meeting comment for the June 2005 NDPSC Meeting supported the foreshadowed amendments with one exception. The OTC Section had initially proposed the following wording for amendment to the reverse schedule entries which mandate label warning statements for exemption from the SUSDP and to the Appendix F general exemption statement:

- "…. the label on the goods complies with the requirements of the *Required Advisory Statements for Medicine Labels*"

The Committee also recalled, however, their decision to change the word 'goods' to 'primary pack' for consistency with the wording used throughout the SUSDP. The resulting foreshadowed change was:

- "… the label on the primary pack complies with the requirements of the Required Advisory Statements for Medicine Labels"

The Committee noted that the OTC Section asserted that the foreshadowed entries with the wording 'primary pack' could potentially be interpreted incorrectly. For example, many medicines to which these changes would apply would be supplied in an immediate container but without a primary pack, as currently defined in the SUSDP. Furthermore, since 'container' was not defined in the SUSDP, it could be argued that information included on a primary pack would not constitute a label. To avoid confusion, the OTC Section suggested that the definition of 'primary pack' and 'label' in the SUSDP be amended as follows to be consistent with the definitions included in the *Therapeutic Goods Act 1989* and TGO 69, i.e.:

- '**Primary pack**' means the pack in which a poison, or a poison and its immediate container or immediate wrapper or measure pack are presented for sale or supply.
- '**Label**' means a statement in writing on, or securely affixed to, an immediate container and any primary pack of a poison.

The Members further noted a submission from XXXXXXXX supporting the foreshadowed amendments to the SUSDP for consistency with the RASML. XXXXXXXX disagreed with some of the comments at the June 2005 NDPSC Meeting which had objected to the foreshadowed changes because RASML should be brought in line with the SUSDP, not the other way around. XXXXXXXX, however, felt that the entries in each document are the same, albeit occasionally phrased differently. XXXXXXXX also noted that, of those particular entries which were of concern to some stakeholders, the entries for essential oils in the RASML were basically correct but XXXXXXXX agreed that they were hard to understand. XXXXXXXX indicated that that they will approach the OTC Section to discuss this and that XXXXXXXX was satisfied with the current SUSDP entries for the essential oils.

The Committee also noted a submission from XXXXXXXX indicating that they do not object to the transfer of label statements to the RASML, as long as there are no amendments to the label statements, particularly for ibuprofen.

A Member advised the Committee that the Joint Expert Committee on trans-Tasman Labelling of Medicines were also looking at definitions including "Primary pack". The Member asserted that it may be premature for the Committee to change its definition, and that it may be more appropriate to wait until such time as the Joint Agency Labelling Order document has been finalised. This document was expected to, among other things, set out the labelling definitions that the Joint Agency would apply to therapeutic products.

In light of this information, a Member proposed that a possible solution with regard to the Appendix F general exemption statement was to refer therapeutic products directly to RASML in a similar way to how agvet products are currently refered to the APVMA. The solution proposed by the Member was that the Committee go ahead with the foreshadowed general exemption statement but avoid the words "the label on the primary pack" i.e.:

[other than agricultural and veterinary chemicals (including pesticides) registered by the Australian Pesticides and Veterinary Medicines Authority and
medicines for human use when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*]

The Committee agreed that if this wording were adopted into Appendix F then therapeutic products would need to comply with the definitions in the RASML, which were expected to align with the TGA definitions, while non-therapeutics (and non-agvets) would continue to fall under the definitions within the SUSDP. The Members agreed in principle that this resolved the problems with definitions raised by the OTC Section and that the entry amendments foreshadowed from the February 2005 NDPSC Meeting could be approved out of session following the Meeting. The out-of-session approval was to allow time for the Draft Advisory Panel (DAP) to go through the proposed amendments in-depth and provide feedback to the Members on whether they supported these amendments.

The Committee was advised that the DAP considered the proposed amendments and agreed that adoption of the wording proposed above for the Appendix F general exemption and replacing the current reverse schedule wording with wording to the effect of "compliant with the requirements of the *Required Advisory Statements for Medicine Labels*" would resolve the problems with definitions raised by the OTC Section. Since this approach would not refer to "Primary Pack" or "Label" there would be no need to amend any of the current SUSDP definitions.

The Committee also noted that the Schedule 4 entry for *Piper methysticum* (kava) in the foreshadowed amendments had been changed to reflect the amendment for kava made at the October Meeting (Item 13.8).

DECISION 2005/45-15

The Committee agreed, out-of-session, to the consequential amendments to the SUSDP, foreshadowed at the February 2005 NDPSC Meeting, for consistency with RASML, with a change to the reverse schedule entries removing reference to "Primary Pack" or "Label" . Additionally, the Committee agreed to adopt wording for the Appendix F exemption statement which indicated that therapeutic products would need to comply with the definitions in the RASML. The Members confirmed that non-therapeutics (and non-agvets) would continue to fall under the definitions within the SUSDP.

Interpretation, Part 1 – New entry

"***Required Advisory Statements for Medicine Labels***" means the document of that name published by the Therapeutic Goods Administration on 1 July 2004, as in force from time to time.

Appendix F – Amendment

WARNING STATEMENTS AND GENERAL SAFETY DIRECTIONS FOR POISONS – amend heading to read:

APPENDIX F
WARNING STATEMENTS AND GENERAL SAFETY DIRECTIONS FOR POISONS

[other than agricultural and veterinary chemicals (including pesticides) registered by the Australian Pesticides and Veterinary Medicines Authority and medicines for human use when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*]

Schedule 2 – Amendments

ASPIRIN – amend entry to read:

ASPIRIN **except**:

(a) when included in Schedule 4, 5 or 6;

(b) in individually wrapped powders or sachets of granules each containing 650 mg or less of aspirin as the only therapeutically active constituent **other than** an effervescent agent when:

(i) enclosed in a primary pack that contains 12 or less such powders or sachets of granules; and

(ii) compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in tablets or capsules each containing no other therapeutically active constituent **other than** an effervescent agent when:

(i) packed in blister or strip packaging or in a container with a child-resistant closure;

(ii) in a primary pack of not more than 25 tablets or capsules, each containing 325 mg or less of aspirin, or in a primary pack of not more than 16 tablets or capsules, each containing 500 mg or less of aspirin; and

(iii) is compliant with the requirements of the *Required Advisory Statements for Medicine* Labels;

(d) in tablets or capsules each containing no other therapeutically active constituent **other than** an effervescent agent when:

(i) packed in blister or strip packaging or in a container with a child-resistant closure;

(ii) in a primary pack containing 100 or less tablets or capsules, each containing 100 mg or less of aspirin when packed and labelled for the prevention of cardiovascular disease or for the inhibition of platelet aggregation; and

(iii) compliant with the requirements of the *Required Advisory Statements for Medicine Labels*.

FLUORIDES – amend entry to read:

FLUORIDES for human use (except in preparations containing 15 mg/kg or 15 mg/L or less of fluoride ion):

(a) as sodium fluoride, in preparations for ingestion containing 2.2 mg or less of sodium fluoride per dosage unit; or

(b) in preparations for topical use containing 2.5 per cent or less of fluoride ion **except**:

(i) pastes, powders or gels for the cleaning of teeth, included in Schedule 3;

(ii) pastes, powders or gels for the cleaning of teeth, containing 1000 mg/kg or less of fluoride ion;

(iii) other dental hygiene products, that are therapeutic goods, containing 220 mg/kg or 220 mg/L or less of fluoride ion, in packs containing not more than 120 mg total fluoride, fitted with a child-resistant closure, when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*; or

(iv) other dental hygiene products, that are not therapeutic goods, containing 220 mg/kg or 220 mg/L or less of fluoride ion, in packs containing not more than 120 mg total fluoride, fitted with a child-resistant closure and labelled with warnings to the following effect:

(A) Do not swallow; and
(B) Do not use [this product/name of product] in children six years of age or less.

IBUPROFEN – amend entry to read:

IBUPROFEN in preparations for oral use when labelled with a recommended daily dose of 1200 mg or less of ibuprofen:

(a) in liquid preparations when sold in the manufacturer's original pack containing 4 grams or less of ibuprofen; or

(b) in divided preparations, each containing 200 mg or less of ibuprofen, in packs of not more than 100 dosage units **except** when:

(i) as the only therapeutically active constituent other than an effervescent agent;

(ii) packed in blister or strip packaging or in a container with a child-resistant closure;

(iii) in a primary pack containing not more than 25 dosage units; and

(iv) compliant with the requirements of the *Required Advisory Statements for Medicine Labels.*

PARACETAMOL – amend entry to read:

PARACETAMOL for therapeutic use **except**:

(a) when included in Schedule 4;

(b) in individually wrapped powders or sachets of granules each containing 1000 mg or less of paracetamol as the only therapeutically active constituent other than effervescent agents when:

(i) enclosed in a primary pack that contains not more than 12 such powders or sachets of granules; and

(ii) compliant with the requirements of the *Required Advisory Statements for Medicine Labels;* or

(c) in tablets or capsules each containing each containing 500 mg or less of paracetamol as the only therapeutically active constituent other than effervescent agents when:

(i) packed in blister or strip packaging or in a container with a child-resistant closure; and

(ii) in a primary pack of not more than 25 tablets or capsules; and

(iii) compliant with the requirements of the *Required Advisory Statements for Medicine Labels.*

PYRITHIONE ZINC – amend entry to read:

PYRITHIONE ZINC for human therapeutic use, **except**:

(a) in semi-solid hair preparations; or

(b) in shampoos containing 2 per cent or less of pyrithione zinc when compliant with the requirements of the *Required Advisory Statements for Medicine Labels.*

SILVER – amend entry to read:

SILVER for therapeutic use **except**:

(a) in chewing gum containing 5 per cent or less of silver per dosage unit when compliant with the requirements of the *Required Advisory Statements for Medicine Labels;*

(b) in solutions for human oral use containing 0.3 per cent or less of silver when compliant with the requirements of the *Required Advisory Statements for Medicine Labels;* or

(c) in other preparations containing 1 per cent or less of silver.

Schedule 4 – Amendments

FLUORIDES – amend entry to read:

FLUORIDES in preparations for human use **except**:

(a) when included in Schedule 2 or 3;

(b) in pastes, powders or gels for the cleaning of teeth, containing 1000 mg/kg or less of fluoride ion;

(c) in other dental hygiene products, that are therapeutic goods, containing 220 mg/kg or 220 mg/L or less of fluoride ion, in packs containing not more than 120 mg total fluoride, fitted with a child-resistant closure, when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(d) in other dental hygiene products, that are not therapeutic goods, containing 220 mg/kg or 220 mg/L or less of fluoride ion, in packs containing not more than 120 mg total fluoride, fitted with a child-resistant closure and labelled with warnings to the following effect:

(A) Do not swallow; and
(B) Do not use [this product/name of product] in children six years of age or less; or

(e) in other preparations containing 15 mg/kg or 15 mg/L or less of fluoride ion.

PIPER METHYSTICUM – amend entry to read:

PIPER METHYSTICUM (Kava) in preparations for human use **except**:

(a) in preparations for oral use containing dried whole or peeled rhizome or containing aqueous dispersions or aqueous extracts of whole or peeled rhizome when labelled with a recommended daily dose of 250mg or less of kavalactones and

(i) if in tablet or capsule form containing 125mg or less of kavalactones per tablet or capsule; or

(ii) if in the form of a teabag when the amount of dried whole or peeled rhizome does not exceed 3g;

and, where containing more than 25mg of kavalactones per dose, compliant with the requirements of the *Required Advisory Statements for Medicine Labels*.

(b) in topical preparations for use on the rectum, vagina or throat containing dried whole or peeled rhizome or containing aqueous dispersions or aqueous extracts of whole or peeled rhizome; or

(c) in dermal preparations.

PYRIDOXINE, PYRIDOXAL or PYRIDOXAMINE – amend entry to read:

PYRIDOXINE, PYRIDOXAL or PYRIDOXAMINE for human therapeutic use **except**:

(a) in oral preparations containing 200 mg or less but more than 50 mg of pyridoxine, pyridoxal or pyridoxamine per recommended daily dose except when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*; or

(b) in oral preparations containing less than 50 mg of pyridoxine, pyridoxal or pyridoxamine per recommended daily dose.

VITAMIN A – amend entry to read:

VITAMIN A for human therapeutic or cosmetic use **except:**

(a) in preparations for topical use containing 1 per cent or less of vitamin A;

(b) in preparations for internal use, containing 100 IU or less of vitamin A per dosage unit of a divided preparation, or 100 IU or less of vitamin A per gram of an undivided preparation; or

(c) in other preparations for internal use when compliant with the requirements of the *Required Advisory Statements for Medicine Labels.*

ZINC COMPOUNDS – amend entry to read:

ZINC COMPOUNDS for human internal use **except:**

(a) in preparations with a recommended daily dose of 25 mg or less of zinc; or

(b) in preparations with a recommended daily dose of more than 25 mg but mot more than 50 mg of zinc when compliant with the requirements of the *Required Advisory Statements for Medicine Labels.*

Schedule 5 – Amendments

ANISE OIL – amend entry to read:

ANISE OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 50 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 50 mL or less fitted with a restricted flow insert, and labelled with the warning:

KEEP OUT OF REACH OF CHILDREN; or

(c) in preparations containing 50 per cent or less of anise oil.

BASIL OIL – amend entry to read:

BASIL OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert, and labelled with the warning:

KEEP OUT OF REACH OF CHILDREN; or

(c) in preparations containing 5 per cent or less of methyl chavicol.

BERGAMOT OIL – amend entry to read:

BERGAMOT OIL **except**:

(a) when steam distilled or rectified;

(b) in preparations for internal use;

(c) in preparations containing 0.4 per cent or less of bergamot oil;

(d) in soaps or bath or shower gels that are washed off the skin;

(e) in preparations other than medicines for human therapeutic use, when packed in containers labelled with the statement:

Application to the skin may increase sensitivity to sunlight; or

(f) in medicines for human therapeutic use, when packed in containers and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*.

CAMPHOR – amend entry to read:

CAMPHOR as a natural component in essential oils containing 10 per cent or less of camphor **except**:

(a) in medicines for human therapeutic use, in essential oils packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, in essential oils packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert, and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(c) in rosemary oil, sage oil (Spanish), or lavindin oils; or

(d) in preparations containing 2.5 per cent or less of camphor.

DIETHYLTOLUAMIDE (DEET) – amend entry to read:

DIETHYLTOLUAMIDE (DEET) **except**:

(a) in medicines for human therapeutic use containing 20 per cent or less of diethyltoluamide, when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations for human use, other than medicines, containing 20 per cent or less of diethyltoluamide, when labelled with the warning statement:

WARNING: May be dangerous, particularly to children, if you use large amounts on the skin, clothes or bedding or on large areas of the body, especially if you keep using it for a long time; or

(c) in preparations other than for human use containing 20 per cent or less of diethyltoluamide.

FLUORIDES – amend entry to read:

FLUORIDES in preparations containing 3 per cent or less of fluoride ion **except**:

(a) when included in Schedule 2, 3 or 4;

(b) in pastes, powders or gels for the cleaning of teeth, containing 1000 mg/kg or less of fluoride ion;

(c) in other dental hygiene products, that are therapeutic goods, containing 220 mg/kg or 220 mg/L or less of fluoride ion, in packs containing not more than 120 mg total fluoride, fitted with a child-resistant closure, when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(d) in other dental hygiene products, that are not therapeutic goods, containing 220 mg/kg or 220 mg/L or less of fluoride ion, in packs containing not more than 120 mg total fluoride, fitted with a child-resistant closure and labelled with warnings to the following effect:

(A) Do not swallow; and
(B) Do not use [this product/name of product] in children 6 years of age or less; or

(e) in other preparations containing 15 mg/kg or 15 mg/L or less of fluoride ion.

LEMON OIL – amend entry to read:

LEMON OIL **except**:

(a) when steam distilled or rectified;

(b) in preparations for internal use;

(c) in preparations containing 0.05 per cent or less of lemon oil;

(d) in soaps or bath or shower gels that are washed off the skin;

(e) in preparations other than medicines for human therapeutic use, when packed in containers labelled with the statement:

Application to the skin may increase sensitivity to sunlight; or

(f) in medicines for human therapeutic use, when packed in containers and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*.

LIME OIL – amend entry to read:

LIME OIL **except**:

(a) when steam distilled or rectified;

(b) in preparations for internal use;

(c) in preparations containing 0.5 per cent or less of lime oil;

(d) in soaps or bath or shower gels that are washed off the skin;

(e) in preparations other than medicines for human therapeutic use, when packed in containers labelled with the statement:

Application to the skin may increase sensitivity to sunlight; or

(f) in medicines for human therapeutic use, when packed in containers and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*.

MARJORAM OIL – amend entry to read:

MARJORAM OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 50 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 50 mL or less fitted with a restricted flow insert, and labelled with the warning:

KEEP OUT OF REACH OF CHILDREN; or

(c) in preparations containing 50 per cent or less of marjoram oil.

NUTMEG OIL – amend entry to read:

NUTMEG OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert, and labelled with the warning:

KEEP OUT OF REACH OF CHILDREN; or

(c) in preparations containing 50 per cent or less of nutmeg oil.

ORANGE OIL – amend entry to read:

ORANGE OIL **except**:

(a) when steam distilled or rectified;

(b) in preparations for internal use;

(c) in preparations containing 1.4 per cent or less of orange oil;

(d) in soaps or bath or shower gels that are washed off the skin;

(e) in preparations other than medicines for human therapeutic use, when packed in containers labelled with the statement:

Application to the skin may increase sensitivity to sunlight;
or

(f) in medicines for human therapeutic use, when packed in containers and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*.

STAR ANISE OIL – amend entry to read:

STAR ANISE OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 50 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 50 mL or less fitted with a restricted flow insert, and labelled with the warning:

KEEP OUT OF REACH OF CHILDREN; or

(c) in preparations containing 50 per cent or less of star anise oil.

THYME OIL – amend entry to read:

THYME OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert, and labelled with the warning:

KEEP OUT OF REACH OF CHILDREN; or

(c) in preparations containing 50 per cent or less of thyme oil.

Schedule 6 – Amendments

AZADIRACHTA INDICA (Neem) – amend entry to read:

(†) AZADIRACHTA INDICA (Neem) including its extracts and derivatives **except**:

(a) when included in Schedule 5;

(b) in preparations for human internal use;

(c) debitterised neem seed oil;

(d) in preparations for human dermal therapeutic use containing cold pressed neem seed oil, when in a container fitted with a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*; or

(e) in preparations for dermal use containing 1 per cent or less of cold pressed neem seed oil.

BAY OIL – amend entry to read:

BAY OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(d) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(e) in preparations containing 25 per cent or less of bay oil.

CAJUPUT OIL – amend entry to read:

CAJUPUT OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(d) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(e) in preparations containing 25 per cent or less of cajuput oil; or

(f) in oils containing 25 per cent or less of cajuput oil.

CAMPHOR – amend entry to read:

CAMPHOR **except**:

(a) when included in Schedule 4 or 5;

(b) when enclosed in an inhaler device which prevents ingestion of its contents;

(c) in solid or semi-solid preparations containing 12.5 per cent or less of camphor;

(d) in liquid preparations containing 2.5 per cent or less of camphor;

(e) in essential oils when the camphor is present as a natural component of the oil:

(i) in medicines for human therapeutic use, packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(ii) in medicines for human therapeutic use, packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(iii) in essential oils other than medicines for human therapeutic use, packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(iv) in essential oils other than medicines for human therapeutic use, packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(f) in rosemary oil, sage oil (Spanish), or lavindin oil as such.

CINEOLE – amend entry to read:

CINEOLE **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(d) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(e) in preparations containing 25 per cent or less of cineole;

(f) in oils containing 25 per cent or less of cineole; or

(g) in rosemary oil or camphor oil (white).

CINNAMON LEAF OIL – amend entry to read:

CINNAMON LEAF OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(d) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(e) in preparations containing 25 per cent or less of cinnamon leaf oil.

CLOVE OIL – amend entry to read:

CLOVE OIL **except**:

(a) when included in Schedule 5;

(b) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted

with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(d) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(e) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(f) in preparations containing 25 per cent or less of clove oil.

EUCALYPTUS OIL – amend entry to read:

EUCALYPTUS OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity

of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(d) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(e) in preparations containing 25 per cent or less of eucalyptus oil.

EUGENOL – amend entry to read:

EUGENOL **except**:

(a) when included in Schedule 5;

(b) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(d) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(e) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity

of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(f) in preparations containing 25 per cent or less of eugenol.

FLUORIDES – amend entry to read:

FLUORIDES **except**:

(a) when included in Schedule 2, 3 ,4 or 5;

(b) in pastes, powders or gels for the cleaning of teeth, containing 1000 mg/kg or less of fluoride ion;

(c) in other dental hygiene products, that are therapeutic goods, containing 220 mg/kg or 220 mg/L or less of fluoride ion, in packs containing not more than 120 mg total fluoride, fitted with a child-resistant closure, when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(d) in other dental hygiene products, that are not therapeutic goods, containing 220 mg/kg or 220 mg/L or less of fluoride ion, in packs containing not more than 120 mg total fluoride, fitted with a child-resistant closure and labelled with warnings to the following effect:

(A) Do not swallow; and
(B) Do not use [this product/name of product] in children six years of age or less; or

(e) in other preparations containing 15 mg/kg or 15 mg/L or less of fluoride ion.

MELALEUCA OIL (Tea tree oil) – amend entry to read:

MELALEUCA OIL (TEA tree oil) **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(c) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN;

(d) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 25 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(e) in preparations containing 25 per cent or less of melaleuca oil.

PENNYROYAL OIL – amend entry to read:

PENNYROYAL OIL **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(c) in preparations containing 4 per cent or less of d-pulgone.

PYRITHIONE ZINC – amend entry to read:

PYRITHIONE ZINC **except**:

(a) when included in Schedule 2;

(b) in semi-solid hair preparations;

(c) in shampoos containing 2 per cent or less of pyrithione zinc when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*; or

(d) when immobilised in solid preparations containing 0.5 per cent or less of pyrithione zinc.

SAGE OIL (Dalmatian) – amend entry to read:

SAGE OIL (Dalmatian) **except**:

(a) in medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and a child-resistant closure and compliant with the requirements of the *Required Advisory Statements for Medicine Labels*;

(b) in preparations other than medicines for human therapeutic use, when packed in containers having a nominal capacity of 15 mL or less fitted with a restricted flow insert and a child-resistant closure and labelled with the warnings:

KEEP OUT OF REACH OF CHILDREN; and
NOT TO BE TAKEN; or

(c) in preparations containing 4 per cent or less of thujone.

13.6 BLOOD PRODUCTS

PURPOSE

The Committee considered the foreshadowed decision to schedule fractionated plasma products and comparable recombinant products that are not currently exempted through the entry in Appendix A of the SUSDP.

BACKGROUND

Historically, the Committee has had a standing policy of not scheduling blood products, given that scheduling may place unwarranted restrictions on the supply of products which already have adequate Commonwealth and State/Territory controls.

The Committee recalled that a recombinant octocog alfa (purified recombinant human antihaemophilic Factor VIII concentrate produced from [sentence deleted]) was previously considered by the NDPSC in May 2001. The May 2001 Committee Meeting discussed the use and distribution of recombinant blood products, and were satisfied that the current use of these products in clinical and hospital settings remained appropriate. The Committee noted that octocog alfa has the same biological activity as Factor VIII derived from human plasma but with reduced potential risk of disease transmission. Members agreed that the safety profile for octocog alfa is consistent with similar blood products exempt from scheduling. There was a suggestion that the Committee consider including a general exemption (Appendix A) for blood products for therapeutic use. However, the Committee decided that it would examine such an entry when recommendations arising from the Review of the Australian Blood Banking and Plasma Product Sector are considered.

The final report of the review was considered by the Committee at the February 2005 Meeting. The Committee was satisfied that appropriate regulatory mechanisms were in place to warrant the exemption of blood products from scheduling requirements. These mechanisms included the licensing institutions where blood transfusions take place at State/Territory level and the National Blood Authority (NBA) managing and overseeing the national blood supply and the TGA regulating the safety, efficacy and quality of blood and blood products at a national level. The Committee then agreed to foreshadow the inclusion of blood products in Appendix A of the SUSDP.

The Committee recalled that comments were sought for the June 2005 Meeting from XXXXXXXX and XXXXXXXX and from XXXXXXXX. Briefly, their comments were as follows:

- XXXXXXXX stated that XXXXXXXX only regulated products derived from human plasma, not whole blood or blood components. XXXXXXXX pointed out that it would seem illogical to exempt product derived from blood and not equivalent recombinant products, especially considering some are only available as recombinant products (eg Factor VIIa). Previously, XXXXXXXX manufactured most plasma derived product and this was distributed by XXXXXXXX. More recently, foreign manufactured product is commercially available directly from sponsors and this situation would only increase. XXXXXXXX also noted that plasma-derived products are intended for the treatment of serious disease and as such require medical supervision and so should not be exempt from scheduling.
- XXXXXXXX stated that blood products should not be exempted as the prescription of such products should rest with a medical practitioner. XXXXXXXX also point out that New Zealand regulate all blood and blood component products as medicines prescribed by medical practitioners, excluding anti-RhD immunoglobulin which can be prescribed by midwives.
- XXXXXXXX endorsed the comments from both XXXXXXXX and XXXXXXXX.

- XXXXXXXX was supportive of the proposal to exempt blood products, including those derived from fractionation of plasma, from scheduling requirements and that such an exemption would have minimal direct impact on XXXXXXXX.

The June 2005 NDPSC Meeting concluded that hospitals and health services have policies and guidelines in place to ensure best practise in the supply and use of blood and blood products and these controls obviate the need for scheduling controls. Furthermore, the Committee felt it inappropriate and impractical for a pharmacist to dispense such product, particularly in an emergency setting. However, the Committee was conscious of the shift in supply arrangements of plasma derived product, including foreign-manufactured and recombinant product. Thus the Committee agreed to include an entry in Appendix A of the SUSDP for whole blood and blood components but to foreshadow the consideration of the scheduling of plasma fractionated and comparable recombinant product at the October 2005 Meeting.

DISCUSSION

The Committee considered pre-meeting comment provided by XXXXXXXX. XXXXXXXX pointed out, as background, that they are the primary supplier for plasma-derived products, with XXXXXXXX distributing Normal Immunoglobulin and some overseas-manufactured product distributed directly from sponsors. XXXXXXXX supply these products to hospital blood banks and these are distributed as part of an order for other blood products (eg whole blood). Thus, hospital blood banks have extensive expertise with inventory management, including traceability and appropriate use. Treating medical practitioners are responsible for prescribing to their patients.

XXXXXXXX pointed out that they were of the understanding that the June 2005 NDPSC Meeting was considering exempting all blood products, including fractionated product and comparable recombinant product. XXXXXXXX reiterated their strong support to exempt all blood products and voiced their concern that this no longer seems the case.

The Committee was informed that a teleconference was held by XXXXXXXX which is a committee made up of [sentence deleted]. At this teleconference, there was unanimous support that fractionated blood product be exempted for the following reasons:

- With the current arrangements, it is staff within hospital blood banks and not pharmacy staff that hold the required skills to manage such product.
- Access to such products is required all day, every day. There is concern that access via pharmacy may therefore compromise patient care.
- As rapid access to such product is essential, broader distribution through pharmacies may result in more stock expiring. Given that such product is sourced from plasma of blood donors, replacement of such product is not a simple task.
- XXXXXXXX staff provide a gate-keeper role for product that is in short supply and requests for such products are reviewed by a medical officer. Such a safety net would not exist if these products were supplied via pharmacies.

- Blood component products and plasma-derived product are always supplied simultaneously and this is both simple and cost effective. Scheduling plasma-derived products would require development of new ordering systems.
- Scheduling plasma-derived products would not add value to the health system and may indeed lead to deterioration in optimal patient care.

The Committee discussed the fact that, while there is an increase in recombinant product being made available in Australia, such product is subject to the same stringent registration requirements that any other prescription medicine marketed in Australia must go through. Thus, whether products are assessed by the TGA or whether they are supplied by XXXXXXXX, they must meet certain safety & efficacy standards as well as manufacturing standards.

It was raised by a Member that, while the points that XXXXXXXX put forward are valid (that they have the required expertise, that access to these products is required at all hours of the day etc), there are up to ten recombinant blood products which are already currently being supplied through pharmacy departments. Several Members went on to voice their concerns that although unscheduled recombinant blood products that are supplied through normal pharmacy wholesalers have not yet been inappropriately accessed by persons without appropriate medical training, such a situation cannot be ruled out from happening in the future, should they remain unscheduled.

The Committee considered whether scheduling recombinant blood products and fractionated blood products would have any consequences in regards to labelling requirements. The Committee was reminded that, even if recombinant blood products remained unscheduled, they must still meet the labelling requirements of *Therapeutic Goods Order 69*, given that they are registered therapeutic goods.

Discussion took place as to whether the matter should be referred to the National Co-ordinating Committee on Therapeutic Goods (NCCTG). It was decided that guidance from the NCCTG would not be required unless the Committee felt it appropriate that the NCCTG should make a broad policy decision in regard to supply chain issues, and not just in relation to blood.

One Committee Member had been contacted by XXXXXXXX of the National Blood Authority's (NBA's) Jurisdictional Blood Committee (JBC). The JBC is responsible for all jurisdictional issues relating to the national blood supply, including planning, production, supply, and budgeting. It is also responsible for considering advice from, and providing advice to, the NBA, on matters related to the national blood supply, overseeing the NBA's role in relation to contracts, and referring proposed changes to the national blood supply for evidence-based evaluation. The JBC member aired concern that comment had not been sought from the NBA in regards to the rescheduling of fractionated blood and recombinant blood products. XXXXXXXX had advised that while they are not opposed to the potential scheduling of fractionated blood product and

recombinant blood product per se, they felt that consideration must be given to the impact on the distribution chain that such a scheduling amendment would result in.

XXXXXXXX considered that, while there are no current concerns of fractionated and recombinant blood product being 'diverted' from the treatment of legitimate conditions, there was potential for such diversion to occur in the future. Particular reference was made by XXXXXXXX to Factor VIII, Factor IX and immunoglobulins.

The Committee recalled that XXXXXXXX had consulted with the NBA when XXXXXXXX were developing their response to the proposal to exempt blood products from scheduling requirements.

OUTCOME

The Committee agreed not to include fractionated plasma products and comparable recombinant products in Appendix A to allow such products to be exempt from the requirements of scheduling at this time. The Committee further agreed to seek input from the NBA's Jurisdictional Blood Committee on the possible ramifications of scheduling fractionated blood products and recombinant blood products. The Committee will then consider this input at the February 2006 Meeting.

13.6.1 OCTOCOG ALFA (RCH)

PURPOSE

The Committee considered the scheduling of a new medicine, octocog alfa (rch).

BACKGROUND

At its 237th meeting in December 2004, the ADEC considered a submission from XXXXXXXX to register XXXXXXXX, containing the new chemical entity octocog alfa (rch). The proposed indication was "for use in haemophilia A for prevention and control of haemorrhagic episodes. Patients with haemophilia A may be treated with Advate as peri operative management. Advate is not indicated in von Willebrand's disease". The following points were raised:

[Section deleted]

The ADEC resolved there should be no objection to approval of the application submitted by XXXXXXXX to register XXXXXXXX, containing octocog alfa (rch). Approval was subject to finalisation of the Product Information to the satisfaction of the TGA. Octocog alfa (rch) contains no human protein components.

At the May 1995 NDPSC Meeting, the Committee considered that scheduling of blood products would place unnecessary and possibly overly restrictive controls on blood

specialised products, and that the regulatory arrangements at both State/Territory and Commonwealth levels were more than adequate at the time.

A non-human derived rch octocog alfa was previously considered at the May 2001 Meeting. In October 2000, the ADEC recommended that XXXXXXXX and XXXXXXXX, containing octocog alfa (recombinant Factor VIII), be approved for the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital Factor VIII deficiency). The Committee noted at the May 2001 NDPSC Meeting that XXXXXXXX and XXXXXXXX are a sterile, stable, purified recombinant human antihaemophilic Factor VIII concentrate produced from [sentence deleted].

The Committee agreed that its policy of leaving blood products for therapeutic use unscheduled remained appropriate.

DISCUSSION

The Committee noted that octocog alfa (rch) was a prescription medicine in New Zealand.

At the June 2005 Meeting, the Committee deferred consideration of this item to the October 2005 meeting when a policy position on those products derived from the fractionation of plasma and comparable recombinant products that are currently not scheduled would be further considered.

OUTCOME

The Committee agreed to again defer the decision to schedule octocog alfa (rch), in line with its decision to defer consideration of the scheduling of products derived from the fractionation of plasma and comparable recombinant products, pending further consultation with jurisdictional stakeholders (see Item 13.6).

13.7 PROCHLORPERAZINE

PURPOSE

The Committee considered the scheduling of prochlorperazine.

BACKGROUND

Prochlorperazine is a phenothiazine antipsychotic. Prochlorperazine and its salts are widely used in the prevention and treatment of nausea and vomiting including that associated with migraine or drug-induced emesis. They are also used for the short-term symptomatic relief of vertigo and in the management of schizophrenia, mania and other psychoses.

At the November 1974 NDPSC Meeting the Committee included prochlorperazine in Schedule 4. At the November 1998 and August 1999 NDPSC Meetings the Committee considered changes to prochlorperazine, arising from Trans-Tasman Harmonisation Working Party recommendations for the purposes of harmonisation. The inclusion of the "buccal use" was prompted by the availability of an OTC NZ product specifically for buccal use at that time. The recommendations from the fourth trans-Tasman harmonisation meeting were supported and the current Schedule 3 prochlorperazine entry allowing for "buccal use" was adopted.

At the June 2005 NDPSC the Committee deferred consideration of minor editorial changes and errata, including an amendment to the Schedule 3 entry for prochlorperazine to remove reference to "buccal use", to the October 2005 NDPSC meeting to allow time to seek comment from the NDPSC Drafting Advisory Panel. Following the meeting the Secretariat noted that the prochlorperazine amendment was a scheduling change rather than an editorial change and therefore included prochlorperazine in the pre-meeting gazette notice.

DISCUSSION

The Committee recalled at the June 2005 NDPSC meeting that the New Zealand Medicines Classifications Committee (MCC) had amended the restricted classification entry for prochlorperazine at its May 2002 meeting as the OTC buccal product had been discontinued. It was noted that the present NZ classification for restricted prochlorperazine is now "in packs containing not more than 10 tablets for the treatment of nausea associated with migraine".

The Committee considered that, in response to the Secretariat's request to the DAP for comments on the proposed prochlorperazine Schedule 3 amendment, a suggestion was received that "tablets" be replaced by "dosage units".

A submission had been received from XXXXXXXX supporting the proposed amendment to remove reference to buccal use. XXXXXXXX noted that the prochlorperazine is not taken orally, or by injection or suppository, and is not indicated for buccal use [Secretariat's note: It was presumed that this comment was referring to Schedule 3 products, as there are Schedule 4 prochlorperazine products on the ARTG].

A Committee member was of the view that the scheduling amendment was not to create a new entry for use of the substance, but to revise the current entry to accommodate oral use, thus proposing that the suggestion to apply the term "dosing units" in the current entry be implemented.

A member of the Committee pointed out that in regards to the potential for side effects, administration via the buccal route is no more likely to result in an adverse reaction in comparison to any other route, especially oral. That is to say that there is no significant safety difference between oral and buccal routes of administration of prochlorperazine.

DECISION 2005/45-16

The Committee agreed that in order to harmonise with New Zealand, the Schedule 3 entry for prochlorperazine be amended by removing reference to "buccal use".

Schedule 3 – Amendment:

PROCHLORPERAZINE – Amend entry to read:

PROCHLORPERAZINE in divided preparations in packs containing not more than 10 dosage units for the treatment of nausea associated with migraine.

13.8 PIPER METHYSTICUM (KAVA)

PURPOSE

The Committee considered the scheduling of *Piper methysticum* (kava).

BACKGROUND

Kava is the rhizome of *Piper methysticum*, a member of the pepper family indigenous to islands of the South Pacific. It contains pyrones including kawain, methysticin and yangonin. Kava has been used in the South Pacific to produce an intoxicating beverage used for recreational purposes and during convalescence. It is reported to have sedative, skeletal muscle relaxant, and anaesthetic properties.

At the October 2003 NDPSC Meeting the Committee noted a safety evaluation report prepared by the Kava Evaluation Group/Office of Complementary Medicines on kava containing medicines, which made recommendations on the regulation of kava as an ingredient in Listed Medicines. Due to the potential risk of liver toxicity from use of non-aqueous extracts of kava plants at high doses, the Committee considered the need to restrict the use of alcohol/acetone extracts of kava including those for bulk supply to health care practitioners for use in extemporaneously compounded preparations. In addition, it was agreed that a schedule entry to minimise the risk, without affecting the current usage of listed complementary products, should be considered by the Committee following a review of products on the ARTG.

The February 2004 NDPSC Meeting was advised that the Complementary Medicines Evaluation Committee (CMEC) Recommendation 41.3 had been included in Schedule 4 of the *Therapeutic Goods Regulations 1990* (TG Regulations) to only allow specified concentrations of aqueous kava extracts in Listed medicines and that all other kava products had been cancelled from the ARTG. The Committee noted that the available information suggested that whole or peeled kava rhizomes and their aqueous preparations containing 250mg or less of kavalactones were acceptable for use in exempt medicines while medical advice was necessary for safe use of other kava preparations due to

toxicity. On this basis, the Committee agreed to foreshadow the inclusion of *Piper methysticum* (kava) in Schedule 4 of the SUSDP with exemptions consistent with those specified in the TG Regulations.

The June 2004 NDPSC Meeting, on the grounds of public health and safety, agreed to include *Piper methysticum* (kava) in Schedule 4 of the SUSDP, as well as adopt the exemptions specified in the TG Regulations. Post-meeting comments were received and considered at the October 2004 NDPSC Meeting. The Committee confirmed the decision from the June 2004 Meeting and agreed that given the toxicity concerns on kava and in the absence of evidence to demonstrate the safety of products containing kava other than those forms recommended by CMEC as suitable for use in Listed medicines, it would be appropriate to allow the supply of such products to the public only under the advice of a medical professional.

At the June 2005 NDPSC the Committee deferred consideration of minor editorial changes and errata, including an amendment to the Schedule 4 entry for *Piper methysticum* (kava) to resolve a possible ambiguity, to the October 2005 NDPSC Meeting to allow time to seek comment from the NDPSC's Drafting Advisory Panel (DAP). Following the meeting the Secretariat noted that the kava amendment was a scheduling change rather than an editorial change and therefore included *Piper methysticum* (kava) in the pre-meeting gazette notice.

The Schedule 4 entry for *Piper methysticum* (kava) at the time of the Meeting was:

PIPER METHYSTICUM (Kava) in preparations for human use **except**:

(a) in preparations for oral use containing dried whole or peeled rhizome or containing aqueous dispersions or aqueous extracts of whole or peeled rhizome when labelled with a recommended daily dose of 250 mg or less of kavalactones:

  (i) containing more than 25 mg of kavalactones per dose, labelled with the statement:

    WARNING: Not for prolonged use. Not recommended for use by pregnant or lactating women. May harm the liver;

  (ii) in tablet or capsule form containing 125 mg or less of kavalactones per tablet or capsule; or

  (iii) in the form of a teabag when the amount of dried whole or peeled rhizome does not exceed 3 g;

(b) in topical preparations for use on the rectum, vagina or throat containing dried whole or peeled rhizome or

containing aqueous dispersions or aqueous extracts of whole or peeled rhizome; or

(c) in dermal preparations.

DISCUSSION

The Committee recalled that a possible ambiguity in the Schedule 4 kava entry was referred to the June 2005 NDPSC Meeting by the XXXXXXXX Member. The Member asserted that the "or" at the end of part (a) (ii) of the kava entry implied that (i), (ii), and (iii) were alternatives, i.e. that tabs, caps and teabags don't have to have the warning statement, which the Member did not believe was the Committee's intention. The Member advised that Schedule 4, Part 4 (Division 2) Item 35 of the TG Regulations indicated that the entries were all expected to carry the warning statement.

The Committee agreed that the Schedule 4 kava entry needed to be reworded to clarify that for oral preparations the warning statement "Not for prolonged use. Not recommended for use by pregnant or lactating women. May harm the liver" was mandatory for all preparations containing more than 25 mg kavalactones for the exception to apply. The Committee further agreed that the rewording would need to indicate the restrictions to tablet, capsule or teabag forms while still clearly covering other forms of oral preparations.

The Committee noted a submission from XXXXXXXX. XXXXXXXX suggested that, as kava may be subject to a yet unpublished harmonization decision in New Zealand, any NDPSC decision be deferred until a future meeting. A submission was also received from XXXXXXXX registering an interest in this issue.

The Committee noted that the June 2005 Medicines Classification Committee (MCC) of New Zealand considered kava and agreed to defer consideration until its next meeting. Members generally agreed, however, that this was no reason to defer a clarification of the SUSDP Schedule 4 entry for kava. Indeed, the XXXXXXXX Member indicated that MCC's deliberations could be usefully informed by NDPSC addressing the perceived ambiguity in the wording.

The Committee also noted that the Schedule 4 entry for *Piper methysticum* (kava) had been changed to incorporate the RASML decision (item 13.5).

DECISION 2005/45-17

The Committee confirmed that all parts of the Schedule 4 exception for oral use for *Piper methysticum* (kava) requires the mandatory warning statement except preparations containing less than 25 mg kavalactones and agreed to amend the SUSDP Schedule 4 entry for *Piper methysticum* (kava) to clarify this ambiguity.

Schedule 4 – Amendment

PIPER METHYSTICUM (Kava) in preparations for human use **except**:

(a) in preparations for oral use containing dried whole or peeled rhizome or containing aqueous dispersions or aqueous extracts of whole or peeled rhizome when labelled with a recommended daily dose of 250mg or less of kavalactones and

(i) if in tablet or capsule form containing 125mg or less of kavalactones per tablet or capsule; or

(ii) if in the form of a teabag when the amount of dried whole or peeled rhizome does not exceed 3g;

and, where containing more than 25mg of kavalactones per dose, compliant with the requirements of the *Required Advisory Statements for Medicine Labels*.

(b) in topical preparations for use on the rectum, vagina or throat containing dried whole or peeled rhizome or containing aqueous dispersions or aqueous extracts of whole or peeled rhizome; or

(c) in dermal preparations.

13.9 PANTOPRAZOLE

PURPOSE

The Committee considered further correspondence relating to the decision to reschedule oral pantoprazole 20mg to Schedule 3.

BACKGROUND

Pantoprazole is a proton pump inhibitor (PPI) similar to esomeprazole, omeprazole, lansoprazole, and rabeprazole. It is a substituted benzimidazole which accumulates in the acidic compartment of parietal cells after absorption where it is converted to the active form, a cyclic sulfenamide. This then binds to the enzyme hydrogen-potassium-ATP-ase (H+/K+-ATPase) at the secretory surface of gastric parietal cells. Inhibition of H+/K+-ATPase blocks the final step of gastric acid production, leading to inhibition of both basal and stimulated acid secretion.

Pantoprazole (XXXXXXXX) was first considered for scheduling at the February 1995 NDPSC Meeting when it was included in S4 following the October 1994 ADEC Meeting's recommendation of approval to register pantoprazole for the treatment of duodenal ulcer, gastric ulcer, reflux oesophagitis and gastrointestinal lesions refractory to histamine-2 receptor antagonists (H2RAs). It has been available through prescription only in Australia since January 1994 and in the USA since May 2000.

At the June 2005 Meeting, the Committee agreed to include in Schedule 3 pantoprazole in oral preparations containing 20 mg or less of pantoprazole for the relief of heartburn and other symptoms of GORD in packs containing not more than 14 days supply. It was also agreed that the implementation date for this decision would be 1 March 2006 to allow adequate time for collaboration with the pharmacy profession and the generation and provision of education materials and supply protocols for pharmacists to supply S3 pantoprazole appropriately. The Committee did not consider an Appendix H listing for pantoprazole as there was insufficient information at the time to make an informed decision.

DISCUSSION

The Committee was informed that, after the June 2005 Meeting, XXXXXXXX was written to and supplied an extract of the Edited Minutes. In that correspondence, it was pointed out that the Committee delayed the implementation date of the scheduling amendment to 1 March 2006 in order to allow time for drafting of the educational materials and supply protocols for S3 pantoprazole. XXXXXXXX was asked to submit the final draft of these materials to the Committee in time for the October 2005 Meeting. XXXXXXXX did not supply these educational materials and could not say with certainty when these materials would be made available. They did, however, confirm that the educational materials for pharmacists were under development.

Advice was noted from XXXXXXXX that XXXXXXXX had not yet engaged professional pharmacy on the development of educational material. Thus Members advocated that there should be a deferral of implementation.

A Member was of the opinion that the underlying reason to defer the rescheduling implementation date cannot be based on the failure of the applicant in providing the Committee the educational material which is to be used by pharmacist, given that educational materials are not approved by the Committee, per se.

Another Member pointed out that the minutes of the June 2005 Meeting stipulated that the required educational material did not necessarily need to be acquired from XXXXXXXX but in fact could be provided by a professional pharmacy body, such as XXXXXXXX.

As such, the final decision to defer the implementation date of the rescheduling was made to provide adequate time to the sponsor and the pharmacy profession to prepare for the imminent scheduling change.

DECISION 2005/45-18

The Committee agreed to vary Decision 2005/ 44 – 24 by delaying the implementation date for the rescheduling of oral pantoprazole 20mg to Schedule 3 to 1 May 2006 to allow the sponsor adequate time to develop pharmacist educational material.

Schedule 3 – New entry

PANTOPRAZOLE in oral preparations containing 20 mg or less of pantoprazole for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days of supply.

Schedule 4 – Amendment

PANTOPRAZOLE – amend entry to read:

PANTOPRAZOLE **except** when included in Schedule 3.

Effective date – 1 May 2006

13.10 ORLISTAT

PURPOSE

The Committee considered the post-meeting comment with regards to the June decision not to include orlistat in Appendix H.

BACKGROUND

Orlistat is a potent, specific and reversible long-acting inhibitor of gastrointestinal lipases which are required for the systemic absorption of dietary triglycerides. It is used in conjunction with dietary modification in the management of obesity.

Orlistat was first considered at the November 1999 NDPSC Meeting, when it was included in Schedule 4 (S4) following a recommendation by the trans-Tasman Harmonisation Working Party. The May 2000 NDPSC Meeting noted that the ADEC, at its December 1999 meeting, recommended the registration of XXXXXXXX containing orlistat XXXXXXXX mg for the treatment of obese patients with a body mass index (BMI) ≥ 30, and overweight patients with a BMI ≥ 27 in the presence of other risk factors, in conjunction with a mildly hypocaloric diet. XXXXXXXX has been marketed in Australia by XXXXXXXX since XXXXXXXX.

The February 2005 NDPSC Meeting considered a proposal to include orlistat in Appendix H of the SUSDP. The Committee did not support the proposal as Members were concerned that omission of information in advertising campaigns about the modest efficacy and reduction of efficacy long-term seen in the clinical trial setting and potential

side effects of orlistat could potentially create a consumer demand based on unrealistic expectations of the product's effectiveness.

At the June 2005 Meeting, the Committee decided not to support a submission from XXXXXXXX to include orlistat in Appendix H. The Committee remained concerned that branded advertising of orlistat would convey an inappropriate public health message that pharmacotherapy is the first-line treatment for obesity. Furthermore, it was felt that branded advertising would make consumers less likely to be influenced by the pharmacist's assessment in determining whether the product is suitable for them. The Committee reaffirmed its view that consumers should be encouraged to undertake appropriate lifestyle changes as a first-line option to achieve safe, long-term weight loss.

DISCUSSION

Correspondence in relation to the June 2005 decision regarding orlistat was received from XXXXXXXX and from XXXXXXXX. The points that XXXXXXXX raised were as follows:

- That the reasons the Committee gave for not supporting Appendix H inclusion sends out a message that they do not have faith in the ability of community pharmacists to be effective decision-makers and advisors on S3 products. Furthermore, advertising does not impact on the skills or abilities of community pharmacists, nor does it alter the fact that a decision to supply an S3 product remains the pharmacists' legal responsibility
- There is no evidence which suggests that consumers who need to lose weight would disregard the primacy of diet and exercise as a result of orlistat being advertised. The reality is quite the opposite: that overweight consumers only turn to medication as an adjunct when struggling with diet or exercise alone.
- The Therapeutic Goods Advertising Code (TGAC) requires that S3 advertising highlight the fact that advice from a pharmacist must be sought. Clause 7.3 of the TGAC requires that all weight management advertising can only be done as part of a balanced message extolling the need for regular exercise and controlled diet. This clause has been strengthened with the new code which was enacted on 19 August 2005 and advertisers can no longer simply insert small print to this effect in order to comply with this clause.
- The Australian Government has identified diabetes, cardiovascular health, arthritis, colorectal cancer and arthritis as National Health Priority Areas. Obesity/ excess weight are major yet modifiable risks across all of these areas. It follows then that allowing the advertising of orlistat (along with pharmacist counselling) would be in line with Australian Government policy.
- The reasons given for not including orlistat in Appendix H are not exclusive to orlistat but are true for all weight-loss treatments. In not allowing the advertising of orlistat, the Committee is producing a "non-level playing field" as no other weight-

loss product has such advertising restrictions, regardless of what schedule it may be in.

- As orlistat is a product grounded in real, rather than "junk" science, advertising would actually raise the standard in terms of advertised weight loss products and therefore address concerns that consumers may have inflated expectations of such products or that consumers may rely on weight loss products alone rather than using such products as an adjunct to balanced diet and regular exercise.

XXXXXXXX also referred to a non-level playing field when raising concerns about the fact that there are many products on the market of untested or of limited efficacy. XXXXXXXX believe that vigorous marketing of such products for rapid and substantial weight loss is inappropriate and not in the public health interest. They too referred to the strengthening of section 7(3) of the TGAC which ensures that messages about the importance of diet and exercise at least match the impact of messages of the benefit of a particular product. XXXXXXXX have suggested that it could be in the public interest to allow the advertising to designated population subgroups of a product for which testing has established efficacy to some degree. They also pointed out that sections 4(2)(a) & 4(2)(c) ensure effective regulating of **any** weight loss product as these sections disallow advertisements arousing unwanted expectations or which mislead directly or by implication. They further noted that any additional requirement deemed necessary by the NDPSC would be enforceable under section 4(1)(a) of the Code.

The Committee recalled that, at the February 2005 NDPSC Meeting, during consideration of XXXXXXXX's proposal for an Appendix H listing for orlistat, the NDPSC evaluator had supported the proposal to include orlistat in Appendix H with the condition that reference to the modest efficacy and reduction of efficacy long-term seen in the clinical trial setting and potential side effects of orlistat need to be presented in any advertising for XXXXXXXX under the rubric of balanced, informed and non-misleading advertising. The evaluator had also suggested statements such as the following to be made in any advertising for XXXXXXXX:

"Orlistat may only lead to minor weight loss in some people"
"Some people may experience side effects with orlistat particularly if diet is not adhered to"
"People may require vitamin replacement during orlistat therapy."

The Committee was reminded that the sponsor did provide a Statutory Declaration which stated their commitment to use the caveats that the evaluator suggested, should orlistat be given an Appendix H listing. One Committee Member then commented that it seemed ironic that, while branded advertising of S3 products must be cleared by TGACC, non-branded advertising needs no such clearance. Concern was raised by a number of Members that there is a potential for non-branded advertising to be overly emotive and unbalanced in the messages it gives. Thus, there is an argument for branded advertising as it is only branded advertising that requires pre-clearance from TGACC. There was

discussion around whether data would be available on the effect that the non-branded advertising has had.

[Sentence deleted]

OUTCOME

The Committee noted the correspondence that was received. The Committee noted in particular that the *Therapeutic Goods Advertising Code 2005* (effective 24 August 2005) has more stringent requirements in regards to the advertising of weight-loss products which should ensure that messages about the importance of diet and exercise do at least match the impact of messages of the benefit of a particular product. [Sentence deleted].

14. PROPOSED CHANGES/ADDITIONS TO THE STANDARD FOR THE UNIFORM SCHEDULING OF DRUGS AND POISONS.

14.1 SUSDP, PART 4

14.1.1 HYDROCORTISONE AND HYDROCORTISONE ACETATE

PURPOSE

The Committee considered an application to reschedule rectal use of hydrocortisone and hydrocortisone acetate (in combination with an anaesthetic), from Schedule 3 (S3) to Schedule 2 (S2).

BACKGROUND

Hydrocortisone, a corticosteroid with both glucocorticoid and mineralocorticoid activity, is used for replacement therapy in chronic adrenocortical insufficiency, salt-losing forms of congenital adrenal hyperplasia syndromes, and as an anti-inflammatory agent.

Hydrocortisone and hydrocortisone acetate were first included in S3 at a concentration of 0.5% or less when present as the only therapeutically active substance at the August 1985 Meeting. At the May 1995 Meeting, the Committee recommended that the Schedule 3 entry for hydrocortisone should be amended to allow a topical combination for rectal use containing cinchocaine to be classified as S3 product. Hydrocortisone and hydrocortisone acetate (dermal use containing 0.5% or less hydrocortisone in packs containing 30 g or less of such preparation, with no other therapeutically active substance or an antifungal as the only other therapeutically active substance) were included in Schedule 2 at the February 1999 Meeting. The November 1999 Meeting included hydrocortisone in Appendix H of the SUSDP, permitting the advertisement of hydrocortisone for rectal use.

XXXXXXXX proposed that the current rectal use indication for hydrocortisone and hydrocortisone acetate (in combination with an anaesthetic) be rescheduled from S3 to

S2. Their intent was to reschedule XXXXXXXX (hydrocortisone and cinchocaine hydrochloride), which is used for the symptomatic relief of haemorrhoids and other anorectal conditions, for rectal use from Schedule 3 to Schedule 2 of the SUSDP. Cinchocaine hydrochloride was already in Schedule 2 of the SUSDP (in preparations for topical use other than eye drops, containing 0.5% or less of total local anaesthetic substances).

DISCUSSION

The Committee considered the arguments XXXXXXXX presented, that the indication, haemorrhoids and other minor anorectal conditions, are often short-termed, short-limited conditions, readily amenable to self-diagnosis, often self-treated and very unlikely to be misdiagnosed by the consumer and therefore potentially masking a serious medical condition. Initial diagnosis will often be confirmed by a doctor and subsequent episodes are likely to be self-treated by patients who are familiar with their disease state. Often patients prefer to access these treatments without consulting a pharmacist due to the perceived embarrassing nature of the condition. Rescheduling of hydrocortisone would therefore give patients easier access to the treatment. XXXXXXXX pointed out that use of the product is restricted to seven days. Advice from a doctor is recommended in event of inadequate relief of the symptoms.

Products for the treatment of haemorrhoids and other anorectal conditions containing hydrocortisone have been allowed to be advertised to the general public in Australia since 1999. Consumers are therefore better educated about haemorrhoidal symptoms and the range of treatments for haemorrhoids and other anorectal conditions. As part of their submission, the sponsor had prepared training modules for pharmacy assistants, to educate/train them in handling enquiries on the product.

The evaluation report for the sponsor's original application, proposing the rescheduling of hydrocortisone and hydrocortisone acetate, concluded that hydrocortisone in topical preparations containing 0.5% or less in a pack size of 30 g or less has demonstrated a high safety profile in over-the-counter use (Schedule 3) for this indication (haemorrhoids and other minor anorectal conditions), with few reports (16) being made on the ADRAC database. Significant post-marketing data are available and do not reveal any toxicity concerns. The adverse reactions reported included arrhythmia (6.25%), hypersensitivity (12.5%), upper respiratory tract infection (6.25%) urticaria (6.25%), pruritus (18.75%) and rash (18.75%). Rectal route of administration reduces risk of systemic toxicity of hydrocortisone/hydrocortisone acetate.

The evaluation report concluded that the dermal tolerability of hydrocortisone/hydrocortisone acetate was reasonable and reactions were mild. Systemic absorption following topical administration of low doses was likely to be low. Since the total dose of hydrocortisone contained in the proposed pack (Proctosedyl) is 150 mg for the ointment and 60 mg for the suppositories, even the oral ingestion of the entire contents of the pack would be very unlikely to cause acute toxicity in either adults or children.

The sponsor had indicated in their submission that hydrocortisone and cinchocaine hydrochloride was registered in 55 countries throughout the world. They had presented information of the current regulatory and classification status of hydrocortisone in other countries. In the United Kingdom (2004), hydrocortisone (0.2%) and lidocaine hydrochloride (1.0%) was changed from Pharmacy (P) to General Sales List (GSL); supplied for the symptomatic relief of anal and perianal itch, irritation and pain associated with external haemorrhoids. Current classification of hydrocortisone (combined with a local anaesthetic) for rectal use in New Zealand is restricted and in the USA is prescription-only.

The Committee noted that the potential for abuse or for drug interactions are minimal.

Two pre-Meeting submissions were received in regards to this scheduling proposal. One was from XXXXXXXX. XXXXXXXX did not support the scheduling amendment for several reasons. They felt that discussion with a pharmacist is necessary with conditions presenting with ano-rectal bleeding to determine when referral is necessary. Furthermore, prolonged use may thin the membrane of the affected area and lead to systemic absorption and local anaesthetics have the potential to cause sensitisation. XXXXXXXX provided no meaningful comment but reserved their right to provide post-Meeting comment.

A Committee Member noted that products other than the sponsor's product would be affected, should this scheduling change be supported. It was further noted that while the evaluator supported a down-scheduling of hydrocortisone in combination with a local anaesthetic for rectal use, this support was only for S2 scheduling for 0.5% hydrocortisone. Furthermore, in New Zealand, 1% hydrocortisone or less by weight of hydrocortisone base in rectal medicines in combination with a local anaesthetic and in a quantity of not more than 35 grams per container or 12 suppositories per pack is a restricted medicine. That is to say that Australia and New Zealand are currently harmonised on the scheduling of this substance. While the UK does schedule hydrocortisone for rectal use as general sales listing, this is limited to 0.2% hydrocortisone in a spray which can only be used on external haemorrhoids.

A Member pointed out that while the submission states that there have been very few reports made on the ADRAC database for hydrocortisone in topical preparations containing 0.5% or less, data on the ADRAC database for over-the-counter preparations should be interpreted cautiously as consumers reporting to ADRAC was only a recent phenomenon. Indeed, consumers may not even be aware that such a mechanism for reporting exists. Also, another Member brought to the Committee's attention that the data garnered from direct reporting to XXXXXXXX did not differentiate well between short term topical rectal use compared to oral/ parenteral/ long term use.

The Committee noted that the methodology used for analysis of safety in regards to systemic absorption relied only on data concerning the acetate salt and not hydrocortisone base. A Committee Member pointed out that the full contents of a tube of 30 grams of

ointment is 30 milligrams of hydrocortisone which is roughly equivalent to 7.5 milligrams of prednisolone and this amount would not suppress adrenal function.

A Committee Member raised concern that while Appendix F requires that hydrocortisone for topical use includes a warning statement limiting it to a five day treatment (unless instructed by a doctor), the packaging gives instructions for up to three weeks. Another Member pointed out that Appendix 1 of the submission did address this issue while another Member still urged that such matters should be referred to the OTC registration section of the TGA for consideration.

The sponsor's argument for down-scheduling this product that some patients may find it embarrassing to consult the pharmacist on such personal matters was discussed. The point was raised that, in some States, the ointment would remain behind the counter so this would negate any advantage in the product becoming S2. Along with this, the suppositories would probably need to be requested because they would be stored in a fridge. Furthermore, a number of Members felt that consumers would tend to assume, as pointed out in texts such as the Therapeutic Guidelines, that all anorectal symptoms are haemorrhoids. If the symptoms were not haemorrhoids but were in fact some type of infection, the use of a topical corticosteroid would be totally inappropriate. This would therefore warrant intervention and such intervention should also include a reiteration that the product should only be used short term.

The Committee concurred with the evaluation report that while the criteria for S2 listing are generally met, requirements of the NDPSC Guidelines for inclusion of a product in Schedule 2 in regards to public health considerations were not addressed adequately. In line with this, one Member contested that, in terms of accessibility, there would be no public benefit in down scheduling such products.

OUTCOME

The Committee agreed that the current scheduling of hydrocortisone remained appropriate for the following reasons:

- Concern that consumers may sometimes have difficulty in differentiating between haemorrhoids and other conditions for which the use of a corticosteroid would be inappropriate. If used on infected skin, there is potential for infection to be masked or exacerbated.
- The safety data presented does not reflect the safety of the product for anorectal use as it includes all adverse events relating to hydrocortisone, regardless of route, dose or duration of treatment.

14.2 SUSDP, PART 5

14.2.1 CETIRIZINE (APPENDIX F AND APPENDIX K)

PURPOSE

The Committee considered an application to amend the wording of Appendix F Part 1 for cetirizine and to remove cetirizine for oral use from Appendix K.

BACKGROUND

Cetirizine hydrochloride, a piperazine derivative and metabolite of hydroxyzine, is described as a non-sedating antihistamine which is long-acting and has some mast-cell stabilising activity. It is used for the symptomatic relief of allergic conditions including rhinitis and chronic urticaria.

At the February and May 1993 Meetings, the Committee noted that the ADEC recommended approval for registration of cetirizine hydrochloride for treatment of seasonal allergic rhinitis, perennial allergic rhinitis, and chronic idiopathic urticaria at its 162nd Meeting. The Committee then recommended Schedule 4 and an Appendix K entry for cetirizine.

A submission to reschedule cetirizine tablets from Schedule 4 to Schedule 3 was considered by the Committee at the May 1997 Meeting. Most other sedating antihistamines were already in Schedule 3 at that time. The ADRAC and toxicology data showed the substance was no more dangerous than other sedating antihistamines. The Committee agreed that, on the basis of the data provided, Schedule 3 listing was acceptable. Oral liquid formulations were considered at the February 1998 Meeting and they were also rescheduled to Schedule 3.

The Committee considered a submission from XXXXXXXX at the August 1998 Meeting to include cetirizine in Appendix H. This submission was jointly considered with similar submissions from XXXXXXXX for loratadine and XXXXXXXX for fexofenadine. The Committee noted at the time that, while cetirizine was not categorised as a non-sedating antihistamine (in contrast to loratadine and fexofenadine), it was considered to have lower sedating potential compared to most first generation antihistamines. Thus, while the Committee agreed to group these three antihistamines in the context of advertising purposes, such grouping should not be taken as an indication that cetirizine's sedation properties were identical to either fexofenadine or loratadine. It was decided at this Meeting to add cetirizine to Appendix H, along with fexofenadine and loratadine.

At the February 1999 Meeting, the Committee supported a recommendation from the Trans Tasman Harmonisation Working Party (TTHWP) that, on grounds of harmonisation, cetirizine in preparations for oral use be rescheduled from Schedule 3 to Schedule 2. A consequence of the deletion from Schedule 3 was the deletion of the Appendix H entry.

DISCUSSION

The Committee noted that the current approved Product Information (PI) states the following in regards to sedation:

- Under *CNS Effects:* 'Studies in normal volunteers using objective measurements, such as sleep latency time, mental alertness and simulated driving performance, showed that cetirizine does not cause CNS depression.'
- Under *Precautions:* 'Some patients may experience a degree of drowsiness…the occurrence of CNS effects has been observed in some individual patients…'

The Committee also noted that the evaluation report which assessed the proposal to remove cetirizine from Appendix K stated the following concerning sedation:

- The studies quoted in the product PIs for cetirizine and loratadine, designed to test for CNS impairment, provided more interpretable evidence for assessing the drug's sedative effects as compared to other studies involving clinical trial patients.
- A total of 23 anti-histamines were assessed regarding sedation potential, based on a calculated 'proportional impairment ratio' (PIR), where a PIR value of 0.00 indicated no potential for CNS impairment and higher PIR values indicated greater CNS impairment. PIR values for cetirizine from 14 studies and for loratadine from 9 studies were 0.92 and 1.94, respectively, and were not significantly different to other second generation anti-histamines.
- In a further extended review, PIR values for single and repeat 10 mg doses of cetirizine and loratadine were compared. No impairment was seen (PIR of 0.00) when a repeat dosage regimen was used for either cetirizine or loratadine.
- Cetirizine and loratadine were non-sedating in four head-to-head comparison studies which used both subjective and objective tests.
- A driving study showed that cetirizine 10 mg did not result in any impairment compared to placebo in all actual driving tests, and psychomotor and cognitive tests.
- The evaluator was of the opinion that cetirizine and loratadine had comparable CNS effects and recommended removal of cetirizine from Appendix K, whilst considering the statements referring to the 'possibility' of sedation in some patients.

The Committee was informed that above data was submitted in an application by XXXXXXXX to change their label statement to 'non-drowsy, lets you stay alert and perform normally and can be used while driving'. The application was approved by Health Canada on 25th March 2005.

The Committee recalled that the New Zealand Medicines Classification Committee Review of anti-histamines undertaken as part of the Trans-Tasman Harmonisation Process recommended that cetirizine be classified as a non sedating anti-histamine.

The pre-Meeting submission from XXXXXXXX in regards to this proposed scheduling amendment was also considered. The following points were made in this submission:

- XXXXXXXX summarised the warnings etc that appear on labelling and on PI documents in countries with similar regulatory systems. The US PI has warning statements regarding drowsiness and has somnolence listed as the most common adverse reaction. Health Canada had approved the following wording for cetirizine but still included statements regarding drowsiness in the PI: *non-drowsy, lets you stay alert and perform normally and can be used while driving.* In New Zealand, the following warning is required on the pack: *although this medicine is unlikely to affect the ability to drive or operate machinery, a few people may be impaired and care should be taken.*
- XXXXXXXX maintained that there are no new data in published literature which justify removing sedation warning requirements for cetirizine. They quoted figures that the incidence of sedation at a dose of 10mg is twice that of placebo and more than three times that of placebo at a dose of 20mg from clinical efficacy trials.
- They pointed out that, in the case of self-selection of medicines, the consumer relied heavily on warning statements on the packaging. Thus, the use of warnings that are supported by scientific evidence is an appropriate part of self-medication with OTC medicines. Furthermore, the Australian warning statement was consistent with warning statements which were required by other countries' drug regulatory agencies. XXXXXXXX also pointed out that adverse reactions were sometimes idiosyncratic and therefore unpredictable.
- XXXXXXXX believed that the proposal to remove the warning statement for cetirizine is commercially-driven as no other second generation antihistamine requires a sedation warning. They stated that it is evident from sales figures that the sedation warning has not been a commercial barrier and that the consumer would not gain from the removal of the sedation warning as the warning does not restrict sales.

The Committee also considered a pre-Meeting submission received from XXXXXXXX which made reference to a number of published trials and the following points were raised:

- A four-way, double blind, randomised controlled trial (RCT) involving 419 patients was quoted. At $P<0.05$, there was a 23% increase in somnolence for patients taking 10mg (compared to placebo) and 25% at the 20mg dose (compared to placebo).
- A literature review (1965 to 1997) found 55 trials firstly investigating differences between first and second-generation antihistamines and secondly investigating differences in sedation between second generation. From this retrospective review, XXXXXXXX had determined that fexofenadine caused no sedation risk (risk: benefit ratio 0.00) while cetirizine did (risk: benefit ration 0.21).
- Another double blind RCT which was a cross-over study ($n = 15$) showed that there was no difference in relation to cognitive and psychomotor function between various doses of fexofenadine and placebo ($P<0.05$).

- Another double-blind RCT (n = 20) compared the sedative effects of cetirizine to fexofenadine where choice reaction time was measured. In comparison to placebo, cetirizine (P = 0.017) was greater than fexofenadine (P = 0.008).
- A double-blind cross-over RCT (n = 16) compared effects of cetirizine 10mg to loratadine 10mg with or without alcohol. When subjective measures were used, cetirizine results showed a significant effect on subjects (P = 0.055) while loratadine did not.
- Two trials in the one paper compared cetirizine separately to both hydroxyzine and diphenhydramine. While cetirizine was found less sedating than either drug, doses of cetirizine 20mg had a greater sedation effect than placebo.
- A double blind seven way cross over RCT compared diphenhydramine to five second-generation antihistamines and cetirizine was found to cause higher incidence of somnolence than other second-generation antihistamines.
- Several studies are quoted as evidence that fexofenadine and loratadine are preferred over cetirizine in what are referred to as safety critical jobs such as military and commercial aircrew.
- Four separate trials are referenced to support the claim that fexofenadine does not have any effect on driving ability, cognitive function tests, reaction time, tracking ability or vigilance tests.
- XXXXXXXX do point out that their submission relies heavily on data on fexofenadine as it is readily available to them but they maintain that this does not detract from the efficacy or safety properties of other non-sedating second generation antihistamines.

The Committee noted that XXXXXXXX would support an amendment to remove cetirizine from Appendix K and to include it in the Appendix F exemption from requiring sedation warnings, along with the other (as XXXXXXXX state) non-sedating antihistamines.

The Committee reflected that Appendix F sets down warning requirements for OTC preparations while Appendix K sets down sedation warning requirements for dispensed medications at any dose.

One Committee Member pointed out that [sentence deleted] most of the data presented in support of XXXXXXXX's application focused on the sedation potential of a dose of 10mg of cetirizine in clinical trials. The Member reminded the Committee that the SUSDP Schedule 2 entry for cetirizine does not have a dosage cut-off but simply lists cetirizine "in preparations for oral use". Thus, regardless of what dosage XXXXXXXX intends, other sponsors could potentially market a 20mg tablet, or a doctor could prescribe a dose of cetirizine higher than XXXXXXXX mg, and neither would require a sedation warning should this scheduling amendment take place.

The point that was made by XXXXXXXX was reiterated by a Member: that Canada is the only country listed in the sponsor's submission which does not require a sedation warning on the package but still requires warning statements within the PI and CMI documents.

The fact that New Zealand requires sedation warnings for both loratadine and cetirizine was discussed. A Member suggested, as XXXXXXXX themselves make the comment that presentations containing up to 10mg of cetirizine and presentations containing 10mg of loratadine should be subject to the same labelling requirements, it might be more appropriate for Australia to take the same stance as New Zealand and require sedation warnings for both rather than for neither. At the very least, the Member felt, should the amendment occur, that the S2 entry for cetirizine should be limited to 10mg.

Comment was made that while the Appendix F warning statements 39 and 40 both warn of the potential for interaction with alcohol, it was unfortunate that XXXXXXXX provided no data regarding the potential interaction between cetirizine and alcohol.

The Committee noted that data presented in submissions by both XXXXXXXX and XXXXXXXX may not have reflected that the balance of current evidence demonstrates that cetirizine should not be considered sedating. XXXXXXXX themselves state that the data they put forward relied heavily on comparisons with fexofenadine.

The issue of consistency was discussed. A Member commented that the Committee should focus on the potential for drowsiness, relative to other non-sedating antihistamines. The same Member was of the view that deliberations in regards to dosage should be dealt with at registration level and not by this Committee. Another Member made a further point about relative drowsiness and stated that all non-sedating antihistamines have the potential to cause sedation and so should have the warning that while drowsiness is unlikely, it may happen. The Committee agreed that adding such a warning statement to Appendix F was inappropriate as it was now an issue for RASML. The Committee thus further agreed that the RASML requirements for all non-sedating antihistamines be referred to the Medicines Evaluation Committee (MEC) and checked for consistency with New Zealand.

A Member raised the point that exclusion from Appendix F does not mean that a product could be promoted as "non-drowsy". Such a claim would need to be separately approved by the MEC.

DECISION 2005/45-19

As the balance of current evidence indicates that cetirizine is no more sedating than loratadine, the Committee agreed to alter the wording of Appendix F Part 3 and remove cetirizine for oral use from Appendix K of the SUSDP. The Committee further agreed to refer the issue of warning statement requirements for all non-sedating antihistamines to the MEC to check for consistency with New Zealand.

Appendix F, Part 3 – Amendment

Antihistamines – Amend paragraph (b) of the entry to read:

(b) oral preparations of astemizole, cetirizine, desloratadine, fexofenadine, loratadine or terfenadine;

Appendix K – Amendment

Cetirizine – Amend entry to read:

Cetirizine **except** when included in Schedule 2.

14.2.2 ITEM DELETED

14.2.3 CLIOQUINOL (APPENDIX C)

PURPOSE

The Committee considered the current Appendix C entry for clioquinol.

BACKGROUND

Clioquinol is a halogenated hydroxyquinoline with antibacterial and antifungal activity and is used in creams and ointments in the treatment of skin infections. Clioquinol was formerly given orally for use in the treatment of intestinal amoebiasis, and for the prophylaxis and treatment of traveller's diarrhoea and similar infections. Oral preparations have been withdrawn from the market because of neurotoxicity. However, oral clioquinol is being investigated for its action as a chelator of copper and zinc in the treatment of Alzheimer's disease.

At the November 1988 DPSSC Meeting, therapeutic substances that were in Schedule 7 (formerly part Two of the Prohibited Substances List) were placed in the new Appendix C. Clioquinol and other halogenated 8-hydroxyquinoline derivatives for internal human use was one of the substances included in Appendix C.

DISCUSSION

The Committee recalled that, at the February 2005 Meeting, the legislative requirements regarding the import and supply of clioquinol in Australia were discussed. It was brought to the Committee’s attention that while clioquinol was not an approved therapeutic good in Australia, it is accessed via the Special Access Scheme (SAS). The usual avenue of access for clioquinol was Category B of the SAS and this required prior approval from a TGA delegate. Further to this, specific approval under relevant State or Territory legislation may be required for possession or use of clioquinol. Clioquinol was not listed

in the *Customs (Prohibited Imports) Regulations 1956*. The Committee was informed that, in 2003, the TGA did not object to a clinical trial investigating the use of clioquinol in the treatment of dementia from taking place, despite the fact that it was listed in Appendix C of the SUSDP. Additionally, it was noted that there have been more recent reports of compounding chemists dispensing preparations of clioquinol.

The Committee also recalled that the NCCTG had established a Working Group to oversee the development of a revised scheduling policy framework including scheduling criteria as well as a review of the SUSDP Appendices. It had been suggested by the NCCTG Working Group that it would be appropriate for the joint therapeutic products legislation to prohibit the importation of those substances for human therapeutic use listed in Appendix C. Should this proposal be supported, consideration could be given to granting an exemption for SAS Category A patients (i.e. with life threatening medical conditions as notified to the Joint Agency) from this prohibition. Should this occur, there may be no need to retain Appendix C. The remaining entries in Appendix C could be transferred to Schedule 7 to allow for uniform controls to be applied by States and Territories.

A minute was sent to the Secretary of the NDPSC from XXXXXXXX who raised the issue of the use of clioquinol in Australia with XXXXXXXX. It was raised with XXXXXXXX that while a trial had taken place around two years ago involving clioquinol, there had been more recent enquiries requesting permission to export trial material for trials being conducted overseas. The TGA was later informed that these trials did not take place.

In the paper that was presented to XXXXXXXX, several possibilities were put forward to overcome the bureaucratic burden. Briefly, these were:

- That the TGA request that the NDPSC amend the Appendix C entry to allow use in lawfully conducted clinical trials. In parallel, the TGA could monitor that the Human Research and Ethics Committee (HREC) approving the trial do consider the association of such compounds with Sub acute Myleo Optic Neuropathy (SMON).
- That the TGA use its powers under their Regulations to prevent trials involving clioquinol or related substances from taking place. This invariably would not be well received by investigators.

The Committee discussed the requirements under the *Therapeutic Goods Act 1989* and its associated regulations in regards to the conduct of clinical trials in Australia. In brief, any clinical trial involving an unapproved therapeutic good or a therapeutic good being used outside of it's marketing approval must be the subject of either a Clinical Trial Notification (CTN) or a Clinical Trial Exemption (CTX). The former involves only notification to the TGA, the latter requires the sponsor to provide pre-clinical, chemistry and clinical data to the TGA for evaluation. With both schemes, the trial must be approved by an HREC beforehand. Further to that, all parties involved (the sponsor, the investigator, the HREC and the Approving Authority) must provide written assurances that the trial will meet both the Note for Guidance on Good Clinical Practice as well as

the NHMRC's National Statement on Ethical Conduct in Research Involving Humans. The legal obligation to meet the requirements of these two guidance documents ensures that any such trial would be conducted to internationally acceptable standards. Furthermore, as one Committee Member pointed out, although the CTN scheme is a notification scheme, the TGA does still have the legislative power to stop clinical trials conducted under this scheme if conducting or continuing the trial would be contrary to public interest.

A pre-meeting submission was received from XXXXXXXX, a biotechnology company developing treatments for neurodegenerative diseases, particularly Alzheimer's disease. [Sentence deleted]. XXXXXXXX discuss the point that very few research institutions routinely hold the appropriate permit which allows them to obtain poisons or controlled substances for use for industrial, educational, advisory or research purposes. XXXXXXXX contests that obtaining such permits is an administrative burden and may well be the rate-limiting step in initiating a clinical trial. The same is true for manufacturers who manufacture investigational products on behalf of institutions conducting clinical trials. [Sentence deleted]. XXXXXXXX supports any move to revise the current scheduling of clioquinol which would streamline administrative requirements for research and development of such substances.

A Committee Member referred to the Bansemer Report and pointed out that one of the recommendations of this report was that trials involving New Chemical Entities (NCEs) should receive both ethics approval and a scientific approval. The Committee Member suggested that such situations would be closer to a CTX than a CTN. However, the Member clarified further that, if the ethics committee was from a tertiary institution which had appropriate scientific expertise, the CTN route would be appropriate. The Committee was further reminded that while the CTN scheme is referred to as a notification scheme, signatures are required from the Principal Investigator, the Sponsor of the trial, the head of the institution where the trial is being conducted and the Chair of the ethics committee. Furthermore, the investigator's brochure, the consent forms and the protocol are all reviewed for CTNs involving NCEs. This certainly was the case with the trials that took place involving clioquinol.

The Committee, noting the thorough review that takes place before a CTN or a CTX trial begins, discussed whether exemption for clinical trials may be warranted for all substances listed in Appendix C. One Member pointed out that making the exemption part of the heading of Appendix C would not work for jurisdictions that have adopted Appendix C only by reference. Furthermore, to exempt all substances in Appendix C to allow use in clinical trials would require a gazettal notification.

DECISION 2005/45-20

Given the safeguards that already exist for clinical trials conducted in Australia, the Committee agreed to amend the Appendix C entry for clioquinol (and related compounds) to allow its use in clinical trials which have met TGA requirements.

Furthermore, the Committee agreed to foreshadow the decision to apply a similar exemption for all substances listed in Appendix C.

Appendix C – Amendment

CLIOQUINOL – amend entry to read:

CLIOQUINOL and other halogenated derivatives of 8-hydroxyquinoline for human internal use **except** when being used solely for experimental purposes in humans and such use:

(a) is in accordance with an approval granted under paragraph 19(1)(b), and the requirements of subsection 19(4A), of the *Therapeutic Goods Act 1989* (as amended from time to time) - otherwise known as the Clinical Trial Exemption (CTX) scheme; or

(b) is in accordance with the requirements of subsection 18(1) of the *Therapeutic Goods Act 1989* and Regulation 12(1A) of the *Therapeutic Goods Regulations 1990* (as amended from time to time) - otherwise known as the Clinical Trial Notification (CTN) scheme.

15. MATTERS REFERRED BY THE AUSTRALIAN DRUG EVALUATION COMMITTEE (ADEC)

15.1 NEW SUBSTANCES

15.1.1 HUMAN PLASMA-DERIVED PROTEIN C

PURPOSE

The Committee considered the scheduling of a new medicine, Human Protein C.

BACKGROUND

Protein C is an endogenous inhibitor of blood coagulation. A preparation of protein C purified from human plasma is used in the management of thromboemboli disorders in patients with congenital deficiency of protein C.

The June 2004 ADEC Meeting recommended the approval of the application submitted by XXXXXXXX to register XXXXXXXX, containing plasma-derived human protein C (XXXXXXXX and XXXXXXXX per vial), indicated for the treatment of purpura fulminans and coumarin-induced skin necrosis in patients with severe congenital protein C deficiency.

ADEC also recommended that approval be subjected to the finalisation of the product information to the satisfaction of TGA.

DISCUSSIONS

The Committee noted that Human Protein C is a prescription medicine in New Zealand. Additionally, the following points raised at the ADEC June 2005 Meeting were noted:

[Section deleted].

OUTCOME

The Committee agreed to defer the decision to schedule Human Protein C, in line with its decision to defer consideration of the scheduling of products derived from the fractionation of plasma and comparable recombinant products, pending further consultation with jurisdictional stakeholders (see Item 13.6).

15.1.2 EPLERENONE

PURPOSE

The Committee considered the scheduling of a new medicine, eplerenone.

BACKGROUND

Eplerenone is an aldosterone antagonist with properties similar to those of spironolactone but with a higher selectivity for the aldosterone receptor. It is used in the management of hypertension and heart failure; in the management of hypertension, eplerenone may be given alone or with other antihypertensives.

The March 2005 ADEC recommended approval of the application submitted by XXXXXXXX to register XXXXXXXX, containing the new chemical entity eplerenone XXXXXXXX mg and XXXXXXXX mg, for the indication: “To reduce the risk of cardiovascular death in combination with standard medical therapy in patients who have evidence of heart failure and left ventricular impairment within 3-14 days of an acute myocardial infarction”.

ADEC also recommended that the approval was subject to the finalisation of the Product Information document to the satisfaction of the TGA.

DISCUSSION

The Committee noted that eplerenone was a prescription medicine in New Zealand. Additionally, the following points raised with the ADEC were noted: [Section deleted]

DECISION 2005/45-21

The Committee agreed to include eplerenone in Schedule 4 of the SUSDP on the grounds that the condition being treated necessitated appropriate medical diagnosis and the safe use of this medicine required patient management and monitoring by a medical professional. The inclusion of eplerenone in Schedule 4 harmonises the scheduling of this substance with New Zealand.

Schedule 4 – New entry

EPLERENONE.

15.1.3 STRONTIUM RANELATE

PURPOSE

The Committee considered the scheduling of strontium ranelate.

BACKGROUND

Strontium ranelate stimulates bone formation as well as reduces bone resorption. It is used in the treatment of postmenopausal osteoporosis to reduce the risk of vertebral and hip fractures.

The March 2005 ADEC Meeting recommended the approval of the application submitted by XXXXXXXX to register XXXXXXXX, containing the new chemical entity, strontium ranelate (XXXXXXXX g), for the indication: “Treatment of postmenopausal osteoporosis to reduce the risk of fracture”.

ADEC also recommended that approval be subjected to the finalisation of the Product Information to the satisfaction of the TGA.

DISCUSSION

The Committee noted that strontium ranelate is a prescription medicine in New Zealand. Additionally, the Committee took into consideration that the March 2005 ADEC noted [section deleted]. It was highlighted that the Product Information (PI) document reported that strontium ranelate was non-genotoxic in *in vitro* and *in vivo* tests. Studies showed no effects on fertility in rats or treatment-related carcinogenicity. No studies on the effects on the ability to drive and use machines had been performed.

The Product Information document stated that strontium ranelate is only intended for use in post menopausal women.

DECISION 2005/45-22

The Committee agreed that strontium ranelate be included in Schedule 4 of the SUSDP on the grounds that the condition being treated necessitated appropriate medical diagnosis and that safe use required patient management and monitoring by a medical professional. The inclusion of strontium ranelate in Schedule 4 would also harmonise the scheduling with New Zealand.

Schedule 4 – New entry

STRONTIUM RANELATE.

15.1.4 SEVELAMER HYDROCHLORIDE

PURPOSE

The Committee considered the scheduling of a new medicine, sevelamer hydrochloride.

BACKGROUND

Sevelamer hydrochloride is a phosphate binder used for treatment of hyperphosphataemia in patients with chronic renal failure on haemodialysis.

The June 2005 ADEC Meeting resolved that there should be no objection to the approval of the application submitted by XXXXXXXX to register XXXXXXXX, containing the new chemical entity sevelamer hydrochloride XXXXXXXX mg and XXXXXXXX mg, for the indication: "XXXXXXXX is indicated for the management of hyperphosphataemia in adult patients with stage IV and V chronic kidney disease".

ADEC also recommended that the approval was subject to finalisation of the Product Information document to the satisfaction of the TGA.

DISCUSSION

The Committee noted that sevelamer hydrochloride is a prescription medicine in New Zealand. Additionally, the following points raised with the ADEC were noted:

[Section deleted].

DECISION 2005/45-23

The Committee agreed to include sevelamer hydrochloride in Schedule 4 on the grounds that the condition being treated necessitated appropriate medical diagnosis and the safe use of this medicine required patient management and monitoring by a medical professional. The inclusion of sevelamer in Schedule 4 also harmonises the scheduling of this substance with New Zealand.

Schedule 4 – New entry

SEVELAMER.

16. OTHER MATTERS FOR CONSIDERATION

16.1 ITEM DELETED

16.2 N,N-DIMETHYLAMPHETAMINE

PURPOSE

The Committee considered the scheduling of N,N-dimethylamphetamine.

BACKGROUND

N,N-dimethylamphetamine is a derivative of amphetamine, which can be synthesized from ephedrine or the ephedra plant, and has comparable central nervous system (CNS) effects to methylamphetamine. Methylamphetamine is a CNS stimulant currently listed in Schedule 8 of the SUSDP.

DISCUSSION

The XXXXXXXX Member referred for consideration by the Committee, the issue of whether N,N-dimethylamphetamine was captured by the Schedule 8 methylamphetamine entry or if it required a separate entry. This was prompted by a query from the XXXXXXXX Police.

The Committee considered the following:

- There was limited information on the toxicity profile of N,N-dimethylamphetamine. In a study comparing the neurotoxic potential of N,N-dimethylamphetamine and methylamphetamine (a structurally-similar drug) in mice and rats, both compounds were found to deplete levels of dopamine and serotonin in mice and rat brains. However, N,N-dimethylamphetamine was a considerably less potent neurotoxic agent.
- No information was located regarding the dependence or abuse potential of N,N-dimethylamphetamine.
- N,N-Dimethylamphetamine was a Schedule 1 controlled substance in the US for reasons of abuse or trafficking.
- There was no current medical use for N,N-dimethylamphetamine.
- While commonly known as N,N-dimethylamphetamine or dimethylamphetamine, the draft guidelines and policies on Joint Agency determination of ingredient names

indicated that the INN should be included where available, in this case dimetamfetamine.

The Committee noted that a submission had been received from XXXXXXXX expressing interest in the scheduling of N,N–dimethylamphetamine.

The XXXXXXXX Member indicated that the inclusion of N,N–dimethylamphetamine in Schedule 9 would be an impediment to further illegal operations. The Committee agreed to recommend to New Zealand that it consider the scheduling N,N–dimethylamphetamine.

DECISION 2005/45-24

The Committee agreed to include N,N–dimethylamphetamine in Schedule 9 on the basis of similar toxicity and abuse potential to methylamphetamine and further agreed to include (dimetamfetamine) in the entry for clarity. The Committee also agreed to recommend to New Zealand to consider the scheduling of N,N–dimethylamphetamine.

Schedule 9 - New entry

N,N–DIMETHYLAMPHETAMINE (Dimetamfetamine).

16.3 SEDATING ANTIHISTAMINES

PURPOSE

The Committee considered comment regarding the June 2005 decision that, in terms of trans–Tasman harmonisation, the current scheduling of sedating antihistamines remained appropriate.

BACKGROUND

The October 2002 trans–Tasman Harmonisation Working Party (TTHWP) recommended that New Zealand harmonise their scheduling of multi–ingredient preparations containing antihistamines with Australia. The October 2003 Meeting foreshadowed consequential amendments to the SUSDP. The February 2004 NDPSC Meeting amended the SUSDP Schedule 2 (S2) entries as foreshadowed for brompheniramine, chlorpheniramine, dexchlorpheniramine, diphenhydramine, diphenylpyraline, doxylamine, pheniramine, promethazine, thenyldiamine, trimeprazine and triprolidine. All these sedating antihistamines were classified as S2 when combined with one or more therapeutically active substance in oral preparations for the treatment of coughs, colds or influenza when either at least one other therapeutically active substance is a sympathomimetic decongestant or contained in the night–time dose of a day-night pack. This amendment

was given effect from 1 September 2004 and it was recognised that this would reclassify a significant number of existing combination products both here and in New Zealand.

The Committee recalled that XXXXXXXX submitted a proposal to the February 2005 NDPSC Meeting to allow multi-ingredient preparations containing diphenhydramine but not containing a sympathomimetic to remain S2. However, the Committee instead foreshadowed the consideration of the scheduling of all oral sedating antihistamines relating to any outcomes on the issue from the June 2005 meeting of New Zealand's Medicines Classification Committee (MCC).

At the June 2005 NDPSC Meeting, the Committee noted the outcomes of the June 2005 MCC Meeting on sedating antihistamines achieved trans−Tasman harmonisation on the scheduling of those oral sedating antihistamines amended at the February 2004 NDPSC Meeting. On the grounds of harmonisation and public health concerns on the potential risks associated with the sedative effects of the antihistamines, the Committee confirmed that the current scheduling of sedating antihistamines remained appropriate.

DISCUSSION

The Committee noted that the June 2005 MCC Meeting referred the following recommendations to the NDPSC in relation to trans-Tasman harmonisation of oral sedating antihistamines:

A. *That the NDPSC should be asked for clarification of why sedating antihistamines for travel sickness have remained classified as S2 medicines when they contain only a sedating antihistamine.* The Committee recalled that dimenhydrinate and promethazine had an S2 entry added for packs of 10 for the prevention or treatment of travel sickness as a result of the TTHWP Decision 9/4. This amendment was foreshadowed at the October 2003 NDPSC Meeting and confirmed at the February 2004 NDPSC Meeting (dimenhyrinate was also discussed under Item 1.8.1.1 in relation to the use exclusion for children under 2 years of age). Thus, the reason for the entries was to harmonise scheduling with New Zealand. The Committee further recalled that diphenhydramine also has an S2 entry for packs of 10 for prevention or treatment of motion sickness. This entry was added after the November 1979 DPSSC Meeting and has remained ever since. In New Zealand, diphenhydramine also has a Pharmacy Only listing for packs of 10 for prevention or treatment of motion sickness. Thus, the current scheduling of diphenhydramine was harmonised with New Zealand. The Committee noted that there are no other sedating antihistamines with an S2 entry for prevention or treatment of travel sickness currently in the SUSDP.

B. *That the exemption for the sale of meclozine for travel sickness at travel terminals or aboard ships or planes should retain the pack size of 12 tablets and that the NDPSC should be asked to harmonise on this pack size for OTC sales.* The Committee noted that there were no products currently registered for use in Australia containing meclozine. The Committee recalled that the decision to

amend the scheduling of meclozine was foreshadowed at the February 2004 NDPSC Meeting as a result of the TTHWP Decision 9/4 and this foreshadowed amendment was confirmed at the June 2004 NDPSC Meeting. At this meeting, a new entry was made in Schedule 2 for primary packs containing 12 or less tablets or capsules for the prevention of motion sickness. Thus, the SUSDP was already harmonised with New Zealand for this substance.

C. *That cyclizine for the prevention of travel sickness should be reclassified as a restricted medicine in New Zealand (i.e. S3) and that the NDPSC be notified of this recommendation.* The Committee noted that there have never been any products containing cyclizine on the Australian Register of Therapeutic Goods (ARTG) and it is listed in S4 of the SUSDP without exemption. This particular antihistamine was not considered along with meclozine, promethazine & dimenhydrinate (as per TTHWP Decision 9/4) most likely because of its borderline sedation effects (i.e. it is not a sedating antihistamine). The Committee further noted that cyclizine had been reclassified as a Restricted Medicine in New Zealand. Previously, as with other antihistamines, it was scheduled as Pharmacy Only for the prevention or treatment of travel sickness. The Committee decided it was appropriate to refer the scheduling of cyclizine to the TTHWP for consideration of harmonisation.

D. *That mepyramine should be classified as a prescription medicine except for dermal use and a pharmacy-only medicine for dermal use and that the NDPSC should be asked to harmonise with the New Zealand classification.* This matter was discussed by the Committee under Agenda Item 18.1.

The Committee also considered correspondence from the TGA's Over The Counter (OTC) Medicines Section concerning the scheduling of sedating antihistamines. One of the matters raised at the June 2005 NDPSC Meeting was that although some products (available in Australia) in S3 containing sedating antihistamines for the treatment of symptoms of coughs, colds and influenza were specifically labelled for night time use, the dosage on the label also recommended a dosing regimen to be taken throughout the day. The Committee noted the following points that the OTC Medicines Section raised in response:

- The current S2 entries refer to products in **day-night packs only** which contain an antihistamine in the bed-time dose. Products intended only for night-time use would not meet the conditions of the current S2 entry. The OTC Medicine Section was unable to find any day-night products where the night dose was labelled for use during the day.
- Because of the recommendations from the June 2005 NDPSC Meeting regarding the scheduling of pseudoephedrine, all products which contain pseudoephedrine and a sedating antihistamine will be included in either S3 or S4.
- The current S2 entries refer only to products indicated for the symptomatic treatment of coughs, colds or influenza. It had come to the attention of the OTC Medicines

Section that there were a number of combination products on the Australian Register of Therapeutic Goods (ARTG) that are either combination day-night products which contain a sedating antihistamine in the night-time dose or else are combination products which contain a sedating antihistamine with a sympathomimetic which are for symptomatic treatment of conditions **other than coughs, colds or influenza**. The OTC Medicines Section point out that, although the formulations of these products address the Committee's concerns regarding the sedation risks of formulations which contain sedating antihistamines, they still remain S3 because of the wording of the current S2 entry for sedating antihistamines.

- The OTC Medicines Section had provided a table of products affected by the change in wording for the S2 entry for sedating antihistamines. Also affected, inadvertently or otherwise, were two newly registered products intended for sinus relief that contain chlorpheniramine, phenylephrine and paracetamol. It was not clear whether it was the Committee's intention for combination products which contain a sedating antihistamine in combination with phenylephrine with or without paracetamol for the treatment of sinusitis or allergies to be classified as Schedule 3 products.

The Committee reiterated the decision at the June 2005 Meeting to restrict combination products containing a sedating antihistamine to S3 unless they were a day-night preparation with the sedating antihistamine only in the bed–time dose or if one of the other therapeutically–active substances were a sympathomimetic (other than pseudoephedrine). With this in mind, and taking into account the correspondence from the OTC Medicines Section, the Committee agreed that the entries for sedating antihistamines should be amended to allow preparations which meet the S2 listing criteria but are intended for conditions other than coughs, colds & influenza to remain in S2.

OUTCOME

The Committee agreed to refer the scheduling of cyclizine to the February 2006 Meeting of the TTHWP. The Committee further agreed to foreshadow an amendment the S2 entries for all oral sedating antihistamines by removing all references to indications. The Committee had, in some cases, taken the approach that the appropriateness of particular indications was an issue that could be effectively dealt with during the registration process. This foreshadowed decision would then allow all combination preparations which also contain a sympathomimetic decongestant (i.e. phenylephrine) to be considered S2 substances. The Committee also agreed to slightly alter the wording of the current entries for sedating antihistamines to avoid possible misinterpretation regarding the cut-off age limit. Thus the statement "2 years of age or less" will be replaced with "under two years of age".

FORESHADOWED DECISION (for consideration at the February 2006 Meeting)

Schedule 2 – Amendment
(sedating antihistamines – brompheniramine, chlorpheniramine, dexchlorpheniramine, diphenhydramine, diphenylpyraline, doxylamine, pheniramine, promethazine, thenyldiamine, trimeprazine and triprolidine)

[SUBSTANCE] – amend entry to read:

[SUBSTANCE] when combined with one or more other therapeutically active substances in oral preparations when:

(a) at least one of the other therapeutically active substances is a sympathomimetic decongestant; or

(b) in a day-night pack containing [substance] in the bed–time dose.

except in preparations for the treatment of children under two years of age.

16.4 POTASSIUM CHLORIDE

PURPOSE

The Committee considered a NSW State Coroner's Report into the death of a child from an overdose of slow release potassium chloride.

BACKGROUND

Potassium chloride has been unscheduled for a number of years.

At the May 1982 NDPSC Meeting the Committee agreed that electrolyte balance control in patients at risk required proper supervision. No recommendations, however, were made by the Committee at this time.

At the February 1985 NDPSC Meeting the Committee agreed that warning on the use of potassium supplementation being given to patients on potassium sparing diuretics was the responsibility of the doctor or pharmacist and that no scheduling action was required. The February 1986 NDPSC Meeting confirmed that no entry was required in the SUSDP for potassium chloride.

DISCUSSION

The Committee were advised that a NSW State Coroner's Report into the death of a child from an overdose of slow release potassium chloride included a number of

recommendations directed to the NSW Minister of Health, the TGA and the NDPSC. These recommendations were:

- As a matter of priority, all slow release potassium products should be given a Schedule 4 classification to ensure that they are taken under medical supervision.
- All manufacturers of slow release potassium products should be required to include on their labels the following warnings:
  - "Do not use for children"
  - "Keep out of reach of children"; and
  - "Seek immediate medical assistance if too many tablets are taken".

  And to amend their Product Information leaflets and Consumer Medicine Information leaflets accordingly.
- Consideration should be given to imposing a similar labelling requirement for all products that are suitable only for adult consumption and could be fatal if ingested by children.

The Committee noted that the current unscheduled status of slow release potassium chloride products technically allowed them to be available through retail outlets. However, a Member noted that these products have been marketed for a long time and have always been supplied through pharmacies. Indeed, a Member observed that many pharmacies keep these products in the dispensary.

[Sentence deleted].

Members noted that potassium chloride has a very wide range of uses. There was general agreement that the consideration of this issue at the February 2006 NDPSC Meeting would be confined to specifically considering the therapeutic uses of potassium chloride.

The Committee was also advised that slow release potassium chloride products for therapeutic use were pharmacy only medicines in New Zealand.

OUTCOME

The Committee noted the NSW State Coroner's Report into the death of a child from an overdose of slow release potassium chloride and agreed to gazette this substance for formal consideration at the February 2006 NDPSC Meeting.

18. MATTERS REFERRED BY THE MEDICINES CLASSIFICATION COMMITTEE (MCC) OF NEW ZEALAND

18.1 MINUTES OF THE NOVEMBER 2004 AND JUNE 2005 MCC MEETINGS

PURPOSE

The Committee considered the outcomes of New Zealand's Medicines Classification Committee (MCC) November 2004 and June 2005 meetings.

BACKGROUND

At these meetings, the MCC considered a number of medicines recommended by the NDPSC for harmonisation of scheduling. In addition, the MCC agreed to classify as prescription medicines all the new chemical entities forwarded by the New Zealand Medicines Assessment Advisory Committee for classification.

DISCUSSION

A member advised that some of the outcomes of the November 2004 and June 2005 MCC meetings were also discussed at the 14th TTHWP Meeting and that it was agreed by Working Party members that the relevant outcomes be forwarded to the NDPSC February 2006 meeting for consideration in an effort to expedite the harmonisation process (item 1.8.1.1). The following items were discussed by the Committee:

<u>November 2004 MCC Meeting</u>

- Ketotifen: Members noted that ketotifen was Schedule 4 (S4) in Australia while in New Zealand it was classified as Prescription medicine except for ophthalmic preparations which were regulated as Restricted medicines. The Committee noted that this issue would be on the agenda of the February 2006 NDPSC meeting as part of a rescheduling application and that the outcome of this consideration was expected to also resolve the harmonisation issue.

- Mercury and Methyl Mercury: The Committee was advised that there was currently no separate schedule entry for methyl mercury in the SUSDP but that this substance would be covered under the entry for mercury in S4. Members also noted that methyl mercury was classified as Prescription medicine in New Zealand except in medicines containing ≤300 μg/kg or or per litre. The Committee noted in the MCC minutes that New Zealand agreed to harmonise with Australia and adopted the exemptions specified for these compounds in Appendix G of the SUSDP and amended the cut-offs for exemption from 10 milligrams per litre or per kilogram to 1 milligram per litre or per kilogram for mercury and to 300 micrograms per litre or per kilogram for methylmercury. MCC based its decision on the rationale that the proposed NDPSC cut–offs, when taken in conjunction with mercury from food and environmental sources,

should fall within the World Health Organisation's provisional tolerable weekly intake of mercury and methylmercury of 0.1 and 0.3 milligrams, respectively, per person (weighing 60 kilograms) per week.

In addition, members noted that the issue of unharmonised nomenclature for mercury between the SUSDP S2 (specified "organic mercury") and Part III (specified "Mercury") was dealt with under item 1.8.1.1.

- Triamcinolone: The Committee noted that the MCC had considered its recommendation to amend the Restricted Medicine entry to harmonise with Australia and restrict the availability of triamcinolone within this classification level to preparations containing 0.1% or less of triamcinolone and in packs containing 5 grams or less of triamcinolone for the treatment of mouth ulcers. Members noted that New Zealand did not harmonise with the indication for triamcinolone in S3 but decided to adopt a formulation based entry which makes the SUSDP S3 and Part II entry for triamcinolone only partially harmonised. Members also pointed out that the S2 entry for triamcinolone was not fully harmonised due to differences in dosage and pack size restrictions and the conditions specified in the S2 entry. To harmonise the S2 and Part III entries for triamcinolone as well as that of all corticosteroid nasal spray for the prophylaxis or treatment of allergic rhinitis, the Committee agreed to recommend that MCC consider adopting the condition "for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over" in Part III. This would be consistent with the approach taken for beclomethasone and budesonide as recommended by the TTHWP Meeting 14 and endorsed by the NDPSC at this meeting (see item 1.8.1.1). Furthermore, in order to fully harmonise the entries in S2 and Part III, the Committee also agreed to remove the pack size restriction specified for all corticosteroid nasal sprays in S2 including mometasone for consistency across the class. The Committee agreed to consider this item at the February 2006 meeting.

- Phenylephrine: The Committee noted that the MCC made a recommendation that phenylephrine for oral use should be a general sale medicine in products containing 50 milligrams or less per recommended daily dose and in packs containing 250 milligrams or less of phenylephrine per pack. Products recommending higher doses or larger pack sizes should be pharmacy-only medicines. Members noted that phenylephrine was on the agenda of the October 2005 (see item 13.4) and that the outcome of this consideration was expected to also address the harmonisation issue.

- The Committee noted the November 2004 MCC meeting had agreed to classify the following new chemical entities Prescription Medicines and agreed to foreshadow their inclusion in S4 at the February 2006 meeting in order to harmonise with New Zealand.

Fulvestrant, palonosetron and terlipressin.

June 2005 MCC Meeting

- Aciclovir: The Committee noted that the MCC June 2005 Meeting agreed to harmonise with Australia on the strength and pack size of general sale products for the treatment of *herpes labialis*. However, members noted that the scheduling of aciclovir remained unharmonised due to the inclusion of preparations for external use for the treatment of herpes labialis when containing more than 5% of acyclovir and packed in tubes containing more than 10 grams of acyclovir in Part III (Pharmacy Only) in New Zealand while preparations other that the exempt products were S4 in Australia. The Committee agreed to make a recommendation to New Zealand to consider reviewing its Pharmacy entry to harmonise with Australia.

- Aconitum spp: Members noted that the MCC had recommended that the NDPSC adopt less restrictive classifications for Aconitum spp in the SUSDP, i.e. S3 and 'unscheduled', to harmonise with New Zealand. It was noted that the only entry for Aconitum spp in the SUSDP was in S4 with no cut-offs to less restrictive schedules. The MCC minutes indicated that it agreed to reclassify Aconitum spp to less restrictive schedules to allow access to complementary products already on the market in New Zealand. This matter was also dealt with under item 1.8.1.1 where the NDPSC agreed to consider harmonising the scheduling of Aconitum spp with New Zealand at the February 2006 meeting. The New Zealand member also offered to make available to the NDPSC a copy of the assessment of the Aconitum spp rescheduling application considered by the MCC at the June 2005 meeting.

- Benzocaine: The Committee noted that the MCC had sought clarification with regard to the inclusion in S2 of preparations for oral use containing 200 mg or less of benzocaine and that this matter was dealt with under item 1.8.1.1. Furthermore, the Committee noted that MCC also considered a proposal from a company seeking to reclassify its mouthwash product containing 0.4% of benzocaine from General Sale medicine to Pharmacy Only medicine in New Zealand. It was noted that on the grounds of harmonisation, the MCC agreed with the proposal and amended Part III of Schedule 1 to include mouthwash preparations containing ≤10% benzocaine.

- Copaiba balsam and pomegranate: The Committee noted that the MCC deleted copaiba balsam and pomegranate from the Pharmacy Only Schedule in New Zealand on the grounds these substances were likely to be obsolete and that the general principle of harmonising on the least restrictive schedule should be adopted unless there was a compelling reason. The NDPSC recalled that these substances were included in S4 at the June 2005 meeting as part of the policy approach for substances where there were no marketed products endorsed by the NCCTG at its April 2005 meeting. However, the NDPSC agreed (discussed under items 12.2 and 12.4) to set aside these decisions and restore the unscheduled status of these substances.

- Cyclizine: The Committee noted that the MCC considered a request from the sponsor company of the only product registered in New Zealand containing cyclizine

proposing that its travel sickness tablets be allowed to remain available as a Pharmacy Only medicine. The MCC was of the view that cyclizine was no less sedating when compared to other sedating antihistamines and in addition, the MCC noted that this substance was identified in pharmacies as being the subject of abuse in New Zealand. On this basis, the MCC agreed that the scheduling of products for oral use containing cyclizine including those indicated for the prevention or treatment of travel sickness remain as Restricted Medicines for consistency with the scheduling of sedating antihistamines as a class. Members noted that the NDPSC had agreed to refer the scheduling of cyclizine to the TTHWP February 2006 as part of the outcome of the NDPSC's consideration of item 16.3.

- Dibrompropamidine and propamidine: The Committee noted the MCC's proposal to harmonise the scheduling of both substances with the New Zealand classification. Members noted that the NDPSC discussed this matter under item 1.8.1.1 where it was agreed to consider the issue at the February 2006 NDPSC meeting.

- Ethyl chloride: The Committee noted that the MCC considered the recommendation that ethyl chloride be classified as Prescription Medicine in New Zealand to harmonise with Australia. In New Zealand, ethyl chloride was classified as a Prescription Medicine for anaesthesia and a Restricted Medicine except for anaesthesia. MCC noted that although Martindale 34 stated that there was no place in modern anaesthesia for ethyl chloride, there was concern about abuse by inhalation of non-medicinal products in the same way as nitrous oxide. On this basis, the MCC considered it appropriate that the substance be retained in the S4 for all uses to curb the potential for abuse and recommended that the NDPSC consider deleting "anaesthesia" from the current S4 entry. The NDPSC noted that the S4 entry for ethyl chloride was already amended to "Ethyl Chloride for human therapeutic use" at the June 2005 meeting to harmonise with New Zealand and that no further action was required.

- Fluticasone: Members noted the MCC recommendation that Australia adopt the New Zealand maximum daily dose limit of 200 μg of fluticasone in S2. The MCC was of the view that fluticasone was twice as potent as the other nasal corticosteroids and that it was appropriate that the dose limit in S2 reflect this accordingly. Members agreed to consider harmonisation with the New Zealand scheduling at the February 2006 meeting.

- Jalap resin: The Committee noted that the June 2005 NDPSC meeting decision to include this substance in S4 was set aside under item 12.3. Members further noted that the substance was also part of a broader consideration in regards to the scheduling harmonisation of stimulant laxatives (see the discussion in relation to stimulant laxatives below).

- Mepyramine: In Australia mepyramine was S3 when in oral preparations and S4 for all other preparations. The Committee was advised that the decision made at the June 2005 NDPSC meeting to remove mepyramine in oral preparations from Schedule 3 was based on incorrect information that there were no products in Australia when in reality

there were three oral products registered on the ARTG containing mepyramine for supply in Australia.
In New Zealand mepyramine was a Pharmacy Medicine for dermal use and Prescription medicine for all other uses. Members noted that the June 2005 MCC meeting considered the June 2005 NDPSC recommendation that New Zealand harmonise with Australia and reschedule mepyramine to S4. Members recalled that this recommendation was made on the basis that whilst there was one Pharmacy Only topical product in New Zealand containing mepyramine, it would be appropriate to reschedule all topical preparations to S4 because of the sensitisation potential of topical antihistamines. The MCC was of the view that the sensitisation issue with mepyramine was not a widespread problem in New Zealand and that its safety profile was comparable to local anaesthetics which had remained available as OTC medicines. On this basis, the MCC agreed that a more restrictive scheduling to harmonise with Australia was not warranted at this time and recommended that the NDPSC consider harmonisation with the New Zealand scheduling of mepyramine.

The NDPSC agreed to set-aside the scheduling amendments relating mepyramine made at the June 2005 NDPSC meeting and foreshadow consideration of harmonisation of scheduling of mepyramine with New Zealand at the February 2006 Meeting, following further investigation of available products and the sensitisation issue with topical mepyramine in Australia.

- Oxiconazole: The Committee noted that MCC recommended that Australia adopt the New Zealand classification to harmonise and reschedule oxiconazole from S4 to OTC availability. MCC pointed out that there were three products on the SMARTI database which were granted consent to market as Pharmacy Only medicines in New Zealand and rescheduling the substance to OTC level of availability in Australia should be consistent with the scheduling of most antifungal agents in the SUSDP. The Committee agreed to consider harmonisation with New Zealand at the February 2006 meeting.

[Paragraph deleted].

- Schoenocaulon Officinale (sabadilla): The Committee noted that the MCC recommended that Australia harmonise with New Zealand on the scheduling of Sabadilla which was reclassified to permit continued sale of complementary products that were already on the market in New Zealand. The MCC also indicated that the material it had reviewed to support reclassification in New Zealand would be forwarded to the NDPSC for consideration at the February 2006 meeting.

The Committee noted the June 2005 MCC had agreed to classify the following new medicines as Prescription Medicines and agreed to foreshadow their inclusion in S4 at the February 2006 meeting in order to harmonise with New Zealand.

Alemtuzumab, Anecortave, Entecavir, Erlotinib, Muraglitazar, Nesiritide, Pegaptanib, Posaconazole, Solifenacin

The Committee discussed the following issues in relation to decisions of the June 2005 MCC meeting to remain unharmonised with Australia:

- Salbutamol and terbutaline: The Committee noted that the MCC reviewed the scheduling of these substances on the basis that 2 years had lapsed since the MCC declined to harmonise with Australia due to differences in the monitoring and management of asthma between the two countries. A member advised that several submissions were received from professional bodies arguing against the proposed rescheduling of salbutamol to S3 in New Zealand due to the severity of asthma and the history of asthma-related deaths in New Zealand. The MCC felt there was no clear management framework for asthma in place within the pharmacy setting and that allowing OTC availability of salbutamol and terbutaline inhalers under current conditions in New Zealand could compromise public health and safety. On this basis, the MCC maintained its position that salbutamol should remain unharmonised at this time and that future proposals to reclassify the scheduling of salbutamol and terbutaline in New Zealand should include a treatment protocol aimed at meeting the requirements of key stakeholders including medical practitioners, asthma educators, pharmacists and consumers.

- Hyoscine butylbromide: The Committee noted that the MCC had considered the NDPSC recommendation to harmonise with the S2 entry in the SUSDP based on the substance's safety record in Australia. Members noted that the MCC declined to harmonise with the scheduling of hyoscine butylbromide on the basis that this medicine should not be made available without advice at the point-of-sale as some of the conditions for which it was indicated were not appropriate for self-diagnosis and required medical intervention. In New Zealand, it was indicated that hyoscine butylbromide was prescribed for conditions such as renal colic which the MCC considered inappropriate for self-diagnosis.

- Stimulant laxatives: The Committee noted the MCC recommendation that stimulant laxatives should be classified more restrictively than bulk laxatives and be included in S2 in order to promote the latter as first line treatment and to afford an element of control over the sale of these products. The Committee noted that the MCC further indicated that pharmacists in New Zealand continued to be aware of attempts by anorexics to abuse stimulant laxatives and that they were able to intervene when necessary. The NDPSC agreed that the issue of harmonising the scheduling of stimulant laxatives required a broader policy approach given the potential regulatory impact in Australia if the New Zealand scheduling for these substances was adopted. The Committee therefore agreed that it would be appropriate to refer this matter to the TGA for consideration.

The members noted that the substances for which the MCC agreed to harmonise with the Australia included alclometasone and clobetasone, antazoline, bethanecol, the antihistamines (with some minor amendments around availability for travel sickness), benzocaine, stramonium, strychnine, fosamprenavir, flunisolide, Juniperus Sabina and naphazoline.

OUTCOME

The Committee noted the outcomes arising from the November 2004 and June 2005 MCC meetings and agreed to foreshadow consideration of the following items at the February 2006 meeting.

Furthermore, the Committee agreed to recommend that New Zealand consider harmonising with Australia by adopting the S2 entry for aciclovir and benzocaine and adopt the condition "for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over" in all nasal corticosteroid entries in Part III.

FORESHADOWED DECISIONS FOR CONSIDERATION AT THE FEBRUARY 2006 NDPSC MEETING:

Schedule 2 – New entries

OXICONAZOLE for dermal use **except** in preparations for the treatment of tinea pedis.

SCHOENOCAULON OFFICINALE (sabadilla)in packs containing 18 milligrams or less of total alkaloids **except** in packs containing 1.8 milligrams or less and labelled with a recommended daily dose of 0.6 milligrams or less of total alkaloids.

Schedule 2 – Amendments

FLUTICASONE in aqueous nasal sprays delivering 50 micrograms or less of fluticasone per actuation when the maximum recommended daily dose is no greater than 200 micrograms for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over.

MOMETASONE in aqueous nasal sprays delivering 50 micrograms or less of mometasone per actuation when the maximum recommended daily dose is no greater than 200 micrograms for the prophylaxis or treatment of allergic rhinitis for up to six months in adults and children 12 years of age and over.

TRIAMCINOLONE in aqueous nasal sprays delivering 50 micrograms or less of triamcinolone per actuation when the maximum recommended daily dose is no greater than 200 micrograms for prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years of age and over.

Schedule 4 – New entries

ALEMTUZUMAB.

ANECORTAVE.

ENTECAVIR.

ERLOTINIB.

FULVESTRANT.

MURAGLITAZAR.

NESIRITIDE.

PALONOSETRON.

PEGAPTANIB.

POSACONAZOLE.

SOLIFENACIN.

TERLIPRESSIN.

Schedule 4 – Amendments

OXICONAZOLE – amend entry to read:

OXICONAZOLE **except**:

(a) when included in Schedule 2;

(b) in preparations for dermal use for the treatment of tinea pedis.

SCHOENOCAULON OFFICINALE (sabadilla) – amend entry to read:

SCHOENOCAULON OFFICINALE **except**:

(a) when included in Schedule 2; or

(b) in packs containing 1.8 milligrams or less of total alkaloids and labelled with a recommended daily dose of 0.6 milligrams or less of total alkaloids.

DECISION 2005/45-25

The Committee agreed to vary its decision from the June 2005 meeting to set-aside the amendments relating to mepyramine. Members noted that the decision to reschedule mepyramine to S4 and delete the S3 entry for oral preparations was based on incorrect

information and that to avoid inadvertent regulatory impact on affected products it would appropriate to set-aside the June 2005 meeting decision and reinstate the current scheduling of mepyramine at this time.

Furthermore, the Committee agreed to review the scheduling of mepyramine at the February 2006 to consider MCC's recommendation that Australia harmonise with the New Zealand classification for mepyramine.

20. MATTERS REFERRED BY THE MEDICAL DEVICES EVALUATION COMMITTEE (MDEC)

The meeting noted the minutes of the 2005/1 (6^{th}) MDEC meeting and that there were no items which required consideration.

21-23. ITEMS DELETED

24. AMENDMENTS TO THE SUSDP

24.1 EDITORIAL CHANGES AND ERRATA

PURPOSE

The Committee considered minor editorial amendments to the SUSDP.

BACKGROUND

At the June 2005 NDPSC Meeting the Committee agreed to defer consideration of a number of minor editorial changes and errata to allow time to seek comment from the NDPSC Drafting Advisory Panel (DAP).

DISCUSSION

A DAP Member responded to the Secretariat's request for consideration of a number of minor editorial changes and errata deferred from the June 2005 NDPSC Meeting. The suggestions in this response were incorporated into the following amendments considered by the Committee.

The Committee agreed to amend:

- the aspirin Schedule 2 entry through removal of "..to the following effect" from (d)(iii) as there is only one warning statement to which it refers.
- the acetanilide Schedule 4 entry by shifting "(excluding when present as an excipient)" to after "alkyl acetanilides" for consistency with other entries, e.g. iron oxide in Schedule 2.
- the tetrahydrocannabinols Schedule 9 entry by shifting the label statements under exception (c) to separate lines for clarity.

The Members agreed to amend the paragraphs in Appendix E and F Introduction under the heading "Poisons Information Centre Telephone Numbers", for simplicity and clarity, to read:

"Companies should use the Poisons Information Centre telephone number(s) (Australia 131 126; New Zealand 0800 764 766) appropriate to the country(ies) of sale for the product."

The Committee agreed, in order to avoid duplication when there already exists chemical entries in Schedule 9, to:

- delete psilocine and psilotsin [common names for 3-(2-dimethylaminoethyl)-4-hydroxyindole] and create individual entries for psilocine and psilotsin in the index referring to 3-(2-dimethylaminoethyl)-4-hydroxyindole. This approach was consistent with the indexing of common names in the SUSDP.
- delete mescaline [the common name for 3,4,5-trimethoxyphenethylamine] and create a separate entry for mescaline in the index referring to 3,4,5-trimethoxyphenethylamine.

The Committee agreed to simplify the Appendix B entry for xanthrophyll to "XANTHROPHYLL (lutein)". Members noted that no reference could be found by the Secretariat in previous NDPSC minutes as to the origin of the other common names included in the existing entry. Xanthrophyll is the AAN for lutein.

The Members considered a possible oversight in the Schedule 3 entry for fluorides which was identified by XXXXXXXX and the XXXXXXXX Member. Amendment 1 of SUSDP 19 amended the entries for fluoride to remove the word "dentifrices…" and replace it with "pastes, powders or gels for the cleaning of teeth…". This has been done for Schedules 2, 4, 5 and 6 but for the Schedule 3 entry the "for the cleaning of teeth" was left out. The Committee considered amending the Schedule 3 entry to include "for the cleaning of teeth" for consistency. However, it was noted that there may be fluoride pastes, powders or gels that were for teeth, but not for cleaning (such as fluoride treatment products) could inadvertently fall out of the Schedule 3 entry. The Committee therefore agreed to amend the Schedule 3 entry to include the general wording "for use on teeth" so as not to inadvertently narrow the entry.

The Committee considered amending the Schedule 6 entry for moxidectin. As it stands, preparations covered by part (b) of the Schedule 6 entry containing < 0.5 % moxidectin for external use in the treatment of animals would also be captured by part (a) of the Schedule 5 entry. The Members agreed to move "except when included in Schedule 5" from the end of part (a) to the end of the whole entry to correct this inadvertent outcome.

The Committee also considered a minor amendment to the Schedule 5 entry for permethrin. The XXXXXXXX Member had recommended amending part (b) of the entry "…containing 50 per cent or less permethrin…" to "…containing 50 per cent or

less of permethrin…". The Members agreed to this proposal as the "of" would add clarity to the entry.

DECISION 2005/45-26

The Committee agreed to the various editorial changes and errata, as discussed above, for inclusion in SUSDP 20 Amendment 2.

Schedule 2 – Amendment

ASPIRIN – amend entry to read:

ASPIRIN **except**:

(a) when included in Schedule 4, 5 or 6;

(b) in individually wrapped powders or sachets of granules each containing 650 mg or less of aspirin as the only therapeutically active constituent other than an effervescent agent:

(i) when enclosed in a primary pack that contains 12 or less such powders or sachets of granules;

(ii) when the primary pack is labelled with warning statements to the following effect:

Don't use [this product / name of the product]:
If you have a stomach ulcer
In the last 3 months of pregnancy
If you are allergic to aspirin or anti-inflammatory medicines;

Unless a doctor has told you to, don't use [this product / name of the product]:
For more than a few days at a time
With other medicines containing aspirin or other anti-inflammatory medicines
If you have asthma
In children under 12 years of age
In children 12-16 years of age with or recovering from chicken pox, influenza or fever
If you are pregnant;

See a doctor before taking [this product / name of the product] for thinning the blood or for your

heart. [*Can be omitted in products for inhibition of platelet aggregation*.];

(c) in tablets or capsules each containing no other therapeutically active constituent **other than** an effervescent agent when:

(i) packed in blister or strip packaging or in a container with a child resistant closure;

(ii) in a primary pack of not more than 25 tablets or capsules, each containing 325 mg or less of aspirin, or in a primary pack of not more than 16 tablets or capsules, each containing 500 mg or less of aspirin; and

(iii) the primary pack is labelled with warning statements to the following effect:

Don't use [this product / name of the product]:
If you have a stomach ulcer
In the last 3 months of pregnancy
If you are allergic to aspirin or anti-inflammatory medicines;

Unless a doctor has told you to, don't use [this product / name of the product]:
For more than a few days at a time
With other medicines containing aspirin or other anti-inflammatory medicines
If you have asthma
In children under 12 years of age
In children 12-16 years of age with or recovering from chicken pox, influenza or fever
If you are pregnant;

See a doctor before taking [this product / name of the product] for thinning the blood or for your heart. [*Can be omitted in products for inhibition of platelet aggregation*.]; or

(d) in tablets or capsules each containing no other therapeutically active constituent **other than** an effervescent agent when:

(i) packed in blister or strip packaging or in a container with a child-resistant closure;

(ii) in a primary pack containing 100 or less tablets or capsules, each containing 100 mg or less of aspirin when packed and labelled for the prevention of cardiovascular disease or for the inhibition of platelet aggregation; and

(iii) the primary pack is labelled with the warning statement:

For use under medical supervision only.

Schedule 3 – Amendment

FLUORIDES – amend entry to read:

FLUORIDES in pastes, powders or gels for use on teeth, containing more than 1000 mg/kg of fluoride ion.

Schedule 4 – Amendment

ACETANILIDE and alkyl acetanilide – amend entry to read:

ACETANILIDE and alkyl acetanilides (excluding when present as an excipient) for human therapeutic use.

Schedule 5 – Amendment

PERMETHRIN – amend entry to read:

PERMETHRIN:

(a) in preparations containing 25 per cent or less of permethrin; or

(b) in preparations for external use, for the treatment of dogs, containing 50 per cent or less of permethrin when packed in single use containers having a capacity of 4 mL or less,

except in preparations containing 2 per cent or less of permethrin.

Schedule 6 – Amendment

MOXIDECTIN – amend entry to read:

MOXIDECTIN for external use:

(a) in preparations containing 2.5 per cent or less of moxidectin when packed in single dose tubes for the treatment of cats and dogs; or

(b) in preparations containing 2 per cent or less of moxidectin for the treatment of animals

except when included in Schedule 5.

Schedule 9 – Amendments

PSILOCIN – delete entry.

PSILOTSIN – delete entry.

MESCALINE – delete entry.

TETRAHYDROCANNABINOLS – amend entry to read:

TETRAHYDROCANNABINOLS and their alkyl homologues **except**:

(a) when separately specified in this Schedule;

(b) when included in Schedule 8;

(c) in hemp seed oil, containing 50 mg/kg or less of tetrahydrocannabinols when labelled with a warning statement:

Not for internal use; or
Not to be taken; or

(d) in products for purposes other than internal human use containing 50 mg/kg or less of tetrahydrocannabinols.

Appendix B – Amendment

XANTHOPHYLL (, -CAROTENE-3,3' –DIOL;LUTEIN;VEGETABLE LUTEIN;VEGETABLE LUTEOL;BO-XAN) – amend entry to read:

SUBSTANCE	**DATE OF ENTRY**	**REASON FOR LISTING**	**AREA OF USE**
XANTHOPHYLL (lutein)	Nov 1974	a	7.1

Appendix E – Amendment

Poisons Information Centre Telephone Numbers
Delete first paragraph, insert:

Companies should use the Poisons Information Centre telephone number(s) (Australia 131 126; New Zealand 0800 764 766) appropriate to the country(ies) of sale for the product.

(Subsequent paragraphs retained)

Appendix F – Amendment

Poisons Information Centre Telephone Numbers
Delete first paragraph, insert:

Companies should use the Poisons Information Centre telephone number (Australia 131 126; New Zealand 0800 764 766) appropriate to the country(ies) of sale for the product.

(Subsequent paragraphs retained)