Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

National Drugs and Poisons Schedule Committee

Record of Reasons

47th Meeting
20-22 June 2006

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GLOSSARY

ABBREVIATION	*NAME*
AAN	Australian Approved Name
AC	Active Constituent
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
ASCC	Australian Safety and Compensation Council
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

1.7 PROCEDURAL MATTERS

1.7.1 OPERATIONS/POLICIES OF THE COMMITTEE

1.7.1.1 DRAFT TEMPLATE FOR SCHEDULING/RESCHEDULING

PURPOSE

The Committee considered a draft template for scheduling/rescheduling applications.

BACKGROUND

The February 2006 NDPSC Meeting considered the following items relating to the process and content for scheduling/rescheduling applications:

- progress of the phased introduction of electronic (e) agenda papers for NDPSC Meetings, including development of an application form/template for submissions.
- the nature of information released with the Record of Reasons, particularly regarding the issues of confidential information and transparency.
- **[**sentence deleted**]**.

While considering the above issues the Committee also recalled that there was general support at the October 2005 NDPSC Meeting for the concept of a form being developed for applicants in which they would have to identify, and justify, what information was to be treated as confidential. The Members concluded that the idea of a form could be extended to a template setting out the preferred format for submissions to the Committee. The Committee therefore agreed to begin to develop a template to facilitate the scheduling/rescheduling process.

DISCUSSION

[Section deleted**]**

Members also recalled that in the February 2006 consideration of **XXXXXXXX** the issue of electronic submissions was discussed. A Member suggested that a template could be developed where applicants had to fill in fields which correlated with the NDPSC scheduling criteria (while still being free to add additional data as the applicants wish). The Committee at that time generally felt that such a template would:

- Provide help and guidance to industry.
- Improve the efficiency with which the Committee could consider applications as all data would be clearly identified and associated with specific criteria.

Another Member noted that if an electronic template were to be introduced then this would enable the Secretariat to only accept applications using the template as valid submissions, resulting in all submissions being electronic. A Member asserted that the

creation of a template for submissions would require considerable drafting and consultation because of the nature of the different types of submissions considered by the Committee from different sectors.

The Committee also considered the New Chemicals Template used by NICNAS, and its associated guidance notes. A Member had suggested that the Committee consider including specific toxicological headings in the proposed NDPSC template and that guidance notes be included for each toxicological heading as was the *Toxicity and Safety of the Substance* section in the NICNAS Template. A Member noted that the NICNAS Template was based on the OECD Robust Industry Summaries and were therefore compliant with an approved international standard. A Member noted, however, that including set toxicological headings may not be appropriate for the broader spectrum of applications received by the Committee. The Committee therefore generally endorsed a generic focus for developing a template appropriate for all applications.

The Members generally agreed on the following plan for developing an NDPSC Template:

- Member's recommended changes to be incorporated into the draft Template.
- Draft Template to be circulated, out of session, to the Committee for refinement.
- Draft Template to be loaded onto the NDPSC website before the October 2006 NDPSC Meeting to allow stakeholder feedback.
- Draft Template, and any stakeholder feedback, to be considered at the October 2006 NDPSC Meeting. The Draft Template could then be finalised.
- Trial the use of the NDPSC Template with some sponsors.

A Member also noted that as this template was for use by the current Committee only it should be very clear that it had nothing to do with templates or procedures envisaged for the new Committees under the proposed Australia New Zealand Therapeutic Products Authority.

OUTCOME

The Committee agreed to foreshadow adoption of a template for scheduling/ rescheduling applications to allow stakeholder input into the drafting of the template. The Committee further agreed to post a draft template onto the NDPSC website, following out-of-session refinement, for stakeholder comments prior to the October 2006 NDPSC Meeting.

1.7.1.2 PROCEDURAL AND GOVERNANCE ISSUES

PURPOSE

The Members considered Committee procedural and governance issues, particularly:

- **[**section deleted**]**;
- pre-meeting lobbying;
- **[**section deleted**]**.

DISCUSSION

Following the February 2006 NDPSC Meeting **XXXXXXXX** wrote to Members raising some issues regarding matters where **XXXXXXXX** felt the NDPSC could improve its current practices. The points discussed included:

[Section deleted**]**

Pre-Meeting Lobbying

- **XXXXXXXX** recommended that Members should not agree to make themselves available for pre-meeting lobbying by applicants/sponsors regarding matters for consideration by the Committee.
- If companies had additional information they wished to bring to the attention of Members, this should be done through the transparent public processes that exist via the Secretariat.

XXXXXXXX advised that industry had raised concerns about a lack of availability of jurisdictional and other Members prior to Meetings. **XXXXXXXX** asserted that if the purpose of industry meeting with any of the Members was to lobby around a specific decision then this was inappropriate. If, however, industry was meeting with Members as part of normal work practices, and discussing general issues not related to a specific matter before the Committee, then this was acceptable.

A Member asserted that while this policy may be appropriate for expert Members, jurisdictional Members needed to remain accessible to applicants, particularly as there may be specific jurisdictional issues that an applicant wished to address in their submission. Members generally felt, however, that there was a distinction between legitimate contact for information gathering and lobbying.

The Members therefore agreed to clarify that contact between Members, particularly jurisdictional Members, and the applicant/sponsor was not precluded, but that lobbying was. A Member asserted that it was important that the Committee's decisions could not be called into doubt through any perception of Members being influenced by lobbying.

A Member felt that perhaps lobbying needed some definition i.e. intention to influence the decision of the Member/Committee. The Committee, however, generally agreed that it could be left to Members, based on their experience and common sense, to interpret whether a contact that was occurring was appropriate or was lobbying. Members would need to keep in mind that such judgements must stand up to public scrutiny so that if there was criticism, it could be justified that the contact was not lobbying. A Member

also noted that the Committee needed to be alert to surreptitious lobbying, particularly by "independent experts" who often did not disclose their links to the applicant/sponsor.

Members therefore agreed that Members should not agree to make themselves available for pre-meeting lobbying by applicants/sponsors regarding matters for consideration by the Committee. Members also agreed to write to industry organisations to request that they disseminate the Committee's view on lobbying to their members.

[Section deleted**]**

OUTCOME

The Members:

- **[**Section deleted**]**
- agreed that Members should not make themselves available for pre-meeting lobbying by applicants/sponsors regarding matters for consideration by the Committee; and
- **[**Section deleted**]**

1.7.1.3 OUTCOMES FROM THE MAY 2006 NCCTG MEETING

1.7.1.3.1 SPONSOR ACCESS TO EVALUATION REPORTS

PURPOSE

The Committee considered the issue of sponsor access to evaluation reports.

BACKGROUND

The February 2004 NDPSC Meeting considered a proposal seeking the release of evaluation reports to the sponsor (for medicines) so that comment could be submitted prior to NDPSC consideration. Members requested that the Secretariat review the proposal and identify implications for consideration by the Committee.

The February 2005 NDPSC Meeting noted that the cut-off for receipt of rescheduling applications was 16 weeks prior to the NDPSC meeting to allow time for the submission to be despatched, assessed (around 8 weeks) and for the evaluation report to be forwarded to the Members. The Secretariat advised that an additional pre-meeting comment on evaluation reports would require medicines rescheduling submissions to be made at least 20 weeks prior to the NDPSC Meeting. This extra time would be required to obtain reports from the evaluators, distribute these to the applicant and allow them reasonable time to comment. The Committee was of the view that the provision of medicines reports to sponsors would be beneficial to the scheduling process and prepared the following model:

- Medicines rescheduling submissions must be made 20 weeks before an NDPSC meeting to allow for company comment.
- Medicines evaluation reports (prepared following assessment of an application) will be sent to the applicant with personal information, e.g. the evaluator's name, deleted.
- The applicant will have a maximum of 10 working days to comment. Responses are to be limited to 6 single sided A4 pages and in a font no smaller than 12 point. The response may only address issues raised in the evaluation report and must not contain any new or additional data.

The June 2005 NDPSC Meeting agreed to proceed with the proposed model for sponsor access to medicines evaluation reports to allow implementation for the February 2006 NDPSC Meeting. The October 2005 NDPSC Meeting confirmed the June 2005 decision and also considered broadening the process for access to evaluation reports to apply to scheduling and rescheduling applications for domestic or other chemicals where an evaluation report was produced (excepting agvet chemicals where there was an existing APVMA process). The Committee agreed to defer consideration of this proposal to allow time for consultation with peak industry groups. The February 2006 NDPSC Meeting subsequently agreed:

- to broaden the process for sponsor access to evaluation reports to also apply to the scheduling and rescheduling for domestic chemicals where an evaluation report had been produced following assessment of a rescheduling application (excepting agvet chemicals where there is an existing APVMA process); and
- that the proposed amendment to the NDPSC guidelines for the provision of medicine and domestic chemicals evaluation reports to sponsors be referred to NCCTG for support and approval.

DISCUSSION

The Committee noted that the May 2006 NCCTG meeting supported the amendment of the NDPSC operational guidelines to allow the release of evaluation reports to sponsors/applicants of medicines and domestic chemicals. The Committee therefore agreed that the following changes be made to the NDPSC Guidelines:

MEDICINES - addition of the following under the "Rescheduling of Medicines" heading immediately following the existing text.

Commenting on Evaluation Reports for Rescheduling of Medicines

The NDPSC can, where warranted, have an application for rescheduling evaluated. Where a submission has been made at least 20 weeks before the meeting, the evaluation report can be distributed to the sponsor/applicant for comment prior to consideration by the NDPSC. Personal information, such as the evaluator's name, and confidential information not belonging to the applicant, will be deleted. Distribution will, where possible, be either fax or email. The applicant will have a maximum of 10 working days

to comment, with comments to be sent by email to the NDPSC mailbox NDPSC@health.gov.au. Comments are to be limited to 6 single sided A4 pages and in a font no smaller than 12 point. The response may only address issues raised in the evaluation report and must not contain any new or additional data. Inclusion of new or additional data is likely to be grounds for consideration of the rescheduling application by the NDPSC to be deferred to a later meeting to allow assessment of this information. Evaluation reports are confidential and are released to sponsor/applicant on the understanding that they are not to be released to third parties without permission.

DOMESTIC CHEMICALS - addition of the following under the "Rescheduling of Domestic or Other Chemicals" heading immediately following the existing text.

Commenting on Evaluation Reports for Domestic Chemicals

The NDPSC can, where warranted, have an application for the scheduling or rescheduling of domestic or other chemicals, evaluated. Where a submission has been made at least 20 weeks before the meeting, the evaluation report can be distributed to the sponsor/applicant for comment prior to consideration by the NDPSC. Personal information, such as the evaluator's name, and confidential information not belonging to the applicant, will be deleted. Distribution will, where possible, be either fax or email. The applicant will have a maximum of 10 working days to comment, with comments to be sent by email to the NDPSC mailbox NDPSC@health.gov.au. Comments are to be limited to 6 single sided A4 pages and in a font no smaller than 12 point. The response may only address issues raised in the evaluation report and must not contain any new or additional data. Inclusion of new or additional data is likely to be grounds for consideration of the rescheduling application by the NDPSC to be deferred to a later meeting to allow assessment of this information. Evaluation reports are confidential and are released to sponsor/applicant on the understanding that they are not to be released to third parties without permission.

OUTCOME

The Committee agreed to proceed with the October 2005 and February 2006 NDPSC decisions to amend the guidelines and webpage to reflect the provision of medicine and domestic chemical evaluation reports to sponsors.

1.7.1.3.2 RELEASE OF INFORMATION IN THE RECORD OF REASONS

PURPOSE

The Committee considered the release of information in the Record of Reasons.

BACKGROUND

The October 2002 NDPSC Meeting, after considering a comment on the inaccuracy of the NDPSC Guidelines, agreed that the Guidelines should be edited to remove outdated or incorrect material (including the section on confidentiality). The Committee flagged that the NDPSC Guidelines Working Party may need to be reconstituted following the Galbally report to re-write the Guidelines. However, re-writing of the Guidelines was not progressed due to work being undertaken with the implementation of Galbally Recommendation 7 (splitting of the NDPSC into two separate committees – the Medicines and Poisons Scheduling Committees) as part of the establishment of the Australia New Zealand Therapeutic Products Authority (ANZTPA).

The October 2005 NDPSC Meeting considered two examples of stakeholder concern about the release of "confidential" information. Members agreed that no changes to the Secretariat's editing of the Record of Reasons were warranted at that time and confirmed the current practice of the Secretariat as appropriate. The Committee further agreed to reconsider this issue at the February 2006 NDPSC Meeting as an opportunity existed to progress some of the moves towards further transparency before the trans-Tasman arrangements come into force. This would allow a smoother transition for stakeholders.

[Sentence deleted**]**. The Committee agreed to refer this issue to NCCTG and to use NCCTG's considerations as a basis for further progression of this issue. Members also agreed to recommend that this consideration remain focused on the specific issue for the NDPSC, as a broader discussion of the full trans-Tasman approach to confidentiality could delay the implementation of a workable solution on the level of transparency the NDPSC was going to provide in the Record of Reasons.

DISCUSSION

Members recalled that the Secretariat currently produced the Record of Reasons from the Ratified Minutes through deletion of material considered by the Secretariat to be commercially sensitive (i.e. formulation detail, manufacturing method, sponsor name, product name, sales information), details from the evaluation reports for new agvet products and extracts from the ADEC minutes. This process was often subjective and the onus for identifying confidential information had fallen on the Secretariat. The Record of Reasons also usually excluded items such as Committee procedures, information items, policy items being developed and Members reports.

The Committee recalled that the October 2005 NDPSC Meeting had noted that under the *Proposed New Model for the Scheduling of Medicines and Poisons within the Joint Agency* (the draft scheduling policy framework), released for public comment in 2005, the onus would be on the person making the submission to justify why information should be treated as confidential, whereas at the moment the Secretariat was making this decision.

The Members also recalled that the current Record of Reasons, with its increased details and information compared to historical standards, was introduced in part because of pressure from stakeholders for increased transparency about the reasons for a decision.

The Secretariat, in including information in the Record of Reasons, advised that it was being pushed by two agendas:

- a drive for transparency about the basis for NDPSC decisions. The opportunity to comment on a decision loses meaning if stakeholders cannot access the details of the reasons behind a decision.
- continuing strong pressure on the Secretariat by some stakeholders to have as little information about their product(s) as possible available to the public.

The Secretariat advised that the above agendas also arise with the issue of the public gazette notices. While in general there was a desire for more transparency in the gazette notices the individual applicants were often reluctant to have additional information in the gazette. The Secretariat had attempted to encourage applicants to include a proposed gazettal notice in their submission but this did not generally occur.

Members also recalled that at the October 2005 NDPSC Meeting there was general agreement that if companies have a particular concern about confidential information in their submission or correspondence with the Secretariat they should be indicating as such. The Committee noted that the issue of identifying and justifying confidential information had also been discussed for the Draft Template (item 1.7.1.1).

The Members also noted, with regard to further input from industry, the following advice from **XXXXXXXX** to the February 2006 Meeting:

- Industry had requested that a formal consultation process be used.
- The Member asserted that this was prompted by industry's experience through the consultation process on the draft scheduling policy framework for ANZTPA. This process had included the issue of confidentiality and industry noted that their submissions had addressed this matter.
- The Member asserted that industry was still awaiting feedback from NCCTG on the issue of confidentiality and did not feel that there had been an appropriate level of transparency on the proposed scheduling arrangements and ANZTPA. Additionally, **XXXXXXXX** asserted that the NDPSC should seek guidance from the NCCTG as it had already received industry's views on the issue of confidentiality.

Members noted that the May 2006 NCCTG meeting had affirmed that it was anticipated that the new Medicines Scheduling Committee would release more information publicly than the NDPSC currently released. The NCCTG Meeting considered whether the NDPSC should take steps now to release more information, noting advice from **XXXXXXXX** that incremental steps towards greater transparency were being taken by all expert committees providing advice to the TGA.

The NCCTG considered that the starting point for consultation with industry stakeholders should be that the only information that should be routinely withheld from public release was commercial-in-confidence information (i.e., formulation detail, manufacturing

method, sponsor name, product name, sales information). In particular, the NCCTG considered that the existence of an application or the identity of a substance that was the subject of a rescheduling application was not commercial-in-confidence information. However, it was suggested that the NDPSC should be prepared to work with industry groups on defining any additional types of information over which industry stakeholders sought confidentiality.

The NCCTG also noted that commercial and market advantage could be gained from the limited release of information from the NDPSC. Once guidelines were in place for wider release of information, applicants would be able to adjust the timing of the lodgement of their submissions to take account of the policies on public release of information (types of information and timing of release).

The NCCTG therefore:

- Supported a greater level of transparency in the release of information, consistent with the requirements of commercial-in-confidence material and public need
- Recommended that the NDPSC consult with industry stakeholders to define the level of transparency that was appropriate
- Recommended that stakeholder responses that were submitted in relation to the consultation on *A proposed new model for the scheduling of medicines and poisons within the Joint Agency* be considered in reviewing the NDPSC guidelines on release of information.

A Member asserted that there was a need to consult with industry to come to an agreed position and to determine how maximum transparency/minimum commercial-in-confidence might work in the scheduling process. **XXXXXXXX** advised that **XXXXXXXX** had not done this consultation, although it did co-ordinate the consultation process in 2005 for the draft scheduling policy framework and that the industry feedback from this included concerns about confidentiality of information.

Another Member noted that there was a partial belief in some forums that industry had used commercial-in-confidence arguments to keep non commercial-in-confidence information out of the public domain.

The Committee discussed what would be an appropriate process for consulting – noting that the issue of commercial-in-confidence/release of information had already been flagged by JAEG in the 2005 consultation document. The Committee wanted to ensure that it did not go outside the scope of this earlier consultation as this could result in inconsistency with the emerging ANZTPA framework. In considering a process a Member enquired about whether NCCTG had considered the industry feedback and if NCCTG could therefore provide guidance prior to initiating another consultation process. The Committee was advised that such detailed consideration had yet to occur.

A Member insisted that sufficient advance notice must be included in any change to the current understanding of what was disclosed in the Record of Reasons and that the Committee would have to be clear about any timelines for change.

Members also recalled that the February 2006 NDPSC Meeting noted that **XXXXXXXX** did not support inclusion of information from agvet evaluations in the Record of Reasons. A Member therefore suggested that the Committee defer consideration of the confidential information issue for the poisons side of scheduling, noting that APVMA had specific legislative requirements that may impede development of a consistent position. The Members agreed that it was appropriate to separate consideration of confidentiality for medicines scheduling from poisons scheduling given that there will shortly be different operation requirements.

OUTCOME

The Committee agreed

- to foreshadow for the October 2006 NDPSC Meeting consideration of changes to the operational requirements for the NDPSC regarding commercial-in-confidence and transparency of information for medicines scheduling. Comments were particularly invited from Stakeholders on the NCCTG's proposed "starting point for consultation" above and on defining any additional types of information over which stakeholders sought confidentiality.
- to consider the stakeholder responses addressing release of information that were submitted in relation to the consultation on *A proposed new model for the scheduling of medicines and poisons within the Joint Agency* at this Meeting.
- to develop a consistent process with **XXXXXXXX** for consulting with industry on this issue to avoid introducing inconsistencies with ongoing ANZTPA consultations.

1.7.1.3.3 A POLICY FOR THE HARMONISATION OF SCHEDULE 4 MEDICINES

PURPOSE

The Committee considered a policy for the harmonisation of Schedule 4 medicines, including outcomes from the May 2006 NCCTG Meeting.

BACKGROUND

The April 2005 NCCTG meeting endorsed the policy approach for dealing with the harmonisation of Schedule 2 or 3 substances where no products containing these substances were being marketed in either Australia or New Zealand. NCCTG agreed to the NDPSC's proposal that such Schedule 2 and/or 3 entries should be deleted and the parent compounds be added or retained in Schedule 4 of the SUSDP. It was noted that

this approach would ensure that all future registration applications for such medicines would be accompanied by contemporary data in keeping with current standards.

The February 2006 NDPSC Meeting agreed to recommend that NCCTG endorse a similar policy approach for harmonising Schedule 4 entries. New and existing substances placed in Schedule 4 of one country should be placed in Schedule 4 of the other country if there was no current entry. Additionally, existing Schedule 4 entries for drugs not marketed or not in current clinical use should be retained. Furthermore, the Committee agreed to the approach of maintaining a cumulative list of all prescription medicines in Schedule 4 to provide an historical record of substances considered by the NDPSC. It was noted that the inclusion of prescription medicines in Schedule 4 also provided control over the importation of such medicines into Australia.

DISCUSSION

Members were advised that the May 2006 NCCTG meeting considered the approach proposed by the NDPSC for harmonising Schedule 4 entries. NCCTG noted some practical difficulties in New Zealand to confirm the absence of products affected by rescheduling decisions. There was currently no comprehensive register in New Zealand of dietary supplements; such products might contain herbal material from species to be included in Schedule 4. NCCTG noted, however, that any rescheduling action entailed a risk of unintended consequences on unidentified products and supported the policy positions that:

- Where one country included a new medicine in Schedule 4/Part 1 as part of a registration application the other country should harmonise and adopt the same classification and nomenclature according to agreed policies, where appropriate.
- Where it had been identified that one country has an existing medicine entry in Schedule 4/Part 1, the other country should harmonise and also adopt the same classification and nomenclature according to agreed policies, where appropriate. This approach should similarly apply to existing Schedule 4/Part 1 entries where no products are currently on the market in either Australia or New Zealand or where they are no longer in current use in other countries including those no longer listed in Martindale (obsolete).

OUTCOME

The Committee noted the NCCTG support for the Schedule 4 harmonisation policy.

1.7.1.3.4 [ITEM DELETED]

1.8 NDPSC WORKING PARTIES

1.8.1 MINUTES OF THE TTHWP FEBRUARY 2006 MEETING (MEETING 15)

The Committee noted the ratified minutes of the February 2006 TTHWP Meeting. It was also noted that the TTHWP recommendations agreed at this meeting were considered at the February 2006 NDPSC meeting which included the proposal to adopt a provision in Part 1 of the SUSDP for recombinant medicines and the recommendation to harmonise the scheduling of cyclizine with New Zealand.

1.8.1.1 NOMENCLATURE OF RECOMBINANT MEDICINES

PURPOSE

The Committee considered its foreshadowed decision in relation to the nomenclature of recombinant medicines.

BACKGROUND

The February 2006 TTHWP meeting agreed to recommend that the NDPSC consider the Working Party's proposal to include a provision in Part 1 of the SUSDP which would cover all recombinant forms of the parent molecules listed in the Schedules. The Working Party agreed that the recommendation should be tabled for consideration at the February 2006 NDPSC meeting to expedite this matter. Under existing arrangements, only specifically listed recombinant medicines were scheduled or covered by the requirements in the SUSDP.

The February 2006 NDPSC meeting considered the proposed TTHWP amendment to Part 1 of the SUSDP. In addition, the Committee also noted the advice sought from **XXXXXXXX** which supported the inclusion of a provision in SUSDP Part 1 to cover in the scheduling of the parent substance every recombinant variant of the scheduled substance. **XXXXXXXX** considered the wording proposed to the TTHWP was appropriate. The Committee noted the **XXXXXXXX** advice which stated that:

[Section deleted**]**

DISCUSSION

The Committee recalled that at the February 2006 NDPSC meeting, a member expressed concern on the potential regulatory impact of the proposed Part 1 amendment on non-therapeutic products. On this basis, the Committee agreed to foreshadow the amendment and to publish the Committee's intent to consider this matter in the June 2006 pre-meeting gazette notice to allow public comment. However, it was noted that no public comment was received in response to the gazette notice.

DECISION 2006/47 - 1

The Committee confirmed its foreshadowed decision and agreed to include a provision in Part 1 of the SUSDP which would cover every recombinant form of substances listed in the Schedules.

Part 1 Interpretation – Amendment

Paragraph 1. (2) – Amend entry [to include a new subparagraph (f)] to read:

(a) that substance prepared from natural sources or artificially; and

(b) where the substance is a plant (other than a plant included in Schedule 8 or 9), that plant or any part of that plant when packed or prepared for therapeutic use; and

(c) every salt, active principle or derivative of the substance, including esters and ethers, and every salt of such an active principle or derivative; and

(d) every alkaloid of the substance and every salt of such an alkaloid; and

(e) except where the substance is levomethorphan or levorphanol, every stereoisomer of the substance and every salt of such a stereoisomer; and

(f) every recombinant form of the substance; and

(g) a preparation or admixture containing any proportion of the substance,

but does not include:

(h) a preparation or product included in Appendix A, or a substance and the reason for its entry in Appendix B; or

(i) a substance included in Appendix G at a concentration not exceeding the concentration specified in column 2 of that Appendix in respect of that substance; or

(j) any other substance included in Schedules 1 to 6, at a concentration not exceeding 10 mg per litre or 10 mg per kilogram, unless that substance is also included in Schedule 7 or 8; or

(k) any substance present as an impurity in a pesticide, at a concentration at or below the maximum content for that substance, specified for the pesticide in the current version of the *Minimum Compositional Standards (MCS) for Active Constituents* or its successor, as published by the Australian Pesticides and Veterinary Medicines Authority.

1.8.1.2 UNHARMONISED MEDICINES IN THE AUSNZ SCHEDULING DATABASE

PURPOSE

The Committee considered the recommendations of the June 2006 TTHWP meeting.

BACKGROUND

The June 2006 TTHWP meeting was advised that processing of medicine records in the AusNZ Scheduling Database for substances listed in S2, S3, S4 and S8 and equivalent New Zealand classifications including General Sale had been completed. Substances identified as unharmonised, i.e. Not Harmonised, Partially Harmonised or Essentially Harmonised which included substances requiring a minor nomenclature change, eg harmonising with New Zealand on the INN and substance parent entry, had been summarised and tabled for consideration at the June 2006 TTHWP meeting.

Working Party members considered each unharmonised substance and agreed on appropriate recommendations to be tabled at the NDPSC June 2006 meeting.

DISCUSSION

The Committee noted that the following policy approaches and principles for harmonisation of scheduling and nomenclature were taken into account by the TTHWP in formulating its recommendations:

- As set out in the *Principles of Harmonisation of Scheduling of Drugs and Poisons* established 1998, there should be equivalent scheduling for drugs and poisons for both countries; equivalent general exemptions from scheduling; a common set of definitions and scheduling criteria and guidelines; consistent interpretation of scheduling criteria; common nomenclature for drugs and poisons; harmonisation of labelling and packaging; and harmonisation of safety directions, warning statements and first aid instructions. Within the Schedules, there should be common descriptions for generic drug and poison classes (eg benzodiazepines, alkaline salts) or any other general classification (eg anabolic steroidal agents).
- Policy for listing botanicals where there is more than one plant or herbal substance of interest for scheduling:

- all species (designated with "spp") are included in the schedule entry when there are 3 or more species appropriate for scheduling, eg Aconitum spp; and
- species are listed individually if 2 or less related species are to be listed in the Schedules, eg podophyllum peltatum and podophyllum emodi.

- Harmonise with New Zealand on the nomenclature of substances, where appropriate, eg harmonising on the INN and substance parent entry;
- S2 and S3 substances where no products containing these substances are being marketed in either Australia or New Zealand should be deleted and the parent compounds be added or retained in S4 of the SUSDP.
- Where one country includes a new medicine in S4/Part I as part of a registration application, e.g. medicines recommended for approval by the ADEC, the other country should harmonise and adopt the same classification and nomenclature according to agreed policies, where appropriate.
- Where it has been identified that one country has an existing medicine entry in S4/Part I, the other country should harmonise and also adopt the same classification and nomenclature according to agreed policies, where appropriate. This approach should similarly apply to existing S4/Part I entries where no products are currently on the market in either Australia or New Zealand or where they are no longer in current use in other countries including those no longer listed in Martindale (obsolete).

The Committee noted a request from industry to consider harmonisation of the scheduling of aspirin, paracetamol and salicylamide with New Zealand at the February 2007 meeting.

OUTCOME

The Committee endorsed the TTHWP recommendations and agreed that substances for consideration of the NDPSC should be included on the agenda and pre-meeting gazette notice of the October 2006 NDPSC meeting. Similarly, the Committee agreed that recommendations to New Zealand should be referred to the MCC consideration at its next meeting.

TABLE 1 –HARMONISATION RECOMMENDATIONS TO NDPSC

Substance	Australian Schedule/ New Zealand Classification		Comment	TTHWP Recommendations
	Australian	**New Zealand**		
PROPOSALS BASED ON LEAST RESTRICTIVE SCHEDULING AND NOMENCLATURE OR WORDING ISSUES				
Australia Actinomycin D (dactinomycin) New Zealand Actinomycin D Dactinomycin	**S4**	**Prescription**	INN is dactinomycin	Australia to consider replacing the substance entry with dactinomycin and New Zealand to consider deleting the entry for Actinomycin D.
Australia: Aspidosperma Quebracho New Zealand: Quebracho	**S4**	**Prescription**	The November 1999 NDPSC meeting minutes stated that the Committee considered the inclusion of Quebracho in S4 would clearly indicate to importers that scheduling applied to the plant itself rather than rely on this being advised via the yohimbine entry. The S4 entry for Quebracho was subsequently amended to read "Aspidosperma quebracho"	Australia and New Zealand to consider retaining the entry for yohimbine. Australia and New Zealand to consider deleting Aspidosperma Quebracho and Quebracho, respectively, from S4.

			at the Feb '01 NDPSC meeting which may have been changed for specificity as Quebracho also captured other species. OCM has advised that if it is the yohimbine content in Aspidosperma quebracho that is the problem, it would be more appropriate to delete the Aspidosperma quebracho entry in the SUSDP and retain the yohimbine entry. It would then be the responsibility of the OCM to identify any and all herbs that are implicated (unless there are other concerns with the species in question). From a public health and safety perspective, no clear rationale for specifically listing the herb, other than what is stated above, could be extracted from old NDPSC minutes.	
Australia: Agalsidase Alfa and Beta	**S4**	**Prescription**		Australia to consider harmonising with New Zealand

New Zealand: Agalsidase				
Australia: Alcuronium Salts New Zealand: Alcuronium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Alendronate sodium New Zealand: Alendronic acid	**S4**	**Prescription**	RecINN Alendronic acid 3 Prescription medicines listed on SMARTI and several Prescription medicines pending registration approval	Australia to harmonise with New Zealand and adopt alendronic acid.
Australia: Benzilonium bromide New Zealand: Benzilonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand
Australia: *Cephaelis Acuminata* (ipecacuanha) New Zealand: ipecacuanha	**S4** except in preparations containing 0.2% or less of emetine.	**General Sale** Ipecacuanha; in medicines containing 0.2% or less of emetine **Prescription** Ipecacuanha; in medicines containing more than 0.2% of emetine	Nomenclature difference. The draft TT_Ingredients List contains *Cephaelis acuminata* and *Cephaelis ipecacuanha.*	Australia to consider adopting *Cephaelis ipecacuanha* and cross-referencing ipecacuanha to both *Cephaelis acuminata* and *Cephaelis ipecacuanha*. New Zealand to consider adopting the entries for *Cephaelis acuminata* and *Cephaelis ipecacuanha* as per

				policy on naming botanicals.
Ciclopirox	**S2** in preparations for dermal use containing 2 per cent or less of ciclopirox. **S3** in preparations for dermal use except when included in Schedule 2.	**General Sale** for dermal use in medicines for tinea pedis only. **Pharmacy Only** for dermal use in medicines containing 2% or less except in medicines for tinea pedis only. **Restricted** for dermal use in medicines containing more than 2%.	The June 2005 NDPSC meeting agreed to harmonise with NZ on the scheduling of antifungals for the treatment of tinea pedis but ciclopirox was not included. No adverse reaction reports received in Australia. New Zealand has received only one report for Batrafen. The indication was "nail lacquer" and the report describes severe local erythema and weeping skin of toes.	Australia to consider harmonising with New Zealand and exempting preparations for the treatment of tinea pedis.
Cimetidine	**S4** except when included in Schedule 3. **S3** for the relief of symptoms of gastro-oesophageal reflux, in packs containing not more than 14 days supply.	**Restricted** in medicines which have received the consent of the Minister or the Director-General to their distribution as restricted medicines and which are sold in the manufacturer's original pack containing not more than 14 days' supply. **Prescription** except when specified elsewhere in this Schedule.	One Restricted medicine on SMARTI containing 200 mg cimetidine indicated for the short-term treatment of proven duodenal or gastric ulcer; maintenance in recurring duodenal ulcer after short-term therapy. ADRU advised that cimetidine is an old drug and it was the first of its class and as such received plenty of attention and generated a	Australia to consider deleting the indication from the schedule entry to harmonise with New Zealand.

			substantial ADR profile. There were some issues in the early days which included interactions and adverse effects in the elderly. It has, however, largely fallen out of favour and is even less used now as proton pump inhibitors have become the treatment of choice in this area. ADRAC would have reviewed cimetidine in the past but not in the past 10 years. Significantly, ADRAC has received no reports concerning cimetidine in 2005, 1 in 2004, none in 2002 or 2003 and 1 in 2001. It is not a cause for concern.	
Clemastine	**S4**	**Restricted** for oral use **Prescription** except for oral use.	Listed as clinical trial medicine on SMARTI. No products on ARTG	Australia to consider harmonising with New Zealand.
Australia: Darbepoetin alfa New Zealand: Darbepoetin	**S4** **Appendix D**	**Prescription**		Australia to amend the entry for darbopoeitin alfa to darbopoeitin.
Australia: Decamethonium Salts	**S4**	**Prescription**		Australia to consider harmonising with New

New Zealand: Decamethonium				Zealand.
Australia: Demecarium bromide New Zealand: Demecarium	**S4**	**Prescription**		Australia to consider adopting the New Zealand nomenclature
Australia: Diphemanil methylsulphate New Zealand: Diphemanil	**S4**	**Prescription**		Australia to consider adopting the New Zealand nomenclature
Australia: Drotrecogin alfa New Zealand: Drotecogin	**S4**	**Prescription**	The rINN is Drotrecogin alfa	Australia to consider adopting the New Zealand nomenclature.
Australia: Edrophonium salts New Zealand: Edrophonium	**S4**	**Prescription**		Australia to consider adopting the New Zealand nomenclature.
Australia: Eformoterol (formoterol) New Zealand: Eformoterol Formoterol	**S4**	**Prescription**	rINN is formoterol and arformoterol	Australia to consider adopting "Formoterol" in S4 and deleting eformoterol (formoterol). New Zealand to consider deleting "Eformoterol"

				and retaining “Formoterol”
Australia: Emepronium salts New Zealand: Emepronium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Epoetin alfa Epoetin beta New Zealand: Epoetins	**S4**	**Prescription**		Australia to consider adopting a class entry in S4 and deleting the individual entries.
Australia: Eprosartan mesylate New Zealand: Eprosartan	**S4**	**Prescription**		Australia to consider adopting the New Zealand nomenclature.
Australia: Etilefrin hydrochloride New Zealand: Etilefrin	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Fluocinolone acetonide New Zealand: Fluocinolone	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia	**S4**	**Prescription** except in	The June 2006 TTHWP	Australia to consider amending

Follicle stimulating hormone Follitropin alpha Follitropin beta Urofollitrophin <u>New Zealand</u> Follitropin Urofollitropin	**(**Follicle stimulating hormone: except when separately specified in this Schedule).	<u>medicines containing 100 micrograms or less per litre or per kilogram.</u>	meeting noted that the scheduling is harmonised and agreed to recommend that the separate listings and class entries be retained as is because of inclusion in Appendix D. Follicle stimulating hormone and follitropin are class entries. Substances in this class include follitropin alpha, follitropin beta and urofollitrophin (all recombinant products). RecINN is Urofollitropin	the entry from Urofollitrophin to Urofollitropin to harmonise with New Zealand.
Australia: Formyldienolone (formebolone) New Zealand: Formyldienolone Formebolone			INN is formebolone.	Australia to consider adopting "Formebolone" in S4 and deleting "Formyldienolone". New Zealand to consider deleting "Formyldienolone" and retaining "Formebolone".
Australia: Fosphenytoin sodium New Zealand: Fosphenytoin	**S4**	**Prescription**		Australia to consider harmonising with New Zealand. .

Australia: Glycopyrrolate (glycopyrronium) New Zealand: Glycopyrronium	**S4**	**Prescription**	INN is Glycopyrronium bromide	Australia to consider harmonising with New Zealand and deleting glycopyrrolate.
Australia: Goserelin acetate New Zealand: Goserelin	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
<u>Australia</u> Heparin <u>New Zealand</u> Heparins	**S4** for internal use except when separately specified in this Schedule.	**Prescription** for internal use.	Other low-molecular weight heparins include, e.g. enoxaparin, logiparin, dalteparin, etc. Enoxaparin and dalteparin are listed in the SUSDP and Part I in New Zealand.	Australia to consider harmonising with New Zealand and adopting the class entry. Australia and New Zealand to list separately logiparin for clarity.
Australia: Hexamethonium Bromide New Zealand: Hexamethonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand and adopting the parent entry.
Australia: Hexocyclium methylsulphate New Zealand:	**S4**	**Prescription**		Australia to consider harmonising with New Zealand and adopting the parent entry.

Hexocyclium				
Australia: Lanatocide C New Zealand: Lanatosides	**S4**	**Prescription**	No products on SMARTI or ARTG	Australia to consider adopting the class entry to harmonise with New Zealand.
Australia: Colaspase (L-asparaginase) New Zealand: L-asparaginase Colaspase	**S4**	**Prescription**	No INN for either drug. Colaspase is the BAN while asparaginase is the USAN.	Australia and New Zealand to consider retaining colaspase, and cross-reference asparaginase to colaspase.
Australia: Laudexium methylsulphate New Zealand: Laudexium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Lauromacrogols Laureth-9 New Zealand: Lauromacrogol	**S4** Lauromacrogols in preparations for injection except when separately specified in these Schedules. **S4** Laureth-9 in preparations for injection	**Prescription** for injection	Lauromacrogol 400 is the INN and Laureth-9 is a synomym. Laureth-9 is listed in the TT Ingredients database. Macrogol lauril ethers have the general formula C(12)H(25)(OCH(2)CH(2))(n)OH. Lauromacrogol 400 is a mixture of monolauril ethers of macrogols where	Australia to consider retaining the entry for Lauromacrogols in S4. Australia to consider cross-referencing Laureth-9 to Lauromacrogols and exempting preparations containing lauromacrogol as an excipient (surfactant). New Zealand to consider adopting the class entry.

			the average value of n in the formula given above is 9. It has sometimes, however, been erroneously described as containing 8, rather than 9, oxyethylene groups. Lauromacrogol 400 is used as a sclerosant in the treatment of oesophageal and gastric varices and varicose veins and has been used as a local anaesthetic and antipruritic in combination topical preparations. Lauromacrogol is contained in topical products as excipient and active ingredient on SMARTI. No products on ARTG.	
Leucovorin	**Covered by the Folinic Acid entry in Australia.**	**Prescription** for injection **Pharmacy Only** in medicines containing more than 500 micrograms per recommended daily dose	RecINN is Calcium folinate. The nomenclature adopted on the ARTG and SMARTI is calcium folinate. New Zealand advised that the entry for leucovorin, which was based on product name, was retained to avoid confusion.	Australia to consider cross-referencing calcium folinate to folinic acid for clarity.

			Folinic acid is not a RecINN but would be the appropriate substance nomenclature to retain in the schedules as calcium folinate would be covered under the provision for derivatives in the SUSDP. Australia and New Zealand are already harmonised on folinic acid.	
Levocetirizine	**S4** (covered by the entry for cetirizine)	**Prescription**	Levocetirizine is a third generation antihistamine and is the active enantiomer of cetirizine.	For clarity, the NDPSC may wish to adopt a separate entry in S4.
Australia: Liothyronine sodium New Zealand: Liothyronine	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Macrogol 3350 New Zealand: Macrogols	**S3** in preparations for oral use for bowel cleansing prior to diagnostic medical and surgical procedures.	**Restricted** in oral preparations for bowel cleansing prior to diagnostic, medical or surgical procedures.		Australia to consider harmonising with New Zealand and adopting the class entry "Macrogols".
Australia: Maldison (malathion) New Zealand: Malathion	**S3** in preparations for human external use except in preparations containing 2 per cent or less of maldison.	**Restricted** for external use in medicines containing more than 2%.	Malathion is the BAN and maldison is a synonym. See also entry for organophosphorus	Australia to consider deleting maldison and retaining malathion to harmonise with New Zealand.

			compounds	
Australia: Methandienone New Zealand: Methandienone Metandienone	**S4**	**Prescription**	Metandienone is the INN. Metandienone is a synonym of methandienone which is already listed in S4 and Part I.	Australia to consider amending the entry to Metandienone. New Zealand to consider deleting "Methandienone".
Australia: Methacholine salts New Zealand: Methacholine	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Methanthelinium bromide New Zealand: Methanthelinium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Metronidazole Metronidazole Benzoate (benzoyl metronidazole) New Zealand: Metronidazole Metronidazole Benzoyl	**S4**	**Prescription**	Metronidazole is the RecINN	Australia and New Zealand to consider retaining only metronidazole and deleting duplicate entries.
Australia: Mitozantrone	**S4**	**Prescription**	RecINN is Mitoxantrone.	Australia to consider harmonising with New

(mitoxantrone) New Zealand: Mitoxantrone				Zealand and deleting mitozantrone.
Australia: Nicotinic acid New Zealand: Nicotinamide Nicotinic Acid	**S3** Nicotinic acid for human therapeutic use except: (a) in preparations containing 100 mg or less of nicotinic acid per dosage unit; or (b) nicotinamide.	**General Sale** in medicines containing 100 milligrams or less per dose form. **Restricted** in medicines containing more than 100 milligrams per dose form.	Rec INN is Nicotinamide The August 1999 NDPSC meeting noted that nicotinamide (nicotinic acid amide) is without the vasodilator effects of nicotinic acid though it has a nutritional effect . The Committee agreed that a recommendation should be made to the NZ MOH that it delete its nicotinamide entry in the interests of harmonisation. Nicotinamide is exempt. High number of Listed medicines containing nicotinamide as active ingredient (dietary supplements) listed on the ARTG.	Australia to consider cross-referencing nicotinamide to nicotinic acid. New Zealand to consider exempting nicotinamide to harmonise with Australia.
Australia: Octatropine methylbromide	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.

New Zealand: Octatropine				
Australia: Oxitropium salts New Zealand: Oxitropium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Oxyphenonium bromide New Zealand: Oxyphenonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Pancuronium bromide New Zealand: Pancuronium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Peginterferon	**No separate entry** (included in the class entry for interferons)	**Prescription**		Australia to consider including a separate entry for clarity and to harmonise with New Zealand.
Australia: Pentaerythritol tetranitrate New Zealand: Pentaerythrityl tetranitrate	**S4**	**Prescription**	Pentaerithrityl Tetranitrate is the Rec.INN. Used in prophylaxis of angina pectoris. 2 discontinued products (approved in late ‘60s) on SMARTI. No products on	Australia to consider harmonising with New Zealand on nomenclature.

			the ARTG.	
Australia: Pentamethonium bromide New Zealand: Pentamethonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Pentolinium salts New Zealand: Pentolinium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Perhexilene New Zealand: Perhexiline	**S4**	**Prescription**	Perhexiline is the INN No products on SMARTI	Australia to consider harmonising with New Zealand.
Permethrin	**S5** 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,	**General Sale** in medicines containing 5% or less. **Prescription** in medicines containing more than 5%.	Head lice and scabies medication Listed on the ARTG contains between 1-5% and should be within the cut-off for General Sale products in New Zealand.	Australia to consider harmonising with New Zealand and adopt the Part I entry in S4.

	except in preparations containing 2 per cent or less of permethrin. **S6** except: (a) when included in Schedule 5; or (b) in preparations containing 2 per cent or less of permethrin.			
Australia: Phenethicillin New Zealand: Pheneticillin	**S4**	**Prescription**	Pheneticillin is the INN	Australia to consider harmonising with New Zealand.
Australia: Phenthimentonium bromide New Zealand: Phenthimentonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Pipecuronium bromide New Zealand: Pipecuronium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Pipenzolate bromide	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.

New Zealand: Pipenzolate				
Australia: Poractant alfa New Zealand: Poractant alpha	**S4**	**Prescription**	Poractant alfa is the BAN	Australia to consider amending the entry to "poractant" . New Zealand to consider amending the entry to "poractant" .
Australia: Prampine salts New Zealand: Prampine	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Pregnenolone acetate New Zealand: Pregnenolone	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Prochlorperazine	**S3** tablets when manufactured, packed and labelled <u>for buccal use</u>, only for the treatment of nausea associated with migraine, in packs containing not more than 10 tablets. **S4** except when included in Schedule 3.	**Restricted** in packs containing not more than 10 tablets for the treatment of nausea associated with migraine. **Prescription** except when specified elsewhere in this Schedule; except when sold for the treatment of nausea associated with emergency contraception		Australia to consider harmonising with New Zealand and deleting "for buccal use" in the S3 entry.

		by pharmacists or nurses accredited to sell levonorgestrel for emergency contraception.		
Australia: Rabies vaccines New Zealand: Rabies vaccine	**S4**	**Prescription**		Australia to consider adopting the New Zealand entry.
Australia: Rapacuronium bromide New Zealand: Rapacuronium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Rifampicin (rifamycin) New Zealand: Rifampicin Rifamycin	**S4**	**Prescription**	Rifamycin is the INN	Australia and New Zealand to adopt Rifamycin and delete duplicate entries.
Australia: Rimiterol hydrobromide New Zealand: Rimiterol	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Rocuronium bromide	**S4**	**Prescription**		Australia to consider harmonising with New

New Zealand: Rocuronium				Zealand.
Silver	**S2** for therapeutic use except: (a) in <u>chewing gum containing 5 mg or less</u> 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.	**General Sale** in oral solutions containing 0.3% or less or other medicines containing 1% or less. **Pharmacy Only** except in oral solutions containing 0.3% or less or other medicines containing 1% or less.	OCM confirmed that there were no chewing gum products containing silver on the ARTG. However there were two cancelled products (oral mouthwash products) that were indicated for non-smoking (both grandfathered) - AUSTR 33394 which contained 5mg of silver nitrate.	Australia to consider deleting the provision for chewing gum under paragraph (a) to harmonise with New Zealand.
Australia: Sodium Valproate Semisodium valproate New Zealand: Valproic acid	**S4**	**Prescription**	Valproic acid and valproate semisodium are both listed as RecINN. However, the TT Ingredients List includes semisodium valproate and sodium valproate.	Australia to consider harmonising with New Zealand and adopting the valproic acid entry. This would allow the definition for derivatives to take effect and

			Sodium valproate is not listed in New Zealand but is covered in the scheduling of valproic acid. No products on SMARTI.	cover all other derivatives and salts. In addition, Australia to cross-reference sodium valproate and semisodium valproate to valproic acid.
Australia: Suxamethonium salts New Zealand: Suxamethonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Suxethonium bromide New Zealand: Suxethonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Terbinafine	**S2** in preparations for dermal use. **S4** except when included in Schedule 2.	**General Sale** <u>for dermal use in medicines for tinea pedis only</u>. **Pharmacy Only** for dermal use except in medicines for tinea pedis only. **Prescription** except when specified elsewhere in this Schedule.	SMARTI includes 2 products for tinea pedis.	Australia to consider harmonising with New Zealand and exempting preparations for the treatment of tinea pedis.
Australia: Tetraethylammonium	**S4**	**Prescription**		Australia to consider harmonising with New

salts New Zealand: Tetraethylammonium				Zealand.
Australia: Thiacetazone New Zealand: Thioacetazone	**S4**	**Prescription**	Thioacetazone is the INN	Australia to consider amending the entry to harmonise with New Zealand.
Thiourea	**S4**	**Prescription** except in medicines containing 0.1% or less.	One product on SMARTI containing 0.2mg/mL thiourea as other ingredient. The ARTG showed two products containing thiourea as excipient. One contained 0.2 mg/mL (0.02%) and the other product did not indicate an amount.	Australia to consider harmonising with New Zealand.
Australia: Thiotepa (triethylene thiophosphoramide) New Zealand: Thiotepa Triethylene thiophosphoramide	**S4**	**Prescription**	Thiotepa is the INN	Australia and New Zealand to consider retaining the substance entry "Thiotepa" and deleting other entries. Both countries to consider cross-referencing triethylene thiophosphoramide to thiotepa.
Australia: Thyrotrophin (TSH) New Zealand:	**S4**	**Prescription**	Micromedex indicated that a recombinant form of thyrotrophin is available, i.e. thyrotrophin alfa.	Australia to consider deleting the descriptor for Thyroid-stimulating Hormone (TSH) to harmonise with New Zealand.

Thyrotrophin				
Australia: Tiemonium iodide New Zealand: Tiemonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Tirofiban hydrochloride New Zealand: Tirofiban	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Tolonium chloride New Zealand: Tolonium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Tolterodine tartrate New Zealand: Tolterodine	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Australia: Traz<u>a</u>done New Zealand: Traz<u>o</u>done	**S4**	**Prescription**	Trazodone is the INN	Australia to consider amending the entry to trazodone to harmonise with New Zealand.
Trometamol	**S4** in preparations for injection.	**General Sale** except for injection in medicines containing more than 3%.	A number of Prescription ophthalmic products and injectable preparations were	Australia to consider harmonising with New Zealand.

		Prescription for injection in medicines containing more than 3%.	listed on SMARTI. S4 injectable products and exempt antiseptic solutions and irrigation solutions included on ARTG	
Valproic acid	**Not listed**	**Prescription**	No products on ARTG	**See semisodium and sodium valproate**
Australia: Vecuronium bromide New Zealand: Vecuronium	**S4**	**Prescription**		Australia to consider harmonising with New Zealand.
Vinyl Ether	**S4** for inhalation anaesthesia.	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand and changing the scheduling condition to therapeutic use.
OTHER HARMONISATION PROPOSALS				
Chlorquinaldol	**S4** for human <u>topical</u> use.	**General Sale** for <u>external</u> use **Prescription** for <u>internal</u> use	No products on ARTG but several Prescription products on SMARTI. MCC Secretary advised that the scheduling of chlorquinaldol dermal preps was most likely based on products available at the time and that only dermal preps	Australia and New Zealand to consider adopting a parent entry in S4 "CHLORQUINALDOL for human therapeutic use" and New Zealand to consider deleting the GS entry.

			containing other S4 active ingredients which cause them to be prescription medicines were available so removal of the GS exemption would not affect any products on the market in New Zealand.	
Chymopapain	**S4** injection for human therapeutic use.	**Prescription**	No products on ARTG and 2 discontinued products for injection on SMARTI.	Australia to consider harmonising with New Zealand and deleting "injection" from the entry.
Cyclopropane	**S4** for inhalation anaesthesia.	**Prescription**	No products found on ARTG or SMARTI	Australia to consider harmonising with New Zealand and amending the entry to "CYCLOPROPANE for therapeutic use".
Enflurane	**S4** for inhalation anaesthesia.	**Prescription**	One product for inhalation on ARTG	Australia to consider harmonising with the New Zealand entry and amending the condition to therapeutic use.
Ephedra	**S4** except in preparations containing 0.001 per cent or less of ephedrine.	**General Sale** Ephedra navadensis.	Ephedra gerardiana and E. sinensis contain ephedrine and have been used in chinese and middle-eastern medicine under the name Ma Huang. E.major, E.helvetica and	Australia to amend the S4 entry to Ephedra spp for consistency with other entries in the SUSDP. New Zealand to adopt a primary entry for Ephedra spp in Part I and harmonise with

			E.dystachia also contain large amounts of ephedrine and were utilised for this in Europe. Ephedra nevadensis is one of the pseudoephedrine containing ephedras, and is used mostly for it's expectorant and stimulating action and has a long history of traditional use.	the Australian exemption on the basis of ephedra's abuse potential.
Ergocalciferol	**Covered under the Vitamin D entry**	**General Sale** in medicines containing 25 micrograms or less per recommended daily dose. **Prescription** in medicines containing more than 25 micrograms per recommended daily dose.	Scheduling for ergocalciferol (New Zealand) and Vitamin D (Australia) is harmonised. 4 General Sale products for injection are listed on SMARTI. A whole range of dietary supplements listed on the ARTG as containing ergocalciferol.	See Vitamin D
Fluroxene	**S4** <u>for inhalation anaesthesia.</u>	**Prescription**		Australia to consider amending the entry to "Fluroxene for human therapeutic use".
Halothane	**S4** for inhalation anaesthesia.	**Prescription**	For therapeutic use in humans.	Australia to consider amending the entry to "Halothane for therapeutic use".
Australia: Hyaluronic acid and	**S4**	**General Sale** Hyaluronidase	Hyaluronidase is used as an adjuvant therapy to increase	Australia to consider adopting a separate entry for

its polymers New Zealand: Hyaluronic acid		**Prescription** Hyaluronic acid	absorption/dispersion of other injected drugs. By catalyzing the hydrolysis of hyaluronic acid, a major constituent of the interstitial barrier, hyaluronidase lowers the viscosity of hyaluronic acid, thereby increasing tissue permeability. It is, therefore, used in medicine in conjunction with other drugs in order to speed their dispersion and delivery. The most common application is in ophthalmic surgery, in which it is used in combination with local anesthetics. 1 injectable product and 1 discontinued topical ointment containing hyaluronidase found on SMARTI. No products containing hyaluronidase on ARTG	Hyaluronidase in S4. New Zealand to consider rescheduling Hyaluronidase to Prescription medicine. .
Isoflurane	**S4** for inhalation anaesthesia.	**Prescription**		Australia to consider amending the entry to "ISOFLURANE for therapeutic use" to harmonise with New Zealand.
Australia:	**S4** for human therapeutic	**Prescription**		Australia to consider

Lead compounds New Zealand: Lead	use			harmonising with New Zealand and amending the entry to "LEAD for human therapeutic use."
Lithium	**S2** (excluding when present as an excipient at 0.25 per cent or less of lithium) in preparations for therapeutic dermal use containing 1 per cent or less of lithium except in preparations containing 0.01 per cent or less of lithium. **S4** (excluding when present as an excipient at 0.25 per cent or less of lithium) for therapeutic use, except: (a) when included in Schedule 2; or (b) in preparations containing 0.01 per cent or less of lithium	**GS** for dermal use in medicines containing 0.01% or less. **Pharmacy Only** for dermal use in medicines containing 1% or less and more than 0.01%. **Prescription except** for dermal use in medicines containing 1% or less.	The New Zealand entry does not exempt preparations containing 0.25 % lithium as an excipient. The February 2003 NDPSC meeting based the exemption level for excipients on the information provided by an applicant in support of a 0.23% cut- off based on a theoretical lithium content for tourmaline of 2.3% and a maximum tourmaline content in dermal products of 10%.	Australia and New Zealand to consider restricting the exemption of 0.25% or less of lithium when present as an excipient to apply only to dermal products. New Zealand to consider adopting the exemption of 0.25% or less lithium when present as an excipient and removing the restriction, i.e for dermal use only on exempt preparations.
Methyl mercury	**S4** MERCURY for cosmetic or therapeutic use except: (a) when separately specified in these Schedules; or (b) in a sealed device	**Prescription** except in medicines containing 300 micrograms or less per litre or per kilogram.	No methyl mercury products on the ARTG	Australia to consider harmonising with New Zealand and adopt a parent entry in S4.

	which prevents access to the mercury. **Appendix G** 300 micrograms or less per litre or per kilogram.			
Methyl salicylate	**S5** in liquid preps containing 25 percent or more of methyl salicylate except when included in S6. **S6** excluding admixtures (see also Schedule 5)	**General Sale**	The ARTG includes Listed medicines containing methyl salicylate in liniments, creams, mouthwash, gel, pastiles and inhalation fluids.	Australia to consider including a primary entry in S4 for preparations for internal use and exempting all other preparations. New Zealand to consider adopting a Part I entry for preparations for internal use.
Nitrous oxide	**S4** for inhalation.	**Prescription**		Australia to consider amending the entry to "Nitrous oxide for therapeutic use" to harmonise with New Zealand.
Australia: Protamine sulfate New Zealand: Protamine sulphate	**S4** except when included in insulins.	**Prescription**	**XXXXXXXX**, an injectable product containing insulin was listed as S3 and 1 injectable antidote listed as unscheduled on the ARTG. All other injectable insulin products containing protamine on the ARTG were S4. All injectable products were	Australia and New Zealand to consider amending the entry to protamine. Australia to consider deleting the exemption for protamine in insulin products and seek comment from DSEB.

			Prescription medicines on SMARTI. No rationale available on e-minutes behind the Australian exemption.	
Quinine	**S4** for human internal use except in preparations containing 50 mg or less of quinine per recommended daily dose.	**General Sale** in medicines containing 50 milligrams or less per recommended daily dose. **Prescription** except in medicines containing 50 milligrams or less per recommended daily dose.		Australia to harmonise with the New Zealand entry and replace "internal" with therapeutic.
Australia: Strophanthin-K Strophantus spp New Zealand: Strophanthin Strophanthin-K Strophantus	**S4**	**Prescription**	**Strophanthin-K** [cardiac glycosides from strophanthus, the seeds of Strophanthus kombe (Apocynaceae)], **G-Strophanthin** [obtained from the seeds of Strophanthus gratus or from the wood of Acokanthera schimperi or A. ouabaio (Apocynaceae)] and **K-strophanthin-alpha** (extracted from Apocynum cannabinum). All strophantins are cardiac glycosides	Australia to consider adopting a class entry for "strophantins" and deleting Strophanthin-K. New Zealand to consider adopting the class entry for "strophanthins" and amending Strophantus to Strophantus spp.

Triamcinolone	**S2** 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. **S3** for the treatment of mouth ulcers in preparations containing 0.1 per cent or less of triamcinolone in a pack of 5 g or less. **S4** except when included in Schedule 2 or 3.	**Pharmacy Only** in aqueous nasal sprays delivering up to 55 micrograms per actuation when the maximum recommended daily dose is no greater than 220 micrograms and medicine has received the consent of the Minister or the Director-General to its distribution as a pharmacy-only medicine. **Restricted** for buccal use in medicines containing 0.1% or less of triamcinolone acetonide and in pack sizes no greater than 5 grams. **Prescription** except when specified elsewhere in this Schedule.	The recommended daily dose for **XXXXXXXX** (triamcinolone nasal spray) in MIMS showed a recommended starting dose of 220 microgram, i.e. 2 sprays in each nostril once daily, and once symptoms are controlled, patients can be maintained on 110 microgram, i.e. 1 spray in each nostril once daily.	Australia to consider adopting the New Zealand dosage per actuation of 55 mcg and recommended daily dosage of 220 mcg for triamcinolone. Furthermore, Australia to consider replacing "for the treatment of mouth ulcers" with "for buccal use" in S3. New Zealand to consider harmonising with the scheduling conditions, i.e. indication and age restriction, specified in the S2.
Trichloroethylene	**S4** for therapeutic use (excluding when present as an excipient).	**Prescription**	No products on SMARTI or ARTG. **Secretariat's Note:** OTC had confirmed its advice that there were no products containing trichloroethylene either in the current or	Australia to consider removing the exclusion for trichloroethylene when used as an excipient to harmonise with New Zealand.

			historical record of the ARTG.	
Australia: Urethane (excluding its derivatives) New Zealand: Urethane	**S4**	**Prescription**	Used as dental bonding agent Used in a large number of medical devices for dental use on the ARTG contain urethane diarylate, urethane dimethacrylate, urethane resin and urethane triacrylate. No products on SMARTI. Dental products should be exempt under the Appendix A exemption for medical devices. However, it would be appropriate to consult ODBT to ensure the proposed entry does not catch dental products.	Australia to consider amending the entry to "Urethane for human therapeutic use" to harmonise with New Zealand.
Australia: Vitamin D New Zealand: Colecalciferol Ergocalciferol Vitamin D	**Covered under the entry for vitamin D** **S4** Vitamin D for <u>human internal</u> therapeutic use except in preparations containing 25 micrograms or less of vitamin D per	**General Sale** in medicines containing 25 micrograms or less per recommended daily dose; in parenteral nutrition replacement preparations. **Prescription** <u>in medicines</u> containing more than 25 micrograms	Scheduling is already harmonised with New Zealand. Colecalciferol is the TT Ingredient Name and RecINN (Index Nominum). MCC supported the current S4 and General Sale	A. Australia to consider cross-referencing colecalciferol and ergocalciferol to vitamin D. Australia to consider amending the nomenclature in S7 to colecalciferol for consistency. B. Australia to consider harmonising with New

	recommended daily dose. **S7** cholecalciferol for use as a rodenticide.	per recommended daily dose except in parenteral nutrition replacement preparations.	classifications. ARTG lists (Colecalciferol) 23 products ranging 900 ng to 5 mg per dose unit No medicine found on SMARTI	Zealand and deleting "internal" from the S4 entry.
PROPOSALS BASED ON THE POLICY FOR OTC AND PRESCRIPTION MEDICINES AND POLICY FOR NAMING BOTANICALS				
4-chlorotestosterone	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand and adopting a separate entry as per policy on S4 medicines.
Chloroxymesterone	**Unscheduled**	**Prescription**	No products on ARTG or SMARTI.	Australia to consider harmonising with New Zealand as per policy on S4 medicines
Cobalt	**Unscheduled**	**Prescription**	One antioxidant product containing 100mcg cobalt per tablet **for export** was found on the ARTG and one discontinued injectable product was listed on SMARTI.	Australia to consider harmonising with New Zealand as per policy on S4 medicines.
Dibotermin	**Unscheduled**	**Prescription**	No products on ARTG (no e-minutes available) but one withdrawn Prescription medicine on SMARTI.	Australia to consider adopting the entry in S4 as per policy on S4 medicines.

Dichlorophen	**S2** for internal human therapeutic use.	**Prescription**	One discontinued product (1969) on SMARTI. No products on ARTG	Australia to consider harmonising New Zealand based on agreed policy where there are no existing products.
Dicyclomine	**S2** in preparations containing 0.1 per cent or less of dicyclomine **S4** except when included in Schedule 2.	**Prescription**	2 export only oral products included on the ARTG. 2 Prescription medicines on SMARTI	Australia to consider harmonising with New Zealand as per policy on OTC entries with no products.
Dihydrotachysterol	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider adopting the entry in S4 as per policy on S4 medicines.
Dimethothiazine	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider adopting the entry in S4 as per policy on S4 medicines.
Duloxetine	**Unscheduled**	**Prescription**	No products on ARTG (SNRI)	Australia to consider adopting the entry in S4 as per policy on S4 medicines.
Epinastine	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider adopting the entry in S4 as per policy on S4 medicines.
Eplerenone	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider adopting the entry in S4 as per policy on S4 medicines.
Ethionamide	**Unscheduled**	**Prescription**	No products on the ARTG.	Australia to consider adopting the entry in S4 as per policy on S4 medicines.
Ethylhexanediol	**Unscheduled**	**Prescription**	No products on the ARTG.	Australia to consider adopting

				the entry in S4 as per policy on S4 medicines.
Fluorescein	**Unscheduled**	**General Sale** except for injection. **Prescription** for injection.	3 disinfectants listed on the ARTG. General Sale ophthalmic and topical preparations on SMARTI.	Australia to consider adopting the S4 entry as per policy on S4 medicines.
Gemifloxacin	**Unscheduled**	**Prescription**	No products on ARTG. One product listed on SMARTI since 2000 but never marketed.	Australia to consider adopting the entry in S4 as per policy on S4 medicines.
Halquinol	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider adopting the entry in S4 as per policy on S4 medicines.
Hexoprenaline	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand as per policy on S4 medicines.
Human protein C	**Unscheduled**	**Prescription**	2 Prescription products (registration pending) on SMARTI No products on ARTG	Australia to consider harmonising with New Zealand as per policy on S4 medicines.
Ibritumomab tiuxetan	**Unscheduled**	**Prescription**		Australia to consider adopting the parent entry in S4 as per policy on S4 medicines. New Zealand to consider amending the entry to read "Ibritumomab".
Levosimendan	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider

				harmonising with New Zealand as per policy on S4 medicines.
Melagatran	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand as per policy on S4 medicines.
Mequitazine	**Unscheduled**	**Prescription**	One export only medicine on ARTG containing 5 mg	Australia to consider harmonising with New Zealand as per policy on S4 medicines.
Mercuric oxide	**S2** in ointments for human ocular use.	**Pharmacy Only** for ophthalmic use.	One discontinued eye Ointment on SMARTI classified as Restricted Medicine (approval date 1962). One homeopathic medicine on the ARTG (Listed medicine).	Australia and New Zealand to delete the S2/Part III entry and adopt a primary entry in S4 as per policy on OTC entries with no products.
Nimorazole	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand as per policy on S4 medicines..
Phenisatin	**Unscheduled**	**Prescription**	Not an INN Phenisatin is a potent stimulant laxative.	Australia to consider harmonising with New Zealand as per policy on S4 medicines..
Piracetam	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New

				Zealand as per policy on S4 medicines..
Rifapentine	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand as per policy on S4 medicines.
Thenyldiamine	**S2 (outcome of the Feb '06 NDPSC meeting)** (a) in nasal preparations for topical use; or (b) when combined with one or more other therapeutically active substances in oral preparations when: (i) at least one of the other therapeutically active substances is a sympathomimetic decongestant; or (ii) in a day-night pack containing thenyldiamine in the bed-time dose; and (iii) not labelled for the treatment of children under 2 years of age. **S4**	**Pharmacy Only** for nasal use; for oral use when combined with one or more other therapeutically active ingredients <u>for the treatment of coughs, colds or influenza</u> when at least one of the other active ingredients is a sympathomimetic decongestant or in a day/night pack containing thenyldiamine in the bed-time dose and in preparations for adults and children over two years of age. **Restricted** for oral use in solid dose form or in liquid form containing 10 milligrams or less per 5 millilitres except when specified elsewhere in	The OTC entries were deleted in June 2005 as part of a group of substances with no products and the S4 entry was retained.	Australia and New Zealand to retain only a primary entry in S4 and delete all other entries as per policy.

		the Schedule. **Prescription** except when specified elsewhere in this Schedule		
Thyrotrophin-releasing factor	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand.
Viprinium	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand as per policy on S4 medicines.
Ximelagatran	**Unscheduled**	**Prescription**	No products on ARTG	Australia to consider harmonising with New Zealand as per policy on S4 medicines.

TABLE 2 – HARMONISATION RECOMMENDATIONS TO MCC

Substance	Australian Schedule/ NZ Classification		Comment	TTHWP Recommendations
	Australian	**NZ**		
PROPOSALS BASED ON THE LEAST RESTRICTIVE SCHEDULING AND NOMENCLATURE OR WORDING ISSUES				
Australia: Aspidosperma Quebracho New Zealand: Quebracho	**S4**	**Prescription**	The November 1999 NDPSC meeting minutes stated that the Committee considered the inclusion of Quebracho in S4 would clearly indicate to importers that scheduling applied to the plant itself rather than rely on this being advised via the yohimbine entry. The S4 entry for Quebracho was subsequently amended to read "Aspidosperma quebracho" at the Feb '01 NDPSC meeting which may have been changed for specificity as Quebracho also captured other species. OCM has advised that if it is the yohimbine content in Aspidosperma quebracho	New Zealand and Australia to consider retaining the entry for yohimbine. Australia and New Zealand to consider deleting Aspidosperma Quebracho and Quebracho, respectively, from S4.

			that is the problem, it would be more appropriate to delete the Aspidosperma quebracho entry in the SUSDP and retain the yohimbine entry. It would then be the responsibility of the OCM to identify any and all herbs that are implicated (unless there are other concerns with the species in question). From a public health and safety perspective, no clear rationale for specifically listing the herb, other than what is stated above, could be extracted from old NDPSC minutes.	
Beclomethasone	**S2** 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 <u>for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and</u>	**Pharmacy Only** in aqueous nasal sprays delivering up to 50 micrograms per actuation when the maximum recommended daily dose is no greater than 400 micrograms and the medicine has received the consent of the Minister or the Director-General to its distribution	Indication and age restriction were already included in New Zealand's registration guidelines and should have no unintended regulatory impact.	New Zealand to consider adopting the scheduling condition specified in S2.

	children 12 years and over. **S4** except when included in Schedule 2.	as a pharmacy-only medicine. **Prescription** except when specified elsewhere in this Schedule.		
Budesonide	**S2** 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. **S4**	**Pharmacy Only** in aqueous nasal sprays delivering up to 50 micrograms per actuation when the maximum recommended daily dose is no greater than 400 micrograms and the medicine has received the consent of the Minister or the Director-General to its distribution as a pharmacy-only medicine.	Same as beclomethasone.	New Zealand to consider adopting the scheduling condition specified in S2.
Australia: Colaspase (L-asparaginase) New Zealand: L-asparaginase Colaspase	**S4**	**Prescription**	No INN for either drug. Colaspase is the BAN while asparaginase is the USAN.	New Zealand and Australia to consider retaining colaspase, and cross-referencing asparaginase to colaspase.
Australia Actinomycin D (dactinomycin)	**S4**	**Prescription**	INN is dactinomycin	New Zealand to consider deleting the entry for Actinomycin D.

New Zealand Actinomycin D Dactinomycin				Australia to consider retaining dactinomycin in S4 and deleting actinomycin D.
Dextromethorphan	**S2** when supplied in a pack containing 600 mg or less of dextromethorphan and with a recommended daily dose of 120 mg or less of dextromethorphan. **S4** except when included in Schedule 2.	**Pharmacy Only** in liquid form containing more than 0.25% or in solid dose form containing more than 15 milligrams per dose form when in packs containing not more than 600 milligrams and with a recommended daily dose of not more than 120 milligrams. **Prescription** except when specified elsewhere in this Schedule.		New Zealand to consider harmonising with the Australian S2 entry.
Dimenhydrinate	**S2** in primary packs of 10 doses or less, for the prevention or treatment of motion sickness, except in preparations for the treatment of children under 2 years of age **S3** in oral preparations except when included in Schedule 2. **S4** except when included in Schedule 2 or 3.	**Pharmacy Only** for oral use in a sealed container of not more than 10 tablets or capsules for the prevention or treatment of motion sickness except when sold at a transport terminal or aboard a ship or plane. **Restricted** for oral use except when specified elsewhere in the Schedule.		New Zealand to consider harmonising with the Australian scheduling condition.

		Prescription except when specified elsewhere in the Schedule.		
Diphenylpyraline	**S2** when combined with one or more 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 diphenylpyraline in the bed-time dose; and not labelled for the treatment of children under 2 years of age. **S3** oral preparations. **S4** except when included in S2 or S3.	**Pharmacy Only** for oral use when combined with one or more other therapeutically active substances <u>for the treatment of coughs, colds or influenza</u> when at least one of the other therapeutically active substances is a sympathomimetic decongestant or in a day/night pack containing diphenylpyraline in the bedtime dose and in preparations for adults or children two years of age or more. **Restricted** for oral use. **Prescription** except when specified elsewhere in this Schedule.	One discontinued and 2 withdrawn Pharmacy Only products listed on SMARTI S2 entry amended at the Feb ’06 to remove the indications. No products on ARTG.	New Zealand to consider harmonising with the Australian entry and removing the indication.
Doxylamine	**S2** when combined with one or more other therapeutically active substances in oral preparations for the	**Pharmacy Only** for oral use when combined with one or more other therapeutically active substances <u>for the</u>	This item was considered at the February ’06 NDPSC meeting where the indication “for the treatment of symptoms of cough, colds or	New Zealand to consider harmonising with the Australian entry and removing the indication.

	treatment of symptoms of coughs, colds or influenza when: (a) at least one of the other therapeutically active substances is a sympathomimetic decongestant; or (b) in a day-night pack containing doxylamine in the bed-time dose, except in preparations for the treatment of children 2 years of age or less. **S3** in oral preparations except when included in S2. **S4** except when included in S2 and S3.	treatment of coughs, colds or influenza when at least one of the other therapeutically active substances is a sympathomimetic decongestant or in a day/night pack containing doxylamine in the bedtime dose and in preparations for adults or children two years of age or more. **Restricted** for oral use except when specified elsewhere in this Schedule **Prescription** except when specified elsewhere in this Schedule	influenza" was removed from the S2 entry. High number of products on both SMARTI and ARTG.	
Australia: Eformoterol (formoterol) New Zealand: Eformoterol Formoterol	**S4**	**Prescription**	RecINN is formoterol and arformoterol	New Zealand to consider deleting "Eformoterol" and retaining "Formoterol" Australia to consider adopting "Formoterol" in S4 and deleting eformoterol (formoterol).
Erythropoietins	**S4** (class entry) **Appendix D**	**Prescription**	The November 2001 NDPSC meeting agreed to include a class entry in addition to the	New Zealand to consider adopting a class entry in Part I in addition to the individual

			individual entries, i.e. erythropoietin, darbepoietin alfa, etc., to promote clarity given these substances have a high potential for abuse and diversion.	entries.
Ethyl chloride	**S4** for human therapeutic use.	**Prescription** for inhalation	1 discontinued topical spray approved in 1969 included on SMARTI.	New Zealand to consider harmonising with Australia and deleting "for inhalation" in the Part I entry.
Australia: Etidronic acid (includes disodium etidronate) New Zealand: Etidronic acid	**S4** (a) for internal use; or (b) in topical preparations except in preparations containing 1 per cent or less of etidronic acid.	**Prescription**	RecINN is etidronic acid No products on ARTG containing Etidronic acid as active ingredient but several products (H_2O_2 solutions and disinfectants) containing the substance as excipient. No products on SMARTI.	New Zealand to consider harmonising with the Australian entry.
Flurbiprofen	**S2** in divided preparations for topical oral use containing 10 mg or less of flurbiprofen per dosage unit. **S4** except when included in Schedule 2.	**Pharmacy Only** in throat lozenges containing 10 milligrams or less per lozenge. **Prescription** except in throat lozenges containing 10 milligrams or less per lozenge.		New Zealand to consider harmonising with Australia.
Fluticasone	**S2** in aqueous nasal sprays delivering 50 micrograms or less of	**Pharmacy Only** in aqueous nasal sprays delivering up to 50	Same as beclomethasone.	New Zealand to consider adopting the scheduling condition specified in S2.

	fluticasone per actuation when the maximum recommended daily dose is no greater than 200 micrograms <u>for the prophylaxis or treatment of allergic rhinitis for up to 6 months in adults and children 12 years and over</u>.	micrograms per actuation when the maximum recommended daily dose is no greater than 200 micrograms and the medicine has received the consent of the Minister or the Director-General to its distribution as a pharmacy-only medicine		
Australia: Formyldienolone (formebolone) New Zealand: Formyldienolone Formebolone			INN is formebolone.	New Zealand to consider deleting "Formyldienolone" and retaining "Formebolone" Australia to consider adopting "Formebolone" in S4 and deleting "Formyldienolone".
<u>Australia</u> Heparin <u>New Zealand</u> Heparins	**S4** for internal use except when separately specified in this Schedule.	**Prescription** for internal use.	Other low-molecular weight heparins include, e.g. enoxaparin, logiparin, dalteparin, etc. Enoxaparin and dalteparin are listed in the SUSDP and Part I in New Zealand.	New Zealand and Australia to list separately logiparin for clarity. Australia to consider adopting the class entry to harmonise with New Zealand.
Australia: Hyaluronic acid and its polymers	**S4**	**General Sale** Hyaluronidase **Prescription** Hyaluronic	Hyaluronidase is used as an adjuvant therapy to increase absorption/dispersion of other injected drugs. By	New Zealand to consider rescheduling Hyaluronidase to Prescription medicine.

New Zealand: Hyaluronic acid		acid	catalyzing the hydrolysis of hyaluronic acid, a major constituent of the interstitial barrier, hyaluronidase lowers the viscosity of hyaluronic acid, thereby increasing tissue permeability. It is, therefore, used in medicine in conjunction with other drugs in order to speed their dispersion and delivery. The most common application is in ophthalmic surgery, in which it is used in combination with local anesthetics. 1 injectable product and 1 discontinued topical ointment containing hyaluronidase found on SMARTI. No products containing hyaluronidase on ARTG	Australia to consider adopting a separate entry for Hyaluronidase in S4.
Isosorbide dinitrate	**S3** in oral preparations containing 10 mg or less of isosorbide dinitrate per dosage unit. **S4** except when included in Schedule 3	**Prescription**	Several products labelled as S2 on the ARTG. No existing products registered on SMARTI. Advise DSEB of products labelled as S2 instead of S3	New Zealand to consider harmonising with Australia.

			on the ARTG.	
Ketoconazole	**S2** in preparations for dermal use except: (a) in preparations for dermal use containing 1 percent or less of ketoconazole for the treatment of the scalp; or (b) in preparations for dermal use for the treatment of tinea pedis. **S4** except: (a) when included in Schedule 2; (b) in preparations for dermal use containing 1 percent or less of ketoconazole for the treatment of the scalp; or (c) in preparations for dermal use for the treatment of tinea pedis.	**General Sale** for dermal use in medicines for tinea pedis only or in shampoos containing 1% or less. **Pharmacy Only** for dermal use except in medicines for tinea pedis only or in shampoos containing 1% or less. **Prescription** except for dermal use.	All dermal preps other than those exempt from scheduling are Pharmacy Only in New Zealand.	New Zealand to consider harmonising with Australia and replace shampoo with the term "for the treatment of the scalp".
Lignocaine	**S2** in preparations for topical use other than eye drops: (a) containing 10 per cent or less of total local anaesthetic substances, except in dermal preparations containing 2 per cent or less of total	**GS** for external use in medicines containing 2% or less; in throat lozenges containing 30 milligrams or less per dose form**.** **Pharmacy Only** for urethral use; for external use in medicines containing 10% or less	Products on SMARTI include anaesthetic wash solutions (GS), suppositories and rectal ointments (Prescription), topical creams and dermal patches 2.5% (Pharmacy Only), topical cream and topical gel ≤2% (GS), eye drops 4%	New Zealand to consider replacing "for external use" with "dermal use" to harmonise with Australia.

	local anaesthetic substances; or (b) in divided preparations containing 200 mg or less of total local anaesthetic substances per dosage unit, except in lozenges containing 30 mg or less of total local anaesthetic substances per dosage unit. **S4 except:** (a) when included in Schedule 2; (b) <u>in dermal preparations</u> containing 2 per cent or less of total local anaesthetic substances; or (c) in lozenges containing 30 mg or less of total local anaesthetic substances per dosage unit.	and more than 2%. **Prescription** for injection except when used as a local anaesthetic in practice by a nurse whose scope of practice permits the performance of general nursing functions or by a registered podiatrist or dental therapist; for oral use except in throat lozenges containing 30 milligrams or less per dose form; for ophthalmic use except when used in practice by a registered optometrist; <u>for external use</u> in medicines containing more than 10%.	(Prescription), lozenges 10mg (GS), oral solutions/spray 2% - 10% (Pharmacy Only)	
Australia: Lobelia Inflata New Zealand: Lobelia	**S2** except for smoking or burning.	**Pharmacy Only** except in medicines for smoking or burning. **GS** in medicines for smoking or burning.		New Zealand to consider adopting the botanical name to harmonise with Australia.
Lobeline	**S2** except for smoking or	**No separate entry**	Scheduled under lobelia in	For clarity and consistency,

	burning.		New Zealand.	New Zealand to consider adopting a separate entry for the alkaloid to harmonise with Australia.
Australia: Lauromacrogols Laureth-9 New Zealand: Lauromacrogol	**S4** Lauromacrogols in preparations for injection except when separately specified in these Schedules. **S4** Laureth-9 in preparations for injection	**Prescription** for injection	Lauromacrogol 400 is the INN and Laureth-9 is a synomym. Laureth-9 is listed in the TT Ingredients database. Macrogol lauril ethers have the general formula C(12)H(25)(OCH(2)CH(2))(n)OH. Lauromacrogol 400 is a mixture of monolauril ethers of macrogols where the average value of n in the formula given above is 9. It has sometimes, however, been erroneously described as containing 8, rather than 9, oxyethylene groups. Lauromacrogol 400 is used as a sclerosant in the treatment of oesophageal and gastric varices and varicose veins and has been used as a local anaesthetic and antipruritic in combination topical preparations. Lauromacrogol is contained	New Zealand to consider adopting the class entry. Australia to consider retaining the entry for Lauromacrogols in S4. Australia to consider cross-referencing Laureth-9 to Lauromacrogols and exempting preparations containing lauromacrogol as an excipient (surfactant).

			in topical products as excipient and active ingredient on SMARTI. No products on ARTG.	
Levonorgestrel	**S3** for emergency post-coital contraception. **S4** except when included in Schedule 3.	**Prescription** except when used for emergency contraception and when sold by nurses or pharmacists recognised by their respective professional bodies as having competency in the field of sexual and reproductive health		New Zealand to consider harmonising with Australia.
Lithium	**S2** (excluding when present as an excipient at 0.25 per cent or less of lithium) in preparations for therapeutic dermal use containing 1 per cent or less of lithium except in preparations containing 0.01 per cent or less of lithium. **S4** (excluding when present as an excipient at 0.25 per cent or less of lithium) for therapeutic use, except: (a) when included in Schedule 2; or	**GS** for dermal use in medicines containing 0.01% or less. **Pharmacy Only** for dermal use in medicines containing 1% or less and more than 0.01%. **Prescription except** for dermal use in medicines containing 1% or less.	The New Zealand entry does not exempt preparations containing 0.25 % lithium as an excipient. The February 2003 NDPSC meeting based the exemption level for excipients on the information provided by an applicant in support of a 0.23% cut- off based on a theoretical lithium content for tourmaline of 2.3% and a maximum tourmaline content in dermal products of 10%.	New Zealand to consider adopting the exemption of 0.25% or less lithium when present as an excipient and removing the restriction, i.e for dermal use only on exempt preparations. New Zealand and Australia to consider restricting the exemption of 0.25% or less of lithium when present as an excipient to apply only to dermal products.

	(b) in preparations containing 0.01 per cent or less of lithium			
Meclozine	**S2** in primary packs containing 12 or less tablets or capsules of meclozine for the prevention or treatment of motion sickness, except in preparations for the treatment of children under 2 years of age. **S4** except when included in Schedule 2.	**Pharmacy Only** in a sealed container of not more than 12 tablets or capsules for the prevention of travel sickness except when sold at a transport terminal or aboard a ship or plane. **Prescription except** when specified elsewhere in the Schedule.		New Zealand to consider harmonising with Australia and adopting the age restriction for consistency with other sedating antihistamines.
Australia: Methandienone New Zealand: Methandienone Metandienone	**S4**	**Prescription**	Metandienone is the INN. Metandienone is a synonym of methandienone which is already listed in S4 and Part I.	New Zealand to consider deleting "Methandienone". Australia to consider amending the entry to the INN.
Methoxamine	**S4** in preparations for injection.	**Prescription** except for external use.		New Zealand to consider harmonising with Australia.
Australia: Metronidazole Metronidazole Benzoate (benzoyl metronidazole) New Zealand:	**S4**	**Prescription**	Metronidazole is the RecINN	New Zealand and Australia to consider retaining only metronidazole and deleting duplicate entries.

Metronidazole Metronidazole Benzoyl				
Miconazole	**S2** for human use in dermal preparations and for application to the nails except in preparations for the treatment of tinea pedis. **S3** for human use in topical preparations: (a) for the treatment of oral candidiasis; or (b) for vaginal use. **S4** except when included in Schedule 2, 3 or 6.	**General Sale** for external use in medicines for tinea pedis only. **Pharmacy Only** for external use except in medicines for tinea pedis only. **Restricted** Miconazole for the treatment of oral candidiasis; for vaginal use. **Prescription** Miconazole; except when specified elsewhere in this Schedule.	Recommendation made to MCC to harmonise with the Australian entry following the October 2005 meeting. Pharmacy Only products on SMARTI were mainly for topical use. Preparations for oral and vaginal use were available as Restricted Medicines on SMARTI.	New Zealand to consider harmonising with the Australian S2 entry and replace external use with dermal use.
Minoxidil	**S2** in preparations for dermal use containing 5 per cent or less of minoxidil. **S4** except when included in Schedule 2.	**Pharmacy Only** for external use in medicines containing 5% or less.	External use in the SUSDP includes use in eyes and ears. Products containing minoxidil have a warning statement against contact with eyes.	New Zealand to consider replacing "for external use" with "for dermal use" and harmonise with Australia.
Mometasone	**S2** in aqueous nasal sprays delivering 50 micrograms or less of mometasone per actuation when the maximum recommended	**Pharmacy Only** in aqueous nasal sprays delivering up to 50 micrograms per actuation when the maximum recommended daily dose	Same as beclomethasone.	New Zealand to consider adopting the scheduling conditions specified in the S2 entry.

	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. **S4** except when included in Schedule 2.	is no greater than 200 micrograms and the medicine has received the consent of the Minister or the Director-General to its distribution as a pharmacy-only medicine. **Prescription** except when specified elsewhere in this Schedule.		
Australia: Nicotinic acid New Zealand: Nicotinamide/ Nicotinic Acid	**S3** Nicotinic acid for human therapeutic use except: (a) in preparations containing 100 mg or less of nicotinic acid per dosage unit; or (b) nicotinamide.	**General Sale** in medicines containing 100 milligrams or less per dose form. **Restricted** in medicines containing more than 100 milligrams per dose form.	Rec INN is Nicotinamide The August 1999 NDPSC meeting noted that nicotinamide (nicotinic acid amide) is without the vasodilator effects of nicotinic acid though it has a nutritional effect . The Committee agreed that a recommendation should be made to the NZ MOH that it delete its nicotinamide entry in the interests of harmonisation. High number of Listed medicines containing nicotinamide as active ingredient (dietary	New Zealand to consider exempting nicotinamide to harmonise with Australia. Australia to consider cross-referencing nicotinamide to nicotinic acid.

			supplements) listed on the ARTG.	
Nystatin	**S2** in dermal preparations. **S3** in preparations for topical use except when included in Schedule 2. **S4** except when included in Schedule 2 or 3.	**Pharmacy Only** for dermal use. **Restricted** for the treatment of oral candidiasis; for vaginal use. **Prescription** except when specified elsewhere in this Schedule.	Existing S3/Restricted products were for vaginal use in both countries.	New Zealand to consider harmonising with the Australian S3 entry.
Oxiconazole	**S2** for dermal use except in preparations for the treatment of tinea pedis. **S3** for vaginal use **S4 except:** (a) when included in Schedule 2 or 3; or (b) in preparations for the treatment of tinea pedis.	**General Sale** for dermal use in medicines for tinea pedis only **Pharmacy Only** for dermal use except in medicines for tinea pedis only **Restricted** for vaginal use.		New Zealand to consider adopting a primary entry in Part I to harmonise with Australia.
Phenacetin	**S4** for therapeutic use (excluding when present as an excipient).	**Prescription**		New Zealand to consider excluding excipients from scheduling to harmonise with Australia.
Australia: Phthalylsulfathiazole New Zealand: Phthalylsulphathiazole	**S4**	**Prescription**	Phthalylsulfathiazole is the INN	New Zealand to consider harmonising with Australia.

Piroxicam	**S4** except in preparations for dermal use.	**General Sale** for external use. **Prescription e**xcept for external use.	No existing product for external use on SMARTI.	New Zealand to consider harmonising with the Australian entry.
Australia: Polyacrylamide New Zealand: Polyacrilamide	**S4**	**Prescription**	A quick search of the internet showed references only to polyacrylamide.	New Zealand to consider harmonising with the Australian nomenclature.
Australia: Poractant alfa New Zealand: Poractant alpha	**S4**	**Prescription**	Poractant alfa is the BAN	New Zealand to consider amending the entry to "poractant" . Australia to consider amending the entry to "poractant" .
Procyclidine	**S2** in preparations containing 5 per cent or less of procyclidine for dermal use. **S4** except when included in Schedule 2.	**Pharmacy Only** for dermal use in medicines containing 0.5% or less. **Prescription** except for dermal use in medicines containing 0.5% or less.		New Zealand to consider harmonising with Australia.
Australia: Protamine sulfate New Zealand: Protamine sulphate	**S4** except when included in insulins.	**Prescription**	**XXXXXXXX**, an injectable product containing insulin was listed as S3 and 1 injectable antidote listed as unscheduled on the ARTG. All other injectable insulin products containing protamine on the ARTG were S4.	New Zealand and Australia to consider amending the entry to protamine. Australia to consider deleting the exemption for protamine in insulin products and advise DSEB accordingly.

			All injectable products were Prescription medicines on SMARTI. No rationale available on e-minutes behind the Australian exemption.	
Pyridoxal	**S4** for human therapeutic use except: (a) in oral preparations containing 200 mg or less but more than 50 mg of pyridoxal per recommended daily dose when compliant with the requirements of the Required Advisory Statements for Medicine Labels; or (b) in oral preparations containing 50 mg or less of pyridoxal per recommended daily dose.	**Not separately listed**	No products on SMARTI	New Zealand to consider adopting the entry in Part I to harmonise with Australia.
Pyridoxamine	**S4** for human therapeutic use except: (a) in oral preparations containing 200 mg or less but more than 50 mg of pyridoxamine per recommended daily dose	**Not separately listed**	No products on SMARTI	New Zealand to consider adopting the entry in Part I to harmonise with Australia.

	when compliant with the requirements of the Required Advisory Statements for Medicine Labels; or (b) in oral preparations containing 50 mg or less of pyridoxamine per recommended daily dose.			
Quassia	**Appendix B** for human therapeutic use and animal use	**Pharmacy Only**	No products on SMARTI.	New Zealand to consider harmonising with Australia.
Australia: Rifampicin (rifamycin) New Zealand: Rifampicin Rifamycin	**S4**	**Prescription**	Rifamycin is the INN	New Zealand and Australia to adopt Rifamycin and delete duplicate entries.
Salicylic acid	**S3** in preparations for dermal use except in preparations containing 40 per cent or less of salicylic acid.	**General Sale** for external use in medicines containing 40% or less. **Restricted** for external use in medicines containing more than 40%.	External use includes application to ears, eyes or nose in the SUSDP.	New Zealand to consider replacing external use with dermal use to harmonise with Australia.
Australia: Schoenocaulon Officinale (Sabadilla)	**S4** except in preparations containing 10 mg/kg (L) of alkaloids of Schoenacaulon	**General Sale** in packs containing 1.8 milligrams or less with a recommended daily dose	Outcome of the June 2006 NDPSC meeting.	New Zealand to consider harmonising with the Australian scheduling and nomenclature.

New Zealand: Sabadilla	officinale.	of not more than 0.6 milligrams of total alkaloids. **Pharmacy Only** in packs containing 18 milligrams or less of total alkaloids except in packs containing 1.8 milligrams or less and a recommended daily dose of not more than 0.6 milligrams of total alkaloids **Prescription** except when specified elsewhere in this Schedule.		
Sodium cellulose phosphate	**S4** for human internal use.	**Prescription**	1 discontinued Prescription oral solution containing 100% of substance on SMARTI.	New Zealand to consider harmonising with Australia.
Sodium nitrite	**S2** for therapeutic use (excluding when present as an excipient)	**Pharmacy Only**	NDPSC August 2001 minutes states that sodium nitrite for the treatment of cyanide poisoning is the reason for inclusion of the substance in S2. A number of products registered on the ARTG containing sodium nitrite as excipient.	New Zealand to consider exempting excipients from scheduling.

Australia: Solasodine New Zealand: Solasadine	**S4**	**Prescription**	Solasodine is the correct spelling	New Zealand to consider amending the spelling to 'solasodine'.
Australia: Strophanthin-K Strophantus spp New Zealand: Strophanthin Strophanthin-K Strophantus	**S4**	**Prescription**	**Strophanthin-K** [cardiac glycosides from strophanthus, the seeds of Strophanthus kombe (Apocynaceae)], **G-Strophanthin** [obtained from the seeds of Strophanthus gratus or from the wood of Acokanthera schimperi or A. ouabaio (Apocynaceae)] and **K-strophanthin-alpha** (extracted from Apocynum cannabinum). All strophantins are cardiac glycosides	New Zealand to consider adopting the class entry for "strophanthins" and amending Strophantus to Strophantus spp. Australia to consider adopting a class entry for "strophantins" and deleting Strophanthin-K.
Thenyldiamine	**S2 (outcome of the Feb '06 NDPSC meeting)** (a) in nasal preparations for topical use; or (b) when combined with one or more other therapeutically active substances in oral preparations when:	**Pharmacy Only** for nasal use; for oral use when combined with one or more other therapeutically active ingredients <u>for the treatment of coughs, colds or influenza</u> when at least one of the other	The OTC entries were deleted in June 2005 as part of a group of substances with no products and the S4 entry was retained.	Australia and New Zealand to retain only a primary entry for all medicines in S4 and delete all other entries.

	(i) at least one of the other therapeutically active substances is a sympathomimetic decongestant; or (ii) in a day-night pack containing thenyldiamine in the bed-time dose; and (iii) not labelled for the treatment of children under 2 years of age. **S4**	active ingredients is a sympathomimetic decongestant or in a day/night pack containing thenyldiamine in the bed-time dose and in preparations for adults and children over two years of age. **Restricted** for oral use in solid dose form or in liquid form containing 10 milligrams or less per 5 millilitres except when specified elsewhere in the Schedule. **Prescription** except when specified elsewhere in this Schedule		
Australia: Thiotepa (triethylene thiophosphoramide) New Zealand: Thiotepa Triethylene thiophosphoramide	**S4**	**Prescription**	Thiotepa is the INN	Australia and New Zealand to consider retaining the substance entry "Thiotepa" and deleting other entries. Both countries to consider cross-referencing triethylene thiophosphoramide to thiotepa.
Other harmonisation proposals				

Creosote	**S2** derived from wood other than beechwood for human therapeutic use, except in preparations containing 10 per cent or less of creosote derived from wood other than beechwood.	**General Sale** in medicines containing 10% or less. **Pharmacy Only** in medicines containing more than 10%.	Creosote was rescheduled at the Oct 2004 NDPSC meeting as an outcome of the consideration of the draft IPCS CICAD report on creosote(s) derived from coal.	New Zealand to consider harmonising with the Australian S2 entry.
Cresols	**S2** PHENOL, or any homologue boiling below 220°C, for human therapeutic use except: (a) when included in Schedule 4; or (b) in preparations for external use containing 3 per cent or less of such substances.	**General Sale** in medicines containing 3% or less. **Pharmacy Only** in medicines containing more than 3%	No products listed on SMARTI	New Zealand to consider harmonising with the Australian entry for phenol. Australia to cross-reference cresol to phenol.
Diclofenac	**S2** in divided preparations for oral use containing 12.5 mg or less of diclofenac per dosage unit in a pack containing 20 or less dosage units and labelled with a recommended daily dose of 75 mg or less of diclofenac. **S3** in divided preparations for oral use containing 25 mg or less	**Pharmacy Only** in solid dose form in medicines containing 12.5 milligrams or less per dose form in packs containing not more than 20 tablets or capsules. **Restricted** in solid dose form in medicines containing 25 milligrams or less and more than 12.5 milligrams per dose form in packs containing	All other Schedule entries are essentially harmonised except for preparations not meeting SUSDP S2 daily dose requirement which would go to S3.	New Zealand to consider harmonising with Australia.

	of diclofenac per dosage unit in a pack containing 30 or less dosage units except when included in Schedule 2. **S4 except**: (a) when included in Schedule 2 or 3; or (b) in preparations for dermal use.	not more than 30 tablets or capsules. **Prescription** except when specified elsewhere in this Schedule; except for external use.		
Ether	**S2** for therapeutic use except: (a) when included in Schedule 4; or (b) in preparations containing 10 per cent or less of ether. **S4** for use in anaesthesia.	**General Sale** except for anaesthesia in medicines containing 10% or less. **Pharmacy Only** except for anaesthesia in medicines containing more than 10%. **Prescription** for anaesthesia.	ARTG lists one product for use as wart paint containing ether as an excipient. One suspension for injection (Prescription) product on SMARTI.	New Zealand to consider harmonising with Australia.
Hexachlorophane	**S2** in preparations for human use containing 3 per cent or less of hexachlorophane except: (a) in preparations containing 0.75 per cent or less of hexachlorophane; or (b) in preparations for use on infants, as specified in Schedule 4. **S4** (a) in preparations for	**General Sale** in medicines containing 0.75% or less. **Pharmacy Only** medicines containing 3% or less but more than 0.75%. **Prescription** in medicines containing more than 3%.	The March 1976 NDPSC meeting considered the ADEC advice and agreed to limit the topical use of hexachlorophene, particularly on infants, because of toxicity issues.	New Zealand to consider harmonising with the Australian scheduling of preparations for use on infants.

	use on infants; or (b) in other preparations except: (i) when included in Schedule 2 or 6; or (ii) in preparations containing 0.75 per cent or less of hexachlorophane.			
Australia: 8-Hydroxyquinoline New Zealand Hydroxyquinoline sulphate 8-Hydroxyquinoline and its non-halegenated derivatives	**S2** and its non-halogenated derivatives for human therapeutic use, except in preparations for external use containing 1 per cent or less of such substances. **Appendix C** Clioquinol and other halogenated derivatives of 8-Hydroxyquinoline for human internal use.	**General Sale** Hydroxyquinoline sulphate for external use. **Pharmacy Only** 8-Hydroxyquinoline and its non-halogenated derivatives in medicines containing more than 1% of such substances.	Hydroxyquinoline sulphate is a synonym of 8-Hydroxyquinoline sulphate. One Pharmacy Only product on SMARTI containing 375µg/mL Hydroxyquinoline sulphate. One solution for injection on ARTG (radioisotope).	New Zealand to consider amending the cut-off of general sale medicines for external use to 1 % or less on the basis of toxicity and include the term "and its non-halogenated derivatives" for consistency.
Ibuprofen	**S2** 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	**General Sale** for external use; for oral use in solid dose form containing 200 milligrams or less per dose form when in packs containing not more than 25 dose units and when		New Zealand to consider harmonising with the 100 mg pack size limit and recommended daily dose of 1200 mg or less ibuprofen. New Zealand to check that all label requirements for exempt

	pack containing 4 grams or less of ibuprofen; or (b) in divided preparations, each containing 200 mg or less of ibuprofen, <u>in packs of not more than 100 dosage units</u> 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.	in medicines which have received the consent of the Minister or the Director-General to their distribution as general sale medicines and are sold in the manufacturer's original pack **Pharmacy Only** for oral use in liquid form in packs containing not more than 4 grams in medicines which have received the consent of the Minister or the Director-General to their distribution as pharmacy-only medicines and which are sold in the manufacturer's original pack; for oral use in solid dose form containing not more than 200 milligrams per dose form in medicines which have received the consent of the Minister or the Director-General to their distribution as pharmacy-only medicines and which are sold in the		and S2 medicines are in the New Zealand registration guidelines for consistency.

		manufacturer's original pack; except in packs containing 200 milligrams or less per oral solid dose form and not more than 25 dose units per pack in medicines which have received the consent of the Minister or the Director-General to their distribution as general sale medicines and which are sold in the manufacturer's original pack. **Prescription** except when specified elsewhere in this Schedule.		
Liquorice deglycyrrhizinised	**Appendix B**	**Prescription**	The May 1999 NDPSC meeting was advised by the NZ Member deglycyrrhizinised liquorice had been classified 'prescription only' in NZ on the basis the only product containing this substance was indicated for the treatment of peptic ulcer. The product was recently discontinued in NZ.	New Zealand to consider harmonising with Australia and reclassifying liquorice deglycyrrhizinised to General Sale.

			Liquorice is used as a flavouring and sweetening agent. It has demulcent and expectorant properties and has been used in cough preparations. It has ulcer-healing properties that may result from stimulation of mucus synthesis. It also has mild anti-inflammatory and mineralocorticoid properties associated with the presence of glycyrrhizinic acid and its metabolite glycyrrhetinic acid, which is an inhibitor of cortisol metabolism. Liquorice may also possess some antispasmodic and laxative properties. Deglycyrrhizinised liquorice has a reduced mineralocorticoid activity and has been used, usually with antacids, for the treatment of peptic ulcer disease. **Secretariat's Note:** The rationale for inclusion in Appendix B is not available	

			from e-minutes. The ARTG lists a number of cough/bronchitis products containing liquorice as an active ingredient. Other Listed products contain extracts of liquorice for flavouring and a number of complementary medicines are also included on the ARTG containing dry liquorice for the treatment of renal water retention and for use as a laxative. NZ has a Pharmacy Only liquorice herbal cough syrup listed on SMARTI in 1990 but never marketed. General Sale products on SMARTI are Fisherman's Friend Lozenge containing Liquorice liquid extract 7.25% and Bonnington's Irish Moss containing Liquorice liquid extract 24mg/mL.	
Phenol	**S2** or any homologue boiling below 220°C, for human therapeutic use	**General Sale** **Pharmacy Only** in medicines other than for		New Zealand to consider adopting the phenol entry and harmonise with Australia.

	except: (a) when included in Schedule 4; or (b) in preparations for external use containing 3 per cent or less of such substances. **S4** in preparations for injection	injection containing more than 3%. **Prescription** for injection		
Prilocaine	**S2** in preparations for dermal use containing 10 per cent or less of total local anaesthetic substances. **S4** except when included in Schedule 2.	**Pharmacy Only** for dermal use in medicines containing 10% or less. **Prescription** for injection except when used as a local anaesthetic in practice by a registered dental therapist; except when specified elsewhere in this Schedule.	2 products for injection on ARTG, containing 30 g/mL of prilocaine HCl	New Zealand to consider harmonising with Australia and adopting "total anaesthetic substances" in Part III based on Recommendation 56 / 6 endorsed at the February 2001 NDPSC meeting. Furthermore, New Zealand to consider harmonising with the S4 entry and include in Part I all preparations not included in S2/Part III.
Triamcinolone	**S2** 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	**Pharmacy Only** in aqueous nasal sprays delivering up to 55 micrograms per actuation when the maximum recommended daily dose is no greater than 220 micrograms and medicine has received	The recommended daily dose for **XXXXXXXX** (triamcinolone nasal spray) in MIMS showed a recommended starting dose of 220 microgram, i.e. 2 sprays in each nostril once daily, and once symptoms are controlled, patients can	New Zealand to consider harmonising with the scheduling conditions, i.e. indication and age restriction, specified in the S2. Australia to consider adopting the New Zealand dosage per actuation of 55 mcg and

	of allergic rhinitis for up to 6 months in adults and children 12 years of age and over. **S3** for the treatment of mouth ulcers in preparations containing 0.1 per cent or less of triamcinolone in a pack of 5 g or less. **S4** except when included in Schedule 2 or 3.	the consent of the Minister or the Director-General to its distribution as a pharmacy-only medicine. **Restricted** for buccal use in medicines containing 0.1% or less of triamcinolone acetonide and in pack sizes no greater than 5 grams. **Prescription** except when specified elsewhere in this Schedule.	be maintained on 110 microgram, i.e. 1 spray in each nostril once daily.	recommended daily dosage of 220 mcg for triamcinolone. Furthermore, Australia to consider replacing "for the treatment of mouth ulcers" with "for buccal use" in S3.
PROPOSALS BASED ON THE POLICY FOR OTC AND PRESCRIPTION MEDICINES AND POLICY FOR NAMING BOTANICALS				
Australia: Acokanthera schimperi and Acokanthera ouabaio New Zealand: Acokanthera	**S4**	**Prescription**	Policy on nomenclature of botanicals considered at TTHWP Meeting 14 and endorsed at the October 2005 NDPSC meeting (<3 plants species individual but if more than 3, schedule all species, e.g. Acokanthera spp.	New Zealand to consider harmonising with Australia and list plant species individually.
Butraconazole	**S4**	**Not listed**	No products on SMARTI	New Zealand to consider harmonising with Australia and adopting the entry in Part I as per policy on S4 medicines.
Australia:	**S4** except in preparations	**General Sale**	The draft TT_Ingredients	New Zealand to consider

Cephaelis Acuminata (ipecacuanha) New Zealand: ipecacuanha	containing 0.2% or less of emetine.	Ipecacuanha; in medicines containing 0.2% or less of emetine **Prescription** Ipecacuanha; in medicines containing more than 0.2% of emetine	List contains *Cephaelis acuminata* and *Cephaelis ipecacuanha.*	adopting the entries for *Cephaelis acuminata* and *Cephaelis ipecacuanha* as per policy on naming botanicals. Australia to consider adopting *Cephaelis ipecacuanha* and cross-referencing ipecacuanha to both *Cephaelis acuminata* and *Cephaelis ipecacuanha*.
Chlorquinaldol	**S4** for human topical use.	**General Sale** for external use **Prescription** for internal use	No products on ARTG but several Prescription products on SMARTI. MCC Secretary advised that the scheduling of chlorquinaldol dermal preps was most likely based on products available at the time and that only dermal preps containing other S4 active ingredients which cause them to be prescription medicines were available so removal of the GS exemption would not likely affect any product on the market in New Zealand.	New Zealand and Australia to consider adopting the parent entry in S4 as "CHLORQUINALDOL for human therapeutic use" and New Zealand to consider deleting the GS entry as per policy on harmonisation of OTC medicines with no existing products.
Australia: Convallaria Keiski and Convallaria Majales	**S4**	**Prescription**	Nomenclature difference.	New Zealand to consider adopting individual entries as per policy on naming

New Zealand: Convallaria				botanicals and harmonise with Australia.
Cortisone	**S4**	**Prescription** Cortisone and other steroidal hormones of the adrenal cortex except when specified elsewhere in this Schedule; except adrenal extract for dermal use in medicines containing 0.02% or less of ketosteroids.	17-ketosteroids are metabolites (break-down products) of androgens and other steroid hormones that are secreted from the adrenal cortex. 1 existing Prescription oral medicine containing 5 mg cortisone acetate was listed on SMARTI. Numerous products containing cortisone were found on the ARTG but none containing adrenal extract. Ketosteroids are not listed on the ARTG. No adverse reaction reports in Australia.	New Zealand to consider adopting the Australian entry.
Australia: Datura spp Datura Stramonium (stramonium) Datura Tatula (stramonium)	**S2** (Datura spp) or oral use: (a) in undivided preparations containing 0.03 per cent or less of total solanaceous alkaloids when labelled	**Pharmacy Only** (Datura spp) for oral use in liquid form in medicines containing 0.03% or less and 0.3 milligrams or less per dose and not more than	Nomenclature only partially harmonised. Australia has separate entries for Datura Stramonium (stramonium), and Datura Tatula (stramonium) while New Zealand has a separate entry	New Zealand to consider adopting the botanical name and entries for Datura Stramonium (stramonium) and Datura Tatula (stramonium) in S2 and S4, and deleting the Part II entry (Restricted

New Zealand: Datura spp Stramonium	with a dose of 0.3 mg or less of total solanaceous alkaloids and a recommended daily dose of 1.2 mg or less of total solanaceous alkaloids, or (b) in divided preparations containing 0.3 mg or less of total solanaceous alkaloids per dosage unit when labelled with a recommended daily dose of 1.2 mg or less of total solanaceous alkaloids, except when separately specified in these Schedules **S2** (Datura Stramonium and Datura Tatula) for oral use when: (a) in undivided preparations containing 0.03 per cent or less of total solanaceous alkaloids when labelled with a dose of 0.3 mg or less of total solanaceous alkaloids and a recommended daily dose	1.2 milligrams per recommended daily dose of total solanaceous alkaloids; in solid dose form in medicines containing 0.3 milligrams or less per dose form and not more than 1.2 milligrams per recommended daily dose of total solanaceous alkaloids. (Stramonium) in solid dose form containing 0.3 milligrams or less per dose and 1.2 milligram or less per recommended daily dose. **Restricted** (Stramonium) for oral use in liquid form; in solid dose form containing more than 0.3 milligrams per dose or more than 1.2 milligrams per recommended daily dose.	for Stramonium. Stramonium has an entry in Part II (Restricted Medicines). No products containing stramonium were found in SMARTI so minimal to nil regulatory impact expected. The MCC Secretary has advised that it was not the intent of MCC to schedule stramonium separately.	Medicine) for Stramonium to harmonise with Australia.

	of 1.2 mg or less of total solanaceous alkaloids; or (b) in divided preparations containing 0.3 mg or less of total solanaceous alkaloids per dosage unit when labelled with a recommended daily dose of 1.2 mg or less of total solanaceous alkaloids, except for smoking or burning. **S4** (Datura spp) except: (a) when included in Schedule 2; or (b) when separately specified in this Schedule **S4** (Datura stramonium and Datura tatula) except: (a) when included in Schedule 2; or (b) for smoking or burning.	**Prescription** (Datura spp) except for oral use when specified elsewhere in this Schedule; except datura stramonium or datura tatula for smoking or burning.		
Deslorelin	**S4**	**Not classified**	No products on SMARTI	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines
Detomidine	**S4**	**Not classified**	No products on SMARTI	New Zealand to consider

				adopting the entry in Part I as per policy on S4 medicines
Diamthazole	**S4**	**General Sale**	No products on ARTG or SMARTI Adopted in the SUSDP at the May 2000 NDPSC on the grounds of harmonisation with New Zealand.	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines.
Difloxacin	**S4**	**Not classified**	No products on SMARTI	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines
Diisopropylamine dichloroacetate	**S4**	**Not classified**	No products on SMARTI NDPSC minutes of May 1984 indicated that the substance was used "as a vitamin for humans and unprescripted use for animals".	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines
Dimethoxanate	**S4**	**Not classified**	No products on SMARTI	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines.
Diphenylpyraline	**S4**	**Pharmacy Only** for oral use when combined with one or more other therapeutically active ingredients for the treatment of coughs, colds or influenza when	2 withdrawn Pharmacy Only medicines (1979) and 1 discontinued product (1969) on SMARTI. No products on ARTG.	New Zealand to consider harmonising with Australia as per policy on OTC medicines with no products.

		at least one of the other active ingredients is a sympathomimetic decongestant or in a day/night pack containing diphenylpyraline in the bed-time dose and in preparations for adults and children over two years of age. **Restricted** for oral use except when specified elsewhere in this Schedule. **Prescription** except when specified elsewhere in the Schedule.		
Disophenol	**S4**	**Not classified**	No products on SMARTI	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines
Ephedra	**S4** except in preparations containing 0.001 per cent or less of ephedrine.	**General Sale** Ephedra navadensis.	Ephedra gerardiana and E. sinensis contain ephedrine and have been used in chinese and middle-eastern medicine under the name Ma Huang. E.major, E.helvetica and E.dystachia also contain large amounts of ephedrine	New Zealand to adopt a primary entry for Ephedra spp in Part I and harmonise with the Australian exemption on the basis of ephedra's abuse potential. Australia to amend the S4 entry to Ephedra spp for consistency with other entries

			and were utilised for this in Europe. Ephedra nevadensis is one of the pseudoephedrine containing ephedras, and is used mostly for it's expectorant and stimulating action and has a long history of traditional use.	in the SUSDP.
Etonogestrel	**S4**	**Not classified**	One Prescription product for subcutaneous implant on SMARTI	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines.
Felbinac	**S2** in preparations for external use. **S4** except when included in Schedule 2.	**Pharmacy Only** for external use.	No products on the ARTG. 1x topical gel product approved in 1992 but not yet marketed in New Zealand.	New Zealand to consider adopting the S4 entry in Part I and both countries to consider deleting the entries in S2 and Part III.
Fomivirsen	**S4**	**Not classified**	No products on SMARTI	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines.
Guanacline	**S4**	**Not classified**	May 1999 NDPSC minutes recommended that New Zealand adopt the entry. No products on SMARTI	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines.
Guanidine	**S4**	**Not classified**	August 1999 NDPSC recommended that New Zealand reschedule the drug	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines.

			from Part II to Part I because of proven toxicity. No products on SMARTI	
Human chorionic gonadatrophin	**S4** except in pregnancy kits	**Not classified**	6 Prescription products on SMARTI containing the active 'chorionic gonadotrophin'	New Zealand to consider adopting the entry in Part I as per policy on S4 medicines. Australia to correct the spelling to Human chorionic gonadotrophin.
Hydrocyanic acid	**S4** for therapeutic use. **Appendix G** exemption at 1 microgram or less per litre or per kilogram.	**General Sale** for oral use in packs containing 0.5 milligrams or less; in medicines containing 1 microgram or less per litre or per kilogram. **Pharmacy Only f**or oral use in packs containing 5 milligrams or less and more than 0.5 milligrams; except in medicines containing 1 microgram or less per litre or per kilogram. **Prescription** except when specified elsewhere in this Schedule; except in medicines containing 1 microgram or less per litre or per kilogram.	The August 1999 NDPSC Meeting considered a TTHWP recommendation that "THE NDPSC SHOULD BE ADVISED TO RECOMMEND TO THE NZ MOH, ON THE GROUNDS OF PUBLIC HEALTH AND SAFETY, TO DELETE ITS PART II AND III ENTRIES FOR HYDROCYANIC ACID AND TO RESCHEDULE THE DRUG TO PART I OF THE MEDICINES REGULATIONS." No products on SMARTI or ARTG.	New Zealand to consider harmonising with the Australian scheduling as per policy.

Ibritumomab tiuxetan	**Unscheduled**	**Prescription**		New Zealand to consider amending the entry to read "Ibritumomab". Australia to consider adopting the parent entry in S4 as per policy on S4 medicines.
Insulin-like Growth Factor I	**S4** **Appendix D**	**Not classified**		New Zealand to consider adopting an entry in Part I for Insulin-like Growth Factor I as per policy on S4 medicines.
Ipriflavone	**S4**	**Not listed**	No products on SMARTI	New Zealand to consider harmonising with Australia as per policy on S4 medicines.
Lefetamine	**S4**	**Not listed**	No products on SMARTI	New Zealand to consider harmonising with Australia as per policy on S4 medicines.
Lodoxamide	**S2** in preparations for ophthalmic use. **S4** except when included in Schedule 2.	**Pharmacy Only** for ophthalmic use.	Only ophthalmic preparations on the ARTG and SMARTI	New Zealand to consider adopting a parent entry to harmonise with Australia.
Mandragora officinarum	**S4**	**Not listed**	No products on SMARTI. New Zealand has advised that the plant is not listed on the MODA.	New Zealand to consider harmonising with Australia as per policy on S4 medicines.
Mercuric oxide	**S2** in ointments for human ocular use.	**Pharmacy Only** for ophthalmic use.	One discontinued eye Ointment on SMARTI classified as Restricted Medicine (approval date 1962).	Australia and New Zealand to delete the S2/Part III entry and adopt a primary entry in S4 as per policy on OTC entries with no products.

			One homeopathic medicine on the ARTG (Listed medicine).	
Methenolone	**S4**	**Not listed**	No products on SMARTI	New Zealand to consider harmonising with Australia as per policy on S4 medicines.
Methyl salicylate	**S5** in liquid preps containing 25 percent or more of methyl salicylate except when included in S6. **S6** excluding admixtures (see also Schedule 5)	**General Sale**	The ARTG includes Listed medicines containing methyl salicylate in liniments, creams, mouthwash, gel, pastiles and inhalation fluids.	New Zealand to consider adopting a Part I entry for preparations for internal use. Australia to consider including a primary entry in S4 for preparations for internal use and exempting all other preparations.
Organophosphorus compounds	**S4** with anticholinesterase activity for human therapeutic use except: (a) when separately specified in these Schedules; or (b) preparations containing 2 per cent or less of maldison for external use.	**Not classified**	No products on SMARTI Several shampoo/topical use products (exempt and S2) on the ARTG.	New Zealand to consider harmonising with Australia as per policy on S4 medicines..
Phenyltoloxamine	**S4**	**Restricted** for oral use. **Prescription** except for oral use.	Oral preparations of this sedating antihistamine were rescheduled from S2 to S3 in	New Zealand to consider harmonising with Australia and deleting the Part II entry as

			August 1985 and the primary was in S4. The June 2003 NDPSC meeting recommended that New Zealand harmonise with this scheduling. The February 2005 NDPSC meeting agreed to delete the S3 entry based on the policy that where there were no OTC products, only the primary entry S4 will be retained to expedite the harmonisation work. No products found on SMARTI or ARTG.	per policy.
Pipradrol	**S4**	**Not listed**	No products on SMARTI	New Zealand to consider harmonising with Australia as per policy on S4 medicines.
Pituitary hormones	**S4**	**Not listed**	No products on SMARTI	New Zealand to consider harmonising with Australia as per policy on S4 medicines.
Polysulfated glycosaminoglycans	**S4** in preparations for injection, except when separately specified in these Schedules.	**Not listed**	No products on SMARTI or ARTG No definite info from e-minutes on the basis for scheduling this substance.	New Zealand to consider harmonising with Australia as per policy on S4 medicines.

			Internet searches indicate that substance is commonly used on veterinary products. Micromedex search indicated that the term heparinoid includes heparin derivatives and has also been used more loosely to include naturally occurring and synthetic highly-sulfated polysaccharides of similar structure. Such compounds have been described in many ways; some of the terms used include sulfated glucosaminoglycans; glycosaminoglycan polysulfate compounds; or sulfated mucopolysaccharides.	
Riluzole	**S4**	**Not listed**	1 Prescription product on SMARTI	New Zealand to consider harmonising with Australia as per policy on S4 medicines..
Scopolia carniolica	**S4**	**Not listed**		New Zealand to consider harmonising with Australia as per policy on S4 medicines.
Tipepidine	**S4**	**Not listed**	Micromedex states that tipepidine hibenzate is a cough suppressant used for	New Zealand to consider harmonising with Australia as per policy on S4 medicines.

			non-productive cough. No products on SMARTI	
Tolpropamine	**S4**	**Not listed**	No products on SMARTI	New Zealand to consider harmonising with Australia as per policy on S4 medicines.
Australia: Veratrum spp New Zealand: Veratrum	**S4**	**Prescription**		New Zealand to consider harmonising with Australia as per policy on naming botanicals.

TABLE 3 – DEFERRED ITEMS

Substance	**Australian Schedule/ NZ Classification**		**Comment**	**TTHWP Recommendations**
	Australian	**NZ**		
Fibrin	**Unscheduled**	**Prescription**	ARTG lists medical devices and formulated medicines including OCTANATE 1000 factor VIII 1000IU powder for injection containing fibrinogen. Fibrin is made from its zymogen fibrinogen, a soluble plasma glycoprotein that is synthesised by the	Deferred pending the outcome of NDPSC consideration of fractionated and recombinant blood products.

			liver. Processes in the coagulation cascade activate the zymogen prothrombin to the serine protease thrombin, which is responsible for converting fibrinogen into fibrin. Fibrin is then cross linked by factor XIII to form a clot.	
Fibrinogen	**Unscheduled**	**Prescription**	**See fibrin**	See fibrin.
Sodium hydroxide	**S5** (excluding its salts and derivatives) in preparations containing 5 per cent or less of sodium hydroxide being: (a) solid preparations the pH of which in a 10 g/L aqueous solution is more than 11.5; or (b) liquid or semi-solid preparations the pH of which is more than 11.5. **S6** (excluding its salts and derivatives) except: (a) when included in Schedule 5; or (b) preparations containing 5 per cent or less of sodium hydroxide being:	**General Sale**	Caught in the entries in S5 and S6 of the SUSDP. Could be addressed by including an exception for therapeutic use. Disinfectants and dental restorative materials containing NaOH found on ARTG. Secretariat to identify other products for therapeutic use if any.	Deferred to February 2007 NDPSC meeting pending the development of a policy for medicines listed in S5-S7

	(i) solid preparations the pH of which in a 10 g/L aqueous solution is 11.5 or less; or (ii) liquid or semi-solid preparations the pH of which is 11.5 or less.			
Aspirin	**S2** 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) compliant with the requirements of the Required Advisory Statements for Medicine Labels: (c) in tablets or capsules each containing no other therapeutically active	**General Sale** except in slow release forms; except in enteric coated forms containing more than 300 milligrams per dose form. **Restricted** in slow release forms; in enteric coated forms containing more than 300 milligrams per dose form	Advice sought from the Australia New Zealand Society of Nephrologist was not received by the TTHWP. NDPSC Chair to advise the Secretariat on an alternative source of expert advice.	The TTHWP agreed to refer this matter back to the NDPSC for consideration of other related substances, i.e. paracetamol and salicylamide and derivatives of these substances. Consideration of this matter would require input from key stakeholders and would be best dealt with under NDPSC processes. Deferred to February 2007 NDPSC meeting.

	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. **S4** (a) when combined with caffeine, paracetamol or salicylamide or any derivative of these substances; or (b) for injection			
Factor VIII inhibitor bypassing fraction	**Unscheduled**	**Prescription**	Await the outcome of the NDPSC's consideration of fractionated and recombinant blood products	Deferred
Hydrocortisone and hydrocortisone acetate	**S2** <u>but excluding other salts and derivatives</u>, in preparations for dermal use containing 0.5 per cent or less of hydrocortisone in packs containing 30 g or less of	**Pharmacy Only** for dermal use in medicines containing 0.5% or less by weight of hydrocortisone base with no other active ingredient except an antifungal and	Secretariat to investigate the rationale for excluding salts and derivatives and advice the October 2006 meeting of findings.	Deferred to a future meeting.

	such preparations containing: (a) no other therapeutically active substance; or (b) an antifungal as the only other therapeutically active substance. **S3** <u>but excluding other salts and derivatives</u>, in preparations containing 1 per cent or less of hydrocortisone: (a) for dermal use, in packs containing 30 g or less of such preparations; and (i) containing no other therapeutically active substance; or (ii) containing an antifungal but no other therapeutically active substance; or (b) for rectal use, when combined with a local anaesthetic but no other therapeutically active substance except unscheduled astringents: (i) in undivided	in a quantity of 30 grams or less or 30 millilitres or less per container. **Restricted** for dermal use in medicines containing 1% or less but more than 0.5% by weight of hydrocortisone base with no other active ingredient except an antifungal and in a quantity of 30 grams or less or 30 millilitres or less per container; in rectal medicines containing 1% or less by weight of hydrocortisone base and in combination with a local anaesthetic and in a quantity of not more than 35 grams per container or 12 suppositories per pack**.** **Prescription** (Hydrocortisone only) except when specified elsewhere in this Schedule.		

	preparations, in packs of 35 grams or less; or (ii) in packs containing 12 or less suppositories, except when included in Schedule 2. **S4** (Hydrocortisone only) except when included in Schedule 2 or 3.			
Immunoglobulins	**S4** for human parenteral use except when separately specified in these Schedules.	**Prescription**	Await the outcome of blood products' consideration by the NDPSC.	Deferred
Iron compounds	**S2** IRON COMPOUNDS (excluding iron oxides when present as an excipient, in divided preparations containing 10 mg or less of total iron oxides per dosage unit or in undivided preparations containing 1 per cent or less of total iron oxides) for human internal use **except**: (a) when included in Schedule 4; or (b) when labelled with a recommended daily dose of 24 mg or less of iron: (i) in undivided	**General Sale** Iron in medicines containing 24 milligrams or less per recommended daily dose; in parenteral nutrition replacement preparations. **Pharmacy Only** Iron in medicines containing more than 24 milligrams per recommended daily dose. **Prescription** Iron for injection except in parenteral nutrition replacement preparations.		Deferred to a future meeting

	preparations supplied in packs each containing 750 mg or less of iron; or (ii) in divided preparations (A) containing more than 5 mg of iron per dosage unit in packs each containing 750 mg or less of iron; or (B) containing 5 mg or less of iron per dosage unit. **S4** IRON COMPOUNDS in injectable preparations for human use.			
Ketoprofen	**S3** in divided preparations for oral use containing 25 mg or less of ketoprofen per dosage unit in a pack containing 30 or less dosage units. **S4** except: (a) in preparations for dermal use; or (b) when included in Schedule 3.	**General Sale** for external use. **Restricted** in solid dose form containing 25 milligrams or less per dose form in packs of not more than 30 capsules or tablets. **Prescription** except when specified elsewhere in this Schedule.	No ophthalmic products on SMARTI. New Zealand products include injectables, oral dose form, topical and suppositories. Secretariat to assess potential regulatory impact.	Deferred to February 2007 NDPSC meeting.
Laxatives: aloes for internal use	**Unscheduled**	**General Sale** except when specified in the	The June 2004 MCC Meeting recommended that	To be referred to the MSC.

aloin bisacodyl colocynth ipomoea jalap resin sennosides sodium picosulphate Phenisatin (S4)		First Schedule of the Medicines Regulations. **Pharmacy Only** (Stimulant laxatives, eg. aloes, aloin, bisacodyl, colocynth, ipomoea, jalap resin, sennosides and sodium picosulphate) **Prescription** Phenisatin	the NDPSC should consider more restrictive scheduling for stimulant laxatives compared to bulk laxatives and include them in S2 to harmonise with New Zealand. Harmonising with NZ is expected to result in significant regulatory impact on Australian products given their unscheduled status. However, several published articles and a recent report[1] have documented the abuse of laxatives by young people in Australia, especially by young females who have anorexia nervosa or bulimia as well as those who have body image problems. Adverse reactions were received on bisacodyl and senna but overall, the unscheduled status of	

[1] Mental Health of Young People in Australia - http://www.health.gov.au/internet/wcms/Publishing.nsf/Content/mental-pubs/$FILE/young.pdf

			stimulant laxatives in Australia did not give rise to safety issues from normal use.	
Mifepristone	**Unscheduled**	**Prescription**	An abortifacient (RU 486) and is related to aglepristone which is a vet drug. See Feb 2001 NDPSC meeting.	Defer to a future meeting of the MSC.
Meptazinol	**Unscheduled**	**Prescription**	Has potential for abuse but not evident from a quick search of the internet. No products on ARTG. One Prescription 200 mg tablet with registration withdrawn on SMARTI.	Deferred to a future meeting.
Nicotine	**S2** for use as an aid in withdrawal from tobacco smoking in preparations for inhalation. **S4** for use as an aid in withdrawal from tobacco smoking (including preparations for nasal administration) except: (a) when included in Schedule 2; (b) in chewing gum; (c) in lozenges; (d) for sublingual use; or	**General Sale** for transdermal use or in chewing gum, lozenges or sublingual tablets. **Pharmacy Only** for inhalation except when sold from a smoking cessation clinic run under the auspices of a registered medical practioner, nurse, pharmacist or psychologist. **Prescription** for nasal		Australia to consider a primary entry for all preparations for therapeutic use in S4 and amend the S7 entry to become the primary for non-therapeutic products. Deferred to a future meeting pending policy for medicines included in non-therapeutic schedules.

	(e) in preparations for transdermal use.	use except when sold from a smoking cessation clinic run under the auspices of a registered medical practitioner; in medicines other than for smoking cessation.		
Octocog alfa	**Unscheduled**	**Prescription**	Pending the outcome of the NDPSC's consideration of fractionated blood products	Deferred
Paracetamol	**S2** 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; (ii) complies with the requirements of the Required Advisory	**General Sale** in tablets or capsules containing 500 milligrams or less and in packs containing not more than 10 grams; in powder form in sachets containing 1000 milligrams or less and not more than 10 grams. **Pharmacy Only** in liquid form; in suppositories; in tablets or capsules containing 500 milligrams or less and in packs containing more than 10 grams; in powder form containing not more than 1000 milligrams per sachet and more than 10 grams per pack		Deferred to the February 2007 meeting as part of the aspirin consideration.

	Statements for Medicine Labels; and (iii) not labelled for the treatment of children 6 years of age or less; or (c) in tablets or capsules 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; (ii) in a primary pack containing not more than 25 such tablets or capsules; and (iv) not labelled for the treatment of children 6 years of age or less. **S4** (a) when combined with aspirin, caffeine or salicylamide or any derivative of these substances except when separately specified in these Schedules; (b) in tablets or capsules	**Prescription** in tablets or capsules containing more than 500 milligrams per dose unit; in powder form containing more than 1000mg per sachet		

	containing more than 665 mg of paracetamol; or (c) in individually wrapped powders or sachets of granules each containing more than 1000 mg of paracetamol.			
Picric acid	**S6** (excluding its derivatives) except in preparations containing 5 per cent or less of picric acid.	**General Sale**	JAEG and TTHWP Secretariat to develop a strategy/policy for dealing with medicines listed in non-medicine schedules.	To be considered as part of a policy for medicines listed in S5, S6 and S7.
Piper methysticum (Kava)	**S4** 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 and (i) if in tablet or capsule form containing 125 mg or less of kavalactones per tablet or capsule; or (ii) if in the form of a teabag when the amount	**Not listed**	The NZ member advised the June 2006 TTHWP that status quo should remain in the interim pending a safety review by the Interim Joint Expert Advisory Committee on Complementary Medicines (IJEACCM) which would be sponsored by MCC.	Await the outcome of the Kava review.

	of dried whole or peeled rhizome dose not exceed 3g; and, where containing more than 25 mg 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.			
Plasma	**Unscheduled**	**Prescription**		See fibrin
Plasma protein fraction	**Unscheduled**	**Prescription**		See fibrin
Plasmin	**Unscheduled**	**Prescription**		See fibrin
Plasminogen activator	**Unscheduled**	**Prescription**		See fibrin
Platelets	**Unscheduled**	**Prescription**		See fibrin
Potassium	**Unscheduled**	**General Sale** for external use; for internal use		Await the outcome of the Potassium chloride

		except when specified in the First Schedule to the Medicines Regulations 1984; for oral rehydration therapy, parenteral nutrition replacement or dialysis. **Pharmacy Only** except when specified elsewhere in this Schedule; for internal use in slow release or enteric coated forms; in medicines containing more than 100 millligrams per recommended dose except in medicines for oral rehydration therapy, parenteral nutrition replacement or for dialysis		consideration by the NDPSC (on the agenda of the October 2006 NDPSC meeting).
Pyrithione zinc	**S2** 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	**Pharmacy Only** for external use in medicines containing more than 2%.	Secretariat to investigate the rationale for restricting the exemption to semi-solid hair preparations and shampoo and advise the October 2006 meeting.	Deferred to the February 2007 NDPSC meeting.

	Statements for Medicine Labels.			
Pyrethrins	**S5** naturally occurring, being pyrethrolone, cinerolone or jasmolone esters of chrysanthemic or pyrethric acids except in preparations containing 10 per cent or less of such substances.	**General Sale**		Will be considered as part of other S5-S7 medicines in non-medicine schedules. Deferred
Salicylamide	**S2** except when included in Schedule 4. **S4** when combined with aspirin, caffeine or paracetamol or any derivative of these substances.	**Pharmacy Only**		To be considered with aspirin and paracetamol. Deferred to February 2007 NDPSC meeting as part of the aspirin consideration.
Serum, dried human	**Unscheduled**	**Prescription**	Part of blood products (may already be covered under the Appendix A exemption)	Deferred
Selenium	**S2** in preparations for human topical therapeutic use **except** in preparations containing 3.5 per cent or less of selenium sulfide. **S3** in preparations for human oral use with a recommended daily dose of 100 micrograms or	**General Sale** for external use in medicines containing 2.5% or less; for internal use containing 150 micrograms or less per recommended daily dose. **Pharmacy Only** for external use in medicines containing more than		Deferred to the February 2007 meeting.

	less of selenium except where the sum of the organic selenium expressed in micrograms and half the inorganic selenium expressed in micrograms, contained in the recommended daily dose of the preparation, does not exceed 26 micrograms. **S4** for therapeutic use except: (a) when included in Schedule 2, 3, 6 or 7; (b) in preparations for human oral use where the sum of the organic selenium expressed in micrograms and half the inorganic selenium expressed in micrograms, contained in the recommended daily dose of the preparation, does not exceed 26 micrograms; (c) in preparations for human topical use containing 35 per cent or less of selenium sulfide;	2.5%; for internal use in medicines containing more than 150 micrograms per recommended daily dose.		

	or (d) for the treatment of animals: (i) in solid, slow release bolus preparations each weighing 100 g or more and containing 300 mg or less of selenium per dosage unit; (ii) in other divided preparations containing 30 micrograms or less of selenium per dosage unit; (iii) as elemental selenium, in pellets containing 100 g/kg or less of selenium; or (iv) in feeds containing 1 g/tonne or less of selenium.			
Sodium picosulphate	**S3** in preparations for oral use for bowel cleansing prior to diagnostic medical or surgical procedures.	**Pharmacy Only** in oral laxative preparations. **Restricted** in oral preparations for bowel cleansing prior to diagnostic, medical or surgical procedures.	Laxatives referred to JAEG for consideration of a policy approach	Seek advice from JAEG re progress of this matter. Deferred
Tar	**S6 (Tar acids)** distilling within the range 230 - 290°C inclusive.	**General Sale**	Caught in the scheduling of tar acids in Schedule 6.	To be considered with the group of medicines listed in S5-S7

				Deferred
Thrombin	**Unscheduled**	**Prescription**	Part of consideration of fractionated and recombinant blood products	Deferred, part of blood products.
Tranexamic acid	**S3** for the treatment of menorrhagia.	**Prescription**	The Committee was advised that the MCC had considered the matter at its June 2006 meeting and did not support harmonisation with Australia. Secretariat to request the MCC minutes.	Australia to consider harmonising with New Zealand. Deferred
Vitamin A	**S4** (a) in preparations for topical use containing 1 per cent or less of vitamin A; or (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 in adults when compliant with the requirements of the Required Advisory Statements for Medicine	**General Sale** in medicines containing 3000 micrograms or less of retinol equivalents per recommended daily dose; in parenteral nutrition replacement preparations. **Prescription** in medicines containing more than 3000 micrograms of retinol equivalents per recommended daily dose except in parenteral nutrition replacement preparations.		Deferred to the February 2007

	Labels.			
Xylenols	**S2 (Phenol)** or any homologue boiling below 220°C, for human therapeutic use except: (a) when included in Schedule 4; or (b) in preparations for external use containing 3 per cent or less of such substances.	**General Sale** in medicines containing 3% or less. **Pharmacy Only** in medicines containing more than 3%.		Australia to review all related entries to ensure that they are cross-referenced to each other. New Zealand to consider cross-referencing the entry to phenols once it is adopted to ensure that there is a parent entry in Part I (Prescription). Deferred

TABLE 4 – SUBSTANCES REMAINING UNHARMONISED AT THIS TIME

Substance	Australian Schedule/ NZ Classification		Comment	TTHWP Recommendations
	Australian	NZ		
Haemophilus influenzae vaccine	**S4** for internal use except when separately specified in this Schedule.	**Restricted** in oral vaccines for the prophylaxis of bacterial complications of colds. **Prescription** except in oral vaccines for the prophylaxis of bacterial complications of colds.		To remain unharmonised pending review by MCC at a future meeting.
Hyoscine butylbromide	**S2** as the only therapeutically active substance, in divided	**Restricted** for oral use in medicines containing not more than 10 milligrams	TTHWP June 2006 meeting was advised that the recommendation to	New Zealand to remain unharmonised with Australia at this time.

	preparations for oral use, containing 20 mg or less of hyoscine butylbromide per dosage unit in a pack containing 200 mg or less of hyoscine butylbromide. **S4** except when included in Schedule 2.	per dose form and in packs containing not more than 20 tablets or capsules. **Prescription** except when specified elsewhere in this Schedule.	harmonise with Australia had been considered and rejected twice by the MCC based on the concern that hyoscine butylbromide was being used for the treatment of irritable bowel syndrome in New Zealand and was associated with adverse reactions in the elderly.	
Ketamine	**S8**	**Prescription**	The June 2006 TTHWP was advised that ketamine would be included in the MODA.	Cannot be Harmonised.
Mitragyna speciosa	**S9**	**S4**		Cannot be harmonised at this time.
Mitragynine	**S9**	**S4**		Cannot be harmonised at this time.
Oxymetazoline	**S2**	**Pharmacy Only** except for nasal use when sold at an airport.		The Committee agreed that the scheduling is "essentially harmonised".
Pentazocine	**S8**	**Prescription**	3 products discontinued in 1969 on SMARTI.	Committee agreed to remain unharmonised at this time.
Pentobarbitone	**S4** when packed and labelled for injection. **S8** except when included in S4.	**Not classified**	The Secretary of the Dental Health Committee wrote to the Committee in 1980 stating that listing pentobarbitone, thiopentone, methohexitone, amylbarbitone and seconal as being necessary-for	Included in the MODA and cannot be harmonised at this time.

			anaesthesia and conscious sedation in dental practice	
Phenobarbitone	**S4**	**Not classified**		Included in the MODA and cannot be harmonised at this time.
Pneumococcal vaccine	**S4**	**Restricted** in oral vaccines for the prophylaxis of bacterial complications of colds. **Prescription** except in oral vaccines for the prophylaxis of bacterial complications of colds.	Only Prescription medicines were found on SMARTI.	New Zealand will remain unharmonised at this time.
Salbutamol	**S3** as the only therapeutically active substance: (a) in metered aerosols delivering 100 micrograms or less of salbutamol per metered dose; or (b) in dry powders for inhalation delivering 200 micrograms or less of salbutamol per dose. **S4** except when included in Schedule 3.	**Prescription**	MCC rejected the proposal to harmonise twice already.	New Zealand to remain unharmonised at this time.
Terbutaline	**S3** as the only therapeutically active substance:	**Prescription**	MCC rejected the proposal to harmonise twice already.	New Zealand to remain unharmonised at this time.

	(a) in metered aerosols delivering 250 micrograms or less of terbutaline per metered dose; or (b) in dry powders for inhalation delivering 500 micrograms or less of terbutaline per dose **S4** except when included in Schedule 3.			
Silicones	**S4** for intra-ocular use. **Appendix C** for injection or implantation except when included in Schedule 4.	**Prescription** for injection.		TTHWP confirmed that the status is essentially harmonised.
Australia: Silver sulfadiazine Sulfadiazine New Zealand: Sulfadiazine, silver (PO) Sulfadiazine (Prescription)	**S4 (**Silver sulfadiazine**)** **S4 (**Sulfadiazine) except when included in Schedule 5.	**Pharmacy Only (**Sulfadiazine, silver) for external use in pack sizes containing 50 grams or less. **Prescription (**Sulfadiazine) except for external use in packs containing 50 grams or less.		New Zealand wishes to remain unharmonised at this time.
Xylometazoline	**S2**	**Pharmacy Only** except for nasal use when sold at an airport.		TTHWP confirmed that entries are essentially harmonised.
Australia:	**S4** for human internal use	**Pharmacy Only** for	Harmonised for zinc	New Zealand wishes to adopt

Zinc Compounds New Zealand: Zinc	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 not more than 50 mg of zinc when compliant with the requirements of the Required Advisory Statements for Medicine Labels.	dermal use in medicines containing more than 5%. **Prescription** for internal use in medicines containing more than 25 milligrams per recommended daily dose except in parenteral nutrition replacement preparations.	chloride.	through the Joint Agency and cannot be harmonised at this time.

1.8.2 GLOBALLY HARMONISED SYSTEM (GHS) FOR CLASSIFICATION AND LABELLING OF CHEMICALS

PURPOSE

The Committee noted progress by the GHS Working Group on the drafting of the report to the Committee on the GHS and its implications for the scheduling of chemicals.

BACKGROUND

At its October 2005 meeting, the NDPSC agreed that further consideration of GHS and its implications was necessary and timely. It therefore agreed that jurisdictions should continue to familiarise themselves with GHS issues. The Committee also supported the reconvening of the GHS Working Group to provide an assessment of GHS and to report to the June 2006 meeting of the NDPSC.

At its February 2006 meeting, the Committee noted the progress being made and the proposed work program for the Working Group. The Committee suggested that, given the importance of the States/Territories in the scheduling and regulation of poisons, it might be useful to expand the Working Party's membership to include a State/Territory member. **XXXXXXXX** indicated support for this proposal and agreed to approach the States/Territories for a nomination.

XXXXXXXX also advised that as the Department of Agriculture, Fisheries and Forestry and the Australian Safety and Compensation Council both had interest in GHS it would be desirable for both those organisations to be kept informed of the Working Group's activities. The Committee supported the need for good communication with these agencies.

DISCUSSION

The Committee noted that the Working Party's membership had been expanded to include a State/Territory member (**XXXXXXXX**), a representative of the Department of Agriculture, Fisheries and Forestry (**XXXXXXXX**) and a representative from the Office of the Australian Safety and Compensation Council (**XXXXXXXX**).

A first draft of the report on the GHS and its implications has been prepared and has been sent to Working Group members for input. The **XXXXXXXX** representative has advised that a similar report is being prepared for consideration by the Product Safety and Integrity Committee which includes representatives from the State/Territory Departments of Agriculture/Primary Industries. A meeting of the OCS Working Group on GHS would be organised in the near future.

OUTCOME

The Committee noted progress to date.

1.9 PROPOSED ROUTINE CHANGES TO THE SUSDP

No items were considered.

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

No items were considered.

2.2 SUSDP, PART 2

2.2.1 STORAGE STATEMENTS FOR SCHEDULE 5 AND 6 PRODUCTS

PURPOSE

The Committee considered inclusion of a new paragraph in Part 3 of the SUSDP setting out the requirements for retail storage of Schedule 5 and 6 poisons.

BACKGROUND

The June 2004 NDPSC Meeting 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. A post-meeting comment, arising from preliminary consideration of the above issue at the February 2004 NDPSC Meeting, highlighted that there were differences between jurisdictions in their requirements for retail storage of Schedule 5 and 6 poisons. The Committee agreed to refer this matter to **[**sentence deleted**]** with a view to the development of a uniform approach to the retail storage of these substances.

The June 2005 NDPSC Meeting considered a **XXXXXXXX** recommendation to include a new paragraph in Part 3 of the SUSDP under "storage" relating to the retail storage of Schedule 5 and 6 poisons to enhance national consistency. **XXXXXXXX** 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 **XXXXXXXX** recommendation and further agreed to add an additional exception to reflect the existence of the definition for "Non-access Packaging" in the SUSDP.

The October 2005 NDPSC Meeting, however, set aside the above decision based on post-meeting comment and to allow further consultation with stakeholders. The Committee also agreed to foreshadow consideration at the February 2006 NDPSC Meeting of the following paragraph for inclusion in Part 3 setting out the requirements for storage of Schedule 5 and 6 poisons in order to enhance national consistency:

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."

At the February 2006 NDPSC Meeting the Committee deferred further consideration to the June 2006 NDPSC Meeting to allow time for Members to collect additional information to help resolve certain jurisdictional issues.

DISCUSSION

The Members recalled the following points raised at the October 2005 and February 2006 NDPSC Meetings:

- 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 inquired whether the label "Keep out of reach of children", the driver behind a uniform storage statement, was more for the domestic than the retail setting. However, another Member advised of a poisoning incident where a Schedule 5 liquid, displayed on a low shelf in a retail outlet, was swallowed by a child. This retailer was subsequently 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 see many more Schedule 5 products with CRCs/CRP because sponsors would be seeking to avoid the cost of displaying their product above 1.2 metres.
- A submission by **XXXXXXXX** to the October 2005 NDPSC Meeting supported the move towards national uniformity but questioned why such a regulatory response in some jurisdictions was not necessary in the past. **XXXXXXXX** also noted that the proposal may have significant cost implications to industry associated with "buying" shelving/display space in the region of 1.2 m or greater.
- **XXXXXXXX**, in response to the above submission, noted that:

- all scheduled poisons carry the statement "Keep out of reach of children" and an entry for storage of Schedule 5 and 6 poisons merely articulated the interpretation of what is considered to be out of children's reach.
- QLD, NSW (for Schedule 6 only) and SA have similar existing requirements.
- a uniform approach would assist retailers (particularly with liability concerns should a child manage to access poisons while in their stores).

- Members recalled the following from February 2006 NDPSC Meeting submissions:

  XXXXXXXX:

  - Asserted that the proposal would restrict sale to above 1.2m except if, (amongst others) the containers were fitted with a CRC (in accordance with AS1928). In review of AS1928, there was no indication of how this could be applied to aerosols. **XXXXXXXX** questioned whether any consideration had been given to these products - i.e. are there any exemptions for aerosols?

  XXXXXXXX:

  - Opposed the proposed storage requirements, particularly for Schedule 5 products. **XXXXXXXX** asserted that this would impact on a wide range of aerosols, especially spray paints and pest control products.
  - Advised that CRP was not readily available for aerosol products and was not applicable for those aerosols which used an integrated actuator.
  - Advised that a number of brands of spray paint had their own display racks which are designed to display the full range of colours available. These go to floor level. **XXXXXX** Reiterated the cost of requiring products to be displayed above 1.2 m.
  - Asserted that the reduced likelihood of accidental ingestion from an aerosol had been recognised by authorities for some time and had seen products packed in the aerosol format exempted from the requirements for CRP in many jurisdictions.

  XXXXXXXX:

  - Proposed that, in the interests of uniformity, the current NSW requirements should be adopted nationally.

  XXXXXXXX:

  - Noted that a range of issues and considerations impact upon this item:
    - The nature of products and packaging that would be impacted, including aerosols, trigger packs and associated refills, products packed as a tube in a box, tablets within foil within a box, powders packed in tubs and composite packaged products.
    - Behavioural considerations of an unsupervised child in a retail outlet, anticipated periods unsupervised and circumstances of any incidents that occurred.

- Identification of the instances of failures of current regulatory controls in states such as NSW (Schedule 6, with certain exemptions) compared with, for instance, QLD, where the regulation applies to all schedules.

The Committee also recalled that a Member had advised the February 2006 Meeting that **XXXXXXXX** had indicated that if the requirement became store above 1.2 m or the product would need a CRC, that **XXXXXXXX** intended to require everything to have a CRC. The Committee at that time agreed that having any retailer requiring all Schedule 5 and 6 products to have CRCs contravened the NDPSC's stated public health policy - CRCs should not appear on products unless there was a real need as doing so would diminish the impact of using a CRC.

A new submission was received from **XXXXXXXX** opposing the foreshadowed paragraph, particularly controls on Schedule 5 products. Members noted that **XXXXXXXX**:

- asserted that there was an absence of impact analysis on the costs to industry and consumers and that the case was yet to be proven that changes would deliver a tangible improvement in child safety. Incident data had not been forthcoming to support the perceived risk for Schedule 5 poisons.
- was supportive of taking all reasonable and practical steps that are commensurate with the identified risk.
- voluntarily restricts all Schedule 6 liquids to a shelf height of at least 1.2 metres above floor level. Staff are trained in chemical handling and have a high service intensity that reduces access to products by unsupervised children.
- asserted that the proposal would have the following negative impacts:
  - due to lack of retail space above 1.2 metres they would have to require suppliers to package Schedule 5 and 6 products in CRC's.
  - cost of implementing CRP will be passed onto customers.
  - an inability to display pallet floor stacks containing high volume lines would reduce sales and be anti-competitive to the hardware industry.
- requested that the NDPSC consider that:
  - supermarket retail environments sell small volumes of Schedule 5 and 6 products in comparison to the hardware industry.
  - **XXXXXXXX** has stringent risk assessment procedures in place and has no record of a poisoning incident involving a Schedule 5 product display.
  - once a Schedule 5 or 6 poison is taken off the shelf and placed into a shopping cart it is within reach of a child. Furthermore, when in the household, chances are it will be stored under the laundry or kitchen sink below 1.2 metres. **XXXXXXXX** asserted that the greatest danger was the household environment and not the supervised retail floor.

- it was impractical to fit a CRC on certain products and therefore it was premature to require Schedule 5 and 6 products that could not be fitted with CRC's to meet strict storage heights.
- the NDPSC description of a Schedule 5 product is "low toxicity and will cause only minor adverse effects to human beings". **XXXXXXXX** questioned whether a product described in this way warranted such tight safety controls.

- would consider it reasonable to store all Schedule 6 poisons less than 5L/kg either at a height of at least 1.2 metres above the floor or packaged in a CRC.

A new submission was received from **XXXXXXXX** reiterating its position that, in the interests of uniformity, the current NSW requirements should be adopted nationally. A similar submission was received from **XXXXXXXX** supporting harmonisation of retail storage requirements throughout Australia and advocating the adoption of the current NSW requirements.

The Committee also considered a submission from **XXXXXXXX** asserting that the safe storage of Schedule 5 and 6 products in the retail environment was already adequately served by the current regulations. Members particularly noted:

- That high volume lines are commonly sold in bulk displays or locations below 1.2m. Many retailers would wish to continue this practise and would therefore require that manufacturers supply CRC packaging on these products. It was asserted:
  - that in some cases the introduction of CRC compliant packaging could increase packaging costs by up to 40%.
  - that the potential widespread use of CRC packaging should not be allowed to overwhelm the basic tenant that Schedule 5 and 6 products should be safely stored in the home as per the directions on the label.
- **XXXXXXXX** expressed concern about the practical application of the change, particularly for certain packaging formats. In many circumstances CRCs are either not yet commercially available or physically not feasible.
- **XXXXXXXX** noted that the risk associated with Schedule 5 and 6 products was far higher in the home than in the retail setting, and asserted that the benefit of improved regulation in a retail environment was low. **XXXXXXXX** recommended an alternative approach - working with retailers and other manufacturers to improve consumer awareness about use and storage of products in the home.

XXXXXXXX resubmitted their February 2006 submission requesting that the Committee again consider their views on this issue.

A number of comments were also received from **XXXXXXXX**. The Committee particularly noted that:

XXXXXXXX:

- NSW Regulation forbids labels which implied that a substance was a poison when it was not, but did not forbid any container or storage for a Schedule 5 which might imply that it was Schedule 6. The fact that retailers may impose additional protocols did not affect the legal situation in any jurisdiction, nor affect other retailers' storage choices.
- The use of CRCs for moderately dangerous products did not 'diminish the impact of using a CRC' because the labelling and other container requirements for Schedule 6s signal that they are more dangerous. On the contrary, the Member asserted that many members of the public assume that any product which does NOT have a CRC must be 'safe'.
- The Member also asserted that there have been very few injuries caused by children accessing Schedule 5s in a retail environment and that generally a larger quantity of a Schedule 5 would need to be consumed to cause injury, unlike Schedule 6s where a mouthful may be injurious.
- The Member therefore supported **XXXXXXXX** proposal that the NSW storage controls for Schedule 6 poisons be incorporated into the SUSDP or that the proposed paragraph be restricted to Schedule 6 poisons with an exemption for aerosols.
- Noted that NSW legislation did not adopt the storage controls in the SUSDP, and asserted that **XXXXXXXX** did not intend to impose additional storage requirements for Schedule 5s in the foreseeable future.

XXXXXXXX:

- Victoria currently does not regulate storage of Schedule 5 or Schedule 6 poisons but would automatically adopt the storage controls in the SUSDP.
- Did not support the introduction of a prescriptive storage statement for Schedule 5 and/or 6 poisons. **XXXXXXXX** asserted that safe storage of these poisons in retail premises was addressed by the statement "Keep out of reach of children" and the need for retailers to store products in accordance with this statement.
- **XXXXXXXX** found little evidence that children accessing Schedule 5 or 6 poisons in retail premises was a problem. A **XXXXXXXX** data search revealed a small number of reported exposures in shops, supermarkets and hardware stores over the last 6 years (22 children and 1 adult- out of 250,000 calls). Six (5 children -aged 1, 3, 4, 6 and 13- and 1 adult) sought medical attention.
- **XXXXXXXX** therefore did not see any need to require the introduction of prescriptive regulation for storage of Schedule 5 or 6 poisons at retail premises, noting that, to date, there did not appear to have been an analysis of the benefits or otherwise of the prescriptive legislation that existed in some jurisdictions.
- Over the last 2-3 years **XXXXXXXX** has conducted a review of drugs and poisons regulations and is about to make new regulations. None of the consultation over this time had raised the issue of retail storage of Schedule 5 or 6 poisons.

- It seemed that the main driver for introducing a storage statement was industry's call for national uniformity, rather than evidence that children accessing Schedule 5 or 6 poisons in retail premises was a problem.
- It was likely that the retailing industry itself was best placed to consider the options available for safe and secure storage of these poisons and to come up with guidelines for storage that could be nationally applied.

The Members considered a number of proposals for progressing national storage requirements, including:

- The above **XXXXXXXX** suggestion to rely on compliance with the label statement "Keep out of reach of children", however:
    - it was noted that this could be a quite restrictive regulatory position in that it may preclude other risk mitigating strategies such as CRCs/CRP. A prescriptive storage statement, such as was foreshadowed or those currently used in QLD, NSW or SA, would allow other risk mitigating strategies to be considered.
    - there was also concern about leaving the interpretation of "Keep out of reach of children" to store managers, and questions were raised about such individual's awareness of the issues.
- A Member was supportive of the above outcome based approach, and suggested a requirement to store poisons in a manner to "preclude access by children" rather than "out of reach".
- Another Member advocated wider use of CRC and CRP and saw no problem with industry widely using such packaging. As such the Member advocated the adoption of a storage requirement for both Schedule 5 and 6 products in line with the current SA controls.
- Other Members support an approach based on the current NSW controls i.e. storage controls for Schedule 6 products only. Some Members noted that this would impose little regulatory impact as most Schedule 6 products were already in CRC or CRP. However, several Members argued that such a position would have to be a 'minimum' recommendation as several jurisdictions would not be removing current requirements on Schedule 5 products.
- A Member, following up the **XXXXXXXX** Member's suggestion, proposed that a guide could be developed to assist industry with storage of scheduled poisons. This guide could describe ways to achieve "Keep out of reach of children" or "Preclude access by children" in the retail setting. Members agreed that review of such a document would help in their consideration of whether there was a need for a storage statement in the SUSDP for Schedule 5 and/or 6 poisons. The **XXXXXXXX** Member agreed to develop such a document for the October 2006 NDPSC Meeting.

Members recalled that the February 2006 NDPSC Meeting agreed that there was a need for a nationally consistent position on retail storage requirements for Schedule 5 and 6

products. Members also recalled advice that, should the current situation of different requirements in different jurisdictions continue, some national retailers had indicated that they would apply the most restrictive requirements nationally because of potential litigation and compliance issues. The Committee noted that while national unity was a worthwhile goal this would be difficult to achieve as there was currently a lack of jurisdictional consensus on the issue. Additionally, while some jurisdictions adopt the storage controls recommended in the SUSDP others do not.

[Section deleted**]**

The Committee also noted that there appeared to be no public health disadvantages to deferring consideration of this issue, while adopting a storage requirement that was less than the most restrictive of the current jurisdictional controls could potentially have some public health implications for those jurisdictions which adopt by reference.

OUTCOME

The Committee agreed to defer consideration until the October 2006 NDPSC Meeting to allow time for the development of a draft guidance document on minimising access by children to Schedule 5 and/or 6 products in the retail setting.

2.3 SUSDP, PART 3

No items were considered.

AGRICULTURAL/VETERINARY, INDUSTRIAL AND DOMESTIC CHEMICALS

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

No items were considered.

4. OTHER OUTSTANDING MATTERS FROM PREVIOUS MEETINGS

4.1 LYE WATER

PURPOSE

The Committee considered the foreshadowed decision on lye water from the February 2006 NDPSC Meeting.

BACKGROUND

Lye water can refer to either sodium hydroxide, potassium hydroxide or a mixture of both in aqueous solution. Lye water can also refer to sodium or potassium carbonate solutions. It is used in the traditional manufacture of soap and as a cleaning agent. Lye water is also an ingredient in asian cooking where it is added in small amounts to bind ingredients such as rice.

At the June 2005 NDPSC Meeting **XXXXXXXX** advised that analysis of a cooking condiment marketed as "Lye Water" was undertaken following the hospitalisation of a child with severe burns to the oesophagus and stomach. The product in question was manufactured by **XXXXXXXX** and had been imported into Australia by a number of distributors. As a result of this, discussions were held with **XXXXXXXX** with a view to having this product recalled from the domestic market as quickly as possible. **XXXXXXXX** also advised that it was his understanding that the regulatory areas dealing with food in some other jurisdictions had chosen not to initiate recall action in relation to this product.

The February 2006 NDPSC Meeting considered the scheduling of the various possible alkaline substances in lye water including the packaging requirements for lye water products. The Committee agreed to foreshadow an amendment to Part 1, Paragraph 25(1) so that food additives captured by the alkaline salts entries (i.e. lye water with a pH > 11.5) were to be required to have a child resistant closure (CRC) where the volume was 2.5 litres or less.

DISCUSSION

Members recalled that at the February 2006 NDPSC Meeting the Committee considered a submission from **XXXXXXXX** raising concerns over the safety of lye water. The Committee particularly noted the following:

- Three incidents of poisonings had been reported from ingestion of lye water.
- **XXXXXXXX** had concerns about the packaging of lye water products and the ease with which they could be accessed by infants and children.
- **XXXXXXXX** recommended that the Schedule 5 entry for alkaline salts be amended to ensure the packaging requirements include the compulsory addition of a CRC. It was recommended that this apply to:
    - Containers of 500 mL or less;
    - Where captured by the Schedule 5 alkaline salts entry, part (d) "in liquid or semi-solid preparations the pH of which is more than 11.5";
    - Products sold for use as food additives; and
    - Retail products intended for use in the home.
- The requirement would not need to apply to products for commercial use.

Members recalled that:

- An analysis of the product referred to by **XXXXXXXX** at the June 2005 NDPSC Meeting determined:
    - The product contained 48.8% (w/w) potassium carbonate and 2.5% (w/w) sodium carbonate with a pH of ~14.
    - The combined potassium and sodium carbonate content represented a total alkalinity equivalent to ~47% (w/v) of sodium hydroxide.
    - The labelling included, in small lettering, a "CAUTION", "FIRST AID" and "SAFETY DIRECTIONS". It stated, again in very small lettering, that "This product is NOT a beverage". However, "NUTRITION INFORMATION" was given. The analyst was of the opinion that to display a "NUTRITION INFORMATION" panel on this product was dangerously misleading as to its nature, in spite of its easily-missed disclaimer that it was not a beverage.
- **XXXXXXXX** considered the above product to be an unlabelled, and therefore non-compliant, Schedule 5 product.
- The Committee also considered:
    - A fact sheet on lye water released by the SA Department of Health.
    - A NSW Food Authority Media Release of 21 July 2005 warning that care is required when handling lye water.

- Brief details of a Food Standards Australia New Zealand recall of a lye water product **XXXXXXXX**.

The Committee also recall that the February 2006 NDSPC Meeting had noted:

- Where sodium or potassium hydroxide are part of a lye water formulation the product would be required to be fitted with a CRC, as set out under Part 1 - Paragraph 25(1), regardless of the pH of the product. Additionally, if the pH of the liquid was more than 11.5 it would also be captured by either the Schedule 5 or 6 entries for sodium or potassium hydroxide, depending on concentration.
- Where lye water had been made from alkaline salts such as sodium or potassium carbonate, with no sodium or potassium hydroxide, then it would be captured by the Schedule 5 alkaline salts entry if it had a pH greater than 11.5, with associated labelling requirements. However, there would be no requirement for a CRC.
- The Committee agreed that lye water was a food additive and therefore did not qualify for the Appendix A general exemption for food. Another Member suggested that perhaps manufacturers did not realise that lye water would be captured by either the alkaline salts entry or the sodium or potassium hydroxide entries. The Committee agreed to the Members suggestion to include a cross reference in the SUSDP index linking lye water to the appropriate schedule entries. The Secretariat advised that these cross references were included in the index for the SUSDP 21 consolidation.
- The Members agreed that the intent was not to eliminate the use of lye water, rather, the intent was to minimise any safety risk by having appropriate safeguards in place. The Committee agreed that the first step in controlling the lye water risk was to introduce a mandatory CRC. Members also agreed that the current failure to comply with the Schedule 5 labelling requirements was an enforcement issue. Members generally agreed that further restrictions, such as a Schedule 6 entry, may need to be considered at a future date should the problem fail to resolve.
- **XXXXXXXX** request that the volume limit for mandating CRC's be 500 mL was also considered. A Member advised that this request had been discussed at the recent **XXXXXXXX** meeting where it was noted that, although current lye water products appeared to be in 500 mL bottles, if a larger bottle was brought to market (i.e. 2 L), this could still find use in a domestic setting. Members agreed that a volume limit of 2.5 litres or less was appropriate to minimise risk posed by lye water products to children.

Members were advised that no pre-meeting submissions had been received.

DECISION 2006/47 - 2

The Committee agreed to amend Part 1, Paragraph 25(1) of the SUSDP to require that food additives captured by the alkaline salts entries (i.e. lye water with a pH > 11.5) are to have a child resistant closure where the volume is 2.5 litres or less as these products have the potential to cause harm if inappropriately access by a child.

Part 2 – Labels and Containers

Child-resistant closures – Amendment

Paragraph 25(1) **–** Amend entry by inserting the following table entry relating to alkaline salts:

25. (1) If a poison listed in column 1 of the following table is sold or supplied in a container having a nominal capacity specified for that poison in column 2 it must be closed with a child-resistant closure.

TABLE

Column 1 **Name of the poison**	**Column 2** **Nominal Capacity**
Alkaline salts included in Schedule 5, when packed and labelled as a food additive.	2.5 litres or less

4.2 N-OLEYL-1,3-DIAMINOPROPANE

PURPOSE

The Committee considered the scheduling of N-oleyl-1,3 diaminopropane.

BACKGROUND

Following the publication of the outcome in relation to C-Treat 6, the APVMA raised the issue of apparent inconsistency between a decision in respect to the inclusion of N-tallow alkyl-1,3-propanediamine acetate and tallow alkylamine acetates in Schedule 6 and the decision taken in 2003 not to refer for scheduling, N-oleyl-1,3-diamineopropane and N-coco-1,3-diaminopropane which were similar products and proposed for similar use ie in the treatment of large industrial seawater cooling systems to control deposits, corrosion and marine growths. The decision not to refer N-oleyl-1,3-diamineopropane and N-coco-1,3-diaminopropane for consideration of scheduling was on the basis of the policy excluding industrial biocides from scheduling.

To establish certainty of decision, consistency in approach, and clarity for all stakeholders, the **XXXXXXXX** undertook to have the NDPSC decision in regard to N-tallow alkyl-1,3-propanediamine acetate & tallow alkylamine acetates reconsidered in light of the use-pattern, toxicological profile and agreed industrial biocides policy, and the policy in relation to industrial biocides reflected in the SUSDP by proposing the inclusion of industrial biocides in Appendix A.

XXXXXXXX therefore suggested that the NDPSC may consider it appropriate to include fatty nitrogen derived ether amines as a group (including amines, tallow alkyl, acetates and amines, N-tallow-alkyltrimethylenedi-, acetates) in Schedule 6 of the SUSDP. In making and agreeing to this proposal, **XXXXXXXX** and the NDPSC did not consider the agreed policy on industrial biocides which may have resulted in these substances being exempted from scheduling – if that policy was relevant to the substances under consideration.

Having regard to the difference in approach to the above substances, the Committee considered it appeared that, in considering these matters, stakeholders were not generally aware of the policy in relation to industrial biocides. To avoid similar occurrences, the Committee agreed it would seem appropriate to reflect the policy in the SUSDP by including industrial biocides falling within the scope of the policy in Appendix A.

The Committee also noted that **XXXXXXXX** had suggested that the NDPSC may also wish to consider whether the substances (N-tallow alkyl-1,3-propanediamine acetate, tallow alkylamine acetates, N-oleyl-1,3-diamineopropane and N-coco-1,3-diaminopropane) should be regarded as industrial biocides. On the basis that these products form a protective surface coating, **XXXXXXXX** had noted that "these products are more like anti-fouling paints than they are like cooling tower treatments. They are mainly for biofouling prevention (including mussels, barnacles, chiton and fan worm) and not for Legionella". Label claims for these products include "for the treatment of freshwater cooling systems in hydroelectricity generating power stations to prevent corrosion, biofilm formation and attachment of freshwater organisms", "for the treatment of seawater cooling systems to prevent corrosion, biofilm formation and attachment of seawater organisms" and "for the control of blue mussel, barnacle, chiton and fanworm in seawater cooling systems".

At the February 2006 meeting, the Committee noted public comment from **XXXXXXXX** who made the following observations.

- Industrial biocides currently fall within the definition of an agricultural chemical.
- Industrial biocides are supplied to and used in workplaces (rather than domestic settings).
- The Record of Reasons of Meeting 44 – June 2005 identified the Committees decision to include N-TALLOW ALKYL-1,3-PROPANEDIAMINE DIACETATE and TALLOW ALKYLAMINEACETATES in Schedule 6
- There are certain labelling considerations that may need to be taken into account for products that fall within the province of the Australian Pesticides and Veterinary Medicines Authority (APVMA). **XXXXXXXX** will be having further dialogue with the APVMA prior to the NDPSC meeting.

XXXXXXXX stressed the need for consistency and that it was the view of the NDPSC that any substance considered by the APVMA should also be considered by the NDPSC.

The Committee agreed that the policy in regard to the consideration of biocides had worked well to date, particularly since biocides were a complex and diverse range of products. It was confirmed that the term biocides should be restricted to bacteriocides, algicides and slimicides though it was recognised that some sectors of industry saw 'biocides' as encompassing a much wider range of products. It was not the intention of the NDPSC (or the APVMA) to broaden the definition. The Committee further confirmed that biocides solely for industrial use did not need to come before the Committee although they would be assessed by **XXXXXXXX**.

The Committee agreed to maintain a watching brief in regard to substances for industrial biocide use and also on the appropriateness of the policy underpinning the approach towards the scheduling of industrial biocides.

It was further agreed to include bacteriocides, algicides and slimicides for industrial biocide use in Appendix A thereby clarifying the NDPSC's policy towards the exemption of these substances in this use situation.

The Committee also requested that N-oleyl-1,3-diaminopropane and N-coco-1,3-diaminopropane be considered for scheduling at the Committee's June 2006 meeting.

DISCUSSION

Consideration of the Scheduling of N-oleyl-1,3-diamineopropane and N-coco-1,3-diaminopropane.

In response to the Committee's request that N-oleyl-1,3-diamineopropane and N-coco-1,3-diaminopropane be considered for scheduling at the Committee's June 2006 meeting, **XXXXXXXX** has provided an assessment which noted the following:

N-oleyl-1,3-diaminopropane

N-oleyl-1,3-diaminopropane has an oral LD_{50} of 200-2000 mg/kg bw in rats, will cause corrosive injury to the mouth, throat and stomach if ingested, and is corrosive to the skin, eyes and the mucous membranes. No data was available on the toxicological effects of repeated exposure.

According to the NDPSC Guidelines for Classification of Medicines and Poisons N-oleyl-1,3-diaminopropane fits the toxicological profile of a substance that should be considered for inclusion in Schedule 6, based on acute oral toxicity and the corrosive effects on skin, eyes and respiratory and alimentary tracts.

N-coco-1,3-diaminopropane

N-coco-1,3-diaminopropane has an acute oral LD_{50} of 200-2000 mg/kg bw in rats, an acute dermal LD_{50} in rats of 2000 mg/kg bw and is corrosive to the skin and eyes. It may cause irritation of nose, throat and respiratory tract if inhaled and cause corrosive injury

to the mucous membranes in the throat, oesophagus and stomach if ingested. No data was available on the toxicological effects of repeated exposure.

According to the NDPSC Guidelines for Classification of Medicines and Poisons N-coco-1,3-diaminopropane fits the toxicological profile of a substance that should be considered for inclusion in Schedule 6, based on acute oral toxicity and the corrosive effects on the skin, eyes, and respiratory and alimentary tracts.

XXXXXXXX noted, that while the committee may wish to include N-oleyl-1,3-diaminopropane and N-coco-1,3-diaminopropane in Schedule 6 based on their toxicology, (particularly their corrosive effects on the eyes, skin and mucosa), the committee may also wish to consider these substances to be an industrial biocide covered by the Schedule A entry for algicides, bacteriocides and slimicides for industrial use.

Inclusion in Schedule 6 would also be consistent with the decision to include N-tallow alkyl-1,3-propanediamine acetate and tallow alkylamine acetates in Schedule 6 based on the highly irritating and/or corrosive effects of these substances on the eyes, skin and mucosa.

Post-meeting correspondence in response to the Committee's decision to include Algicides, Bacteriocides or Slimicides for Industrial Use in Appendix A was received from **XXXXXXXX** which provided the following comments:

- **XXXXXXXX** had concerns with the inclusion of 'industrial biocides' in Appendix A as identified in its submission to the February 2006 NDPSC meeting.
- Inclusion in Appendix A means that the SUSDP does not apply to the nominated group of substances/products.
- At its meeting, NDPSC "further agreed to include bacteriocides, algicides and slimicides for industrial use in Appendix A". Whilst this may have been perceived as further defining or reducing the scope of the general term 'biocides' the decision still has significant coverage.
- **XXXXXXXX** noted the NDPSC Purpose Statement of "including industrial biocides, algicides and slimicides in Appendix A to reflect the policy established by the Committee in August 1993 which excludes industrial biocides (except when available in the home) from scheduling."
- **XXXXXXXX** understands that, for other than those products that are clearly identifiable as retail consumer products (household aerosols, domestic swimming pool, domestic garden products etc), most products registered by the APVMA are in fact industrial products in that they are used in workplaces (including on farms, in industry and by employees, contractors, government workers etc).
- **XXXXXXXX** understands, for example, the term 'industrial bacteriocide' to include disinfectants and sanitisers that may be used in a number of industrial/workplace settings (e.g. dairy, poultry, mushroom productions etc - these products are registered by the APVMA and are not 'available in the home' uses). Products such as cooling

tower treatments currently remain within the scope of the APVMAs jurisdiction. Similarly, they wonder whether any products are registered for the control of algae in farm dams or other industrial, non-domestic situations. From a quick search of PubCris, **XXXXXXXX** states that there also seem to be a number of agricultural combination products that may fall within the NDPSC definition (i.e. contain a bactericide or algicide effective active constituent with attendant claims and are used in industrial settings such as farms). There is also the example of a pool chemical that may be specifically packed and labelled for use in public pools and spas. Such products are registered by the APVMA but used in an industrial setting.

- Inclusion of this group of substances/products in Appendix A would create a significant precedent for products that are registered by the APVMA – indeed **XXXXXXXX** was not aware of any APVMA registered product that currently falls outside the jurisdiction of the SUSDP.
- In dialogue with the APVMA they have suggested qualifying wording to provide for inclusion of words in the Appendix A entry to the effect of ALGICIDES, BACTERIOCIDES OR SLIMICIDES for industrial use, except those within the jurisdiction of the Agvet Code Act 1994. Whilst **XXXXXXXX** can understand the rationale for this proposal they wonder whether the argument has come full circle and indeed that no Appendix A entry is required at all.

The Committee noted that **XXXXXXXX** had advised that it has discussed the **XXXXXXXX** proposal and suggested that the Appendix A entry established at the February 2006 meeting be replaced by the wording "ALGICIDES, BACTERIOCIDES OR SLIMICIDES that do not fit the definition of an Agvet chemical product - for industrial use."

Members again discussed the overall appropriateness of including algicides, bacteriocides or slimicides in Appendix A given that inclusion in Appendix A would exempt these biocides from scheduling. It was highlighted, however, that the exclusion of algicides, bacteriocides or slimicides would only be in those situations when they were for industrial use and when their purpose did not fit the definition of an agvet chemical product under the Agvet Code Act. Specific substances could still be included in the schedules. The regulatory arrangements in place would also capture individual substances/products proposed for use in agricultural or domestic use situations.

The **XXXXXXXX** member reiterated that the **XXXXXXXX** did not wish to regulate industrial biocides. The **XXXXXXXX** saw no harm in clarifying the policy towards industrial biocides which would help reinforce possible future legislative proposals as well as keeping in mind the potential overlap between agvet and industrial chemicals. The proposal had limited policy effects and could be best regarded as an exercise in communication.

OUTCOME

The Committee agreed, based upon their highly irritating and corrosive effects on skin, eyes and mucosa, to foreshadow inclusion of N-oleyl-1,3 diaminopropane and N-coco-1,3- diaminopropane in Schedule 6 for consideration at the October 2006 NDPSC Meeting.

FORESHADOWED DECISION (for consideration at the October 2006 Meeting)

Schedule 6 - New entries

N-OLEYL -1,3 - DIAMINOPROPANE.

N-COCO - 1,3 – DIAMINOPROPANE.

DECISION 2006/47 – 3 (Variation of Decision 2006/46-18)

The Committee agreed that, having regard to the post-meeting comments, to vary the February 2006 decision, to include an entry in Appendix A for algicides, bacteriocides or slimicides, as this entry should only apply if the use of the substance does not fit the definition of an agvet chemical product.

Appendix A – New Entry

ALGICIDES, BACTERIOCIDES OR SLIMICIDES for industrial use that do not fit the definition of an agvet chemical product.

4.3 AMINES USED AS CURING AGENTS FOR EPOXY RESINS

PURPOSE

The Committee considered the scheduling of aliphatic and aromatic amines when used as curing agents.

BACKGROUND

At the February 2006 NDPSC meeting, the Committee was advised that the Secretariat had recently received a request concerning the SUSDP approved name for 2,4,6-tri(dimethyl-aminomethyl)phenol, an aromatic amine, when used for curing epoxy resins. 2,4,6-tri(dimethyl-aminomethyl)phenol, when used for curing epoxy resins, was captured by the Schedule 5 general entry for “amines”. A consequence of this scheduling however, was that an approved name for amines when used for curing epoxy resins was “aliphatic amines” as set out under Labels and Containers, sub-clause 7(1)(k)(iii).

The Committee agreed that there were two issues viz a minor labelling clarification involving the approved name for those amines captured already by the Schedule 5 entry,

and the broader issue of the toxicity of aliphatic versus aromatic amines for curing epoxy resins. The Committee agreed to defer consideration of the broader issue until **XXXXXXXX** had undertaken a review of the toxicity of aromatic and aliphatic amines in general. To clarify an inconsistency, the Committee also agreed to amend the entry in the primary pack and immediate containers provisions, subclause 7(1)(k)(iii) to allow either 'aromatic amines' or 'aliphatic amines' to be used as an approved name.

DISCUSSION

The NDPSC received advice from **XXXXXXXX** regarding the chemical nature and toxicity of 2,4,6-tri(dimethylamino) Sphenol and consideration of toxicity data of a number of aliphatic and aromatic amines used as epoxy hardeners as well as several relevant model amines.

XXXXXXXX noted that the term "aromatic amine" was specifically defined as "those in which nitrogen is attached directly to an aromatic ring". Therefore, this term encompassed compounds derived from aniline, such as 4,4'-methylenebisaniline and 4,4'-oxybisaniline. It did not include the aromatic ring-containing compounds where the nitrogen atom was attached to an alkyl group which was then bonded to an aromatic ring, such as benzylamine (aminomethylbenzene) and m-xylenediamine (MXDA; 1,3-di(aminomethyl)benzene). These alpha aminoalkyl benzenes are considered to be aliphatic amines, and the chemical properties are more consistent with simple aliphatic amines such as ethylenediamine. This group includes 2,4,6-tris(dimethyl-aminomethyl)phenol.

XXXXXXXX also noted that several aromatic amines are used as epoxy hardeners, as located by searching chemical inventories for terms such as **XXXXXXXX**. These include 4,4'-methylenebisaniline (MDA), 4,4'-oxybisaniline and 4,4'-sulfonylbisaniline (dapsone), and possibly N-methyl derivatives. It is not clear whether any of these are available to the public. An OECD Screening Information Data Set (SIDS) document for 4,4'-methylenebisaniline, prepared in Europe, indicates that "there is no information about the use of MDA in consumer products, hence consumer exposure seems not to exist". The US High Production Volume (HPV) Challenge test plan for 4,4'-oxybisaniline, indicates that this chemical is only used in industrial processes.

Toxicity of Aliphatic Amines

Acute toxicity

It was noted by **XXXXXXXX** that, as a class, the aliphatic amines are characterised by strong basicity. The alpha aminoalkyl benzenes such as 2,4,6-tris(dimethylaminomethyl)phenol are similar to the simpler aliphatic amines in this respect. Benzylamine is a strong base, with a pKa for the conjugate acid of 9.33, comparable with methylamine (10.66), trimethylamine (9.81) and ammonia (9.25). 2,4,6-tris(dimethylaminomethyl)-phenol has a pH of 11 as a 100 g/L solution at 22°C, indicating that it has a comparable basicity to other aliphatic amines. Due to the high

basicity, the major toxicity issues with these chemicals arise from irritant properties, to the skin, eyes, respiratory tract and gastrointestinal tract. In many cases, toxicity examinations have focussed on these acute effects, particularly as the high irritancy of the parent amine restricts the likelihood of repeat exposure.

With respect to the Schedule 5 description, some major aliphatic amines used in epoxy hardeners, such as diethylenetriamine (DETA) and triethylenetetramine (TETA), do not meet this description. DETA and TETA are classified in the OASCC Hazardous Substances Information System (HSIS) as corrosive (R34) and sensitising (R43), which is more consistent with the requirements of Schedule 6.

Benzylamine, an alpha aminoalkyl benzene, is classified in the HSIS as corrosive (R34). MXDA is also reported to be corrosive to rabbit skin and sensitising to humans.

2,4,6-tris(dimethylaminomethyl)phenol was reported as being corrosive but not sensitising to skin, and the results of acute oral toxicity testing indicated gastric irritation. It is classified in the OASCC HSIS as R36/38 (irritating to skin and eyes) and R22 (Harmful if swallowed).

Repeat Dose Toxicity

The aliphatic amine, ethylenediamine, is reported not to be genotoxic; and the main target organs for subchronic toxicity were the kidney and retina.

DETA and TETA also showed comparatively low repeat dose toxicity when administered in salt form.

Dermal repeat dose studies have been conducted for 2,4,6-tris(dimethylaminomethyl)-phenol, for up to 28 days. Effects were mainly confined to the skin. This compound was also negative in a single Ames Test.

For MXDA, a 3 day inhalation study was insufficient to draw conclusions about the effects of long term repeated exposure.

The problems associated with gastrointestinal irritation during repeat dosing may be overcome by use of salts, but no oral repeat dose studies on alpha aminoalkyl benzenes or their salts were identified. However the quaternised derivative benzyltrimethylammonium chloride has been tested. While toxicity related to the neurological effects of the quaternary ammonium group was seen, specific target organ toxicity was not seen.

Toxicity of Aromatic Amines

Acute toxicity

The aromatic amines as a class were noted to have much lower basicity than the aliphatic amines. The prototypical aromatic amine, aniline, is a weak base with the pKa of the conjugate acid being 4.63, compared with 9-10 for the aliphatic amines. The difference in

basicity has a major effect on the skin irritancy or corrosivity of the amine. Aniline is only mildly irritating to rabbit skin, although a long lasting severe irritation with pannus formation in rabbit eyes is seen. The derivatives, 4,4'-methylenebisaniline and 4,4'-oxybisaniline, are only slightly irritating to eyes and skin.

Repeat Dose Toxicity

The major issue with the aromatic amines relates to effects following repeated exposure. Haemolytic anaemia was observed in rats treated with aniline orally at 7 mg/kg bw/day and genotoxicity has been demonstrated. Aniline is classified as carcinogen category 3 (R40) and danger of serious damage to health by prolonged exposure (R48), as well as for acute toxicity.

4,4'-methylenebisaniline induces liver damage in humans and animals. 4,4'-oxybisaniline, 4,4'-methylenebisaniline and 4,4'-methylenebis(2-methylaniline) are classified by IARC as Group 2B carcinogens with animal evidence of carcinogenicity. The OASCC HSIS classification for 4,4'-methylenebisaniline includes carcinogen category 2 (R45), mutagen category 3 (R63), danger of very serious irreversible effects (R39), danger of serious damage to health by prolonged exposure (R48) and sensitising (R43).

Neither 4,4'-methylenebisaniline nor aniline are classified for irritancy or corrosivity.

XXXXXXXX summarised the situation by saying that the aliphatic group shows major effects due to their high basicity, such as corrosivity, and may be skin sensitisers. Aromatic amines show lower primary irritancy effects, although some have also been reported to be skin sensitisers. The aromatic amines have specific effects by repeat dose, including carcinogenicity, which have not been observed for the aliphatic amines, including alpha aminoalkyl benzenes. There is insufficient information available to fully characterise the repeat dose toxicity of the alpha aminoalkyl benzenes, but the acute effects are likely to limit exposure. Aromatic amines used as epoxy hardeners, with the possible exception of dapsone, do not appear to be available to the public.

XXXXXXXX also noted that it is not known if any aromatic amines are in use as epoxy hardeners in Australia. Internationally they are used in industrial processes in which they are completely consumed. These do not share a class based toxicity with aliphatic amines and may be considered on a case by case basis should any come to the attention of the NDPSC.

XXXXXXXX Proposals to NDPSC

XXXXXXXX proposed that the NDPSC consider:

- listing the chemical 2,4,6-tris(dimethylaminomethyl)phenol as an aliphatic amine, requiring no change to the approved name to cover this chemical.

- listing aliphatic amines as a class in Schedule 6. The severely irritant to corrosive nature of these chemicals does not appear fully consistent with the criteria for Schedule 5

OUTCOME

The Committee noted the advice provided by **XXXXXXXX** but agreed at this stage not to amend the current Schedule 5 entry for amines for use as curing agents for epoxy resins. The Committee further agreed to consider individual substances on a case by case basis should the need arise. In this regard the **XXXXXXXX** offered to look at amines used as curing agents and to advise the Committee if further action in relation to the scheduling of specific amines should be considered.

5. PROPOSED CHANGES/ADDITIONS TO THE STANDARD FOR THE UNIFORM SCHEDULING OF DRUGS AND POISONS.

5.1 SUSDP, PART 4

5.1.1 POTASSIUM AZELOYL DIGLYCINATE, AZELAIC ACID AND THE DEFINITION OF DERIVATIVE

PURPOSE

The Committee considered the scheduling of potassium azeloyl diglycinate (PAD). The Committee also considered the broad issue of defining the term “derivative”.

BACKGROUND

PAD is the potassium salt of a condensation product of azelaic acid and glycine. Currently there is no entry for PAD in any of the Schedules.

The August 1995 NDPSC Meeting agreed to include a new entry for azelaic acid in Schedule 4 following registration approval of a topical preparation containing azelaic acid. Azelaic acid is used by dermatologists as an anti-seborrheic, anti-acne and anti-micotic. Azelaic acid is produced naturally as an oxidation product of oleic acid and secreted by the sebaceous gland onto the skin.

The November 1996 NDPSC Meeting considered a request to reschedule 20% azelaic acid, for the treatment of acne, from Schedule 4 to 3. The Committee agreed, however, that inclusion in Schedule 2 for azelaic acid preparations for dermal use was appropriate in view of its toxicity and its use for an easily diagnosed condition. The February 1997 NDPSC Meeting considered a post-meeting comment asserting that this rescheduling could lead to inappropriate use and lack of counselling when using azelaic acid for acne which may result in a severe skin reaction. The Committee noted the sponsor’s response, including the opportunity for on-going counselling at the pharmacy when repeat

purchasing the product and support materials provided to the pharmacist. The Committee considered that this information addressed the issues raised and that the rescheduling decision remained appropriate.

The June 2005 NDPSC Meeting considered a submission from **XXXXXXXX** requesting that PAD, asserted to be a derivative of azelaic acid, be exempt from the requirements of scheduling when used in cosmetic products at low concentrations. The Committee, noting that the available toxicity data for PAD was deficient, agreed that the current scheduling of azelaic acid remained appropriate.

DISCUSSION

The Committee considered a new **XXXXXXXX** submission, on behalf of **XXXXXXXX**, that again requested that PAD be exempt when used in cosmetic products at low concentrations. This submission included new toxicological data as well as the information considered at the June 2005 NDPSC Meeting.

The Committee recalled the following from its June 2005 consideration:

- **[**Sentence deleted**]**. **XXXXXXXX** asserted that it was unable to retail products in Australia because PAD, as a derivative of azelaic acid, was captured under Schedule 2 by the azelaic acid entry. The Committee noted that **XXXXXXXX** were expected to use PAD at levels of between **XXXXXXXX**.
- The Members were advised that there were four products on the ARTG containing azelaic acid as an anti-acne or anti-bacterial. These products had concentrations of azelaic acid from 15 to 20%. There were no products listed on ARTG using PAD.
- The Committee noted advice from **XXXXXXXX**. Some issues identified were:
    - PAD was not listed on the Australian Inventory of Chemical Substances (AICS). **[**Section deleted**]**
    - The data provided by the applicant was of a limited nature which did not enable a proper **XXXXXXXX** assessment to support a recommendation on scheduling.
- Toxicity data from **XXXXXXXX** indicated that even at 100% concentration PAD was found to be a non-irritant to eyes. A test **[**sentence deleted**]** found no skin irritancy or allergenic reaction.
- The Committee generally agreed that the data as submitted was deficient in a number of areas, particularly noting:
    - No oral toxicity studies; **XXXXXXXX** estimated an oral LD50 ≥ 5000 mg/kg, but this was an extrapolation from other substances.
    - The eye irritancy test did not appear to be an OECD regulated test.
    - The skin sensitization studies had limitations.

- No dermal or inhalation acute studies and no repeat dose, mutagenicity, carcinogenicity, reproductive toxicity or respiratory sensitisation studies.
- There were no photo sensitisation studies and no data on UV effects.

- The Committee generally agreed that from the limited toxicity data PAD could be classified as exempt or Schedule 5 but the data did not provide the level of detail needed to support a definitive decision.

The Committee also noted the following new toxicity data in the submission:

- *In vitro* testing indicated that PAD was not an eye irritant.
- *In vitro* and patch testing indicated that PAD was not a dermal irritant.
- Testing indicating that PAD was not allergenic.
- Testing of 5 rats in a 2000 mg/kg dose indicated that PAD had a GHS category 5 (2000 mg/kg bw > LD_{50} < 5000 mg/kg bw) acute oral toxicity.
- A 5% diluted sample of PAD had a minimal skin sensitisation potential.
- Phototoxicity UV *in vitro* testing indicated that PAD was non-phototoxic and non-photoirritating.

XXXXXXXX asserted that the above new information, along with the previous data considered, demonstrated that products containing PAD for cosmetic use, for the proposed concentrations and use pattern, posed no clinically significant safety issue.

The new **XXXXXXXX** submission was forwarded to **XXXXXXXX** for comment. The Members particularly noted the following from the **XXXXXXXX** response:

- **XXXXXXXX** noted the applicant's assertion that PAD was a derivative of azelaic acid and was of the opinion that the status of PAD as a derivative of azelaic acid required clarification. PAD contained two amino acid glycine molecules compared to azelaic acid, which could be regarded as sufficiently different in structure (and likely characteristics) to disqualify it from being considered a derivative (i.e. not subject to the azelaic acid entry and therefore may require a specific PAD entry in the SUSDP). The Secretariat also advised the Members that numerous cosmetic websites had indicated an industry perception that PAD was an azelaic acid derivative used for its greater solubility in water.
- **XXXXXXXX** advised that it would require the following data to undertake a proper assessment for PAD:
  - Physical and chemical specifications: Given the purity of the chemical is quoted as 30%, additional characterisation of the impurities was required.
  - Acute dermal toxicity (OECD Test Guidelines (TG) 402 or equivalent).
  - Skin irritation (TG 404 or equivalent). Skin sensitisation (TG 406 or equivalent).

- Eye irritation (TG 405 or equivalent).
- Dermal/percutaneous absorption.
- Repeated dose toxicity.
- Mutagenicity/genotoxicity (combined TG 471 and TG 473 or equivalent).

- **XXXXXXXX** noted that the majority of the above toxicological tests involve the use of animals and that there were to date no validated *in vitro* alternative methods capable of replacing these tests. **XXXXXXXX** therefore asserted that all deviations from this required set of data, including omissions, must be explained and scientifically justified. For example, given the toxicity tests submitted have not been formally validated, justification on their relevance and reliability was required.

The **XXXXXXXX** evaluation was forwarded to **XXXXXXXX** for comment. The Members noted the following points from this comment:

- Prior to consideration of the submission **XXXXXXXX** wished for a determination as to whether PAD was a derivative of azelaic acid. If PAD was a derivative, and hence scheduled, **XXXXXXXX** wished to continue with the application. If PAD was not a derivative, and thus not scheduled, **XXXXXXXX** wished to withdraw the application as PAD could be used for cosmetic application and the rules under NICNAS applied. (The Secretariat advised Members that **XXXXXXXX** was informed that any determination as to whether PAD was a derivative of azelaic acid was up to the Committee and could not be determined by the Secretariat prior to NDPSC consideration. **XXXXXXXX** therefore agreed not to withdraw the application.)
- That there was insufficient time to provide the toxicological and chemical data required in the **XXXXXXXX** comment.
- **XXXXXXXX** also asserted that industry appeared to be confused as what was meant in Part 1, Paragraph (2)(c) a substance in a schedule or appendix includes “every salt, active principle or derivative of the substance including esters and ethers, and every salt of such active principle or derivative”.

The Committee noted that the data indicated a low toxicological profile for PAD and agreed that PAD was most likely to be either unscheduled or Schedule 5 based on this information. However, concerns remained over the acceptability of the test methods employed to generate the toxicological information. The Members generally agreed, therefore, to defer consideration to allow additional evaluation of the submission in light of the Committee’s test method concern.

The Members also considered the question of derivative raised by the **XXXXXXXX** submission. The Committee noted that there was currently no definition of derivative in the SUSDP but generally agreed that in this instance it was appropriate to consider PAD as a separate substance as it had different biological properties and a different use to azelaic acid. However, Members remained concerned by the lack of clarity about what

was meant by the reference to derivative in Part 1, Paragraph (2)(c). The Committee noted the following:

- Several Members felt that there was a need for an SUSDP definition of derivative.
- A strict chemical definition of derivative could potential capture a vast number of compounds which may, in many cases, result in an inappropriate level of scheduling. A suggested solution was to specify a limit on the complexity of the chemistry required to get from the parent to the derivative for the substance to still be considered a derivative. Members generally agreed that it would be difficult to craft a workable complexity limit and that this may require broad stakeholder input.
- A Member noted that perhaps a definition of derivative could be based on, or include a rider of, "similar characteristics in use". Alternatively, the definition could be based around "mechanism of action". A Member noted, however, that currently esters and ethers were specifically included and that these often had dissimilar characteristics in use, or mechanisms of action, to that of the parent compound.
- An alternative approach was a suggestion that reference to derivative be removed from Part 1, Paragraph (2)(c) i.e. "every salt or active principle of the substance, including esters and ethers, and every salt of such an active principle". This left the issue of minor chemical tinkering of substances to avoid scheduling (for example, alternative halogenation for some compounds) despite these substances having a strong risk of similar toxicological effects etc to that of the scheduled substance.
- Following on from the above suggestion to remove reference to "derivative", a Member proposed that a pragmatic approach to the issue would be to consider all substances brought to the Committee as individual substances and as such, if scheduling were warranted, move to capture these through specific entries. No ready solution was proposed to deal with those substances which had previously not had specific entries because they were deemed to be captured as derivatives, or on how to apply group entries if derivatives were not to be captured.

The Committee generally agreed that consideration of the above issues should be deferred to the October 2006 NDPSC Meeting to allow time for Members to further consider the problem and to allow stakeholders to highlight additional concerns or issues they have with the application of "derivative" in the SUSDP.

OUTCOME

The Committee agreed to defer consideration of the scheduling of potassium azeloyl diglycinate to allow time for an additional evaluation of toxicological data and the testing methods used. The Committee further agreed to foreshadow consideration of the usage of "derivative" in the SUSDP, including the possibility of including a definition.

5.1.2 EYELASH AND EYEBROW TINTS (PHENYLENEDIAMINES AND TOLUENEDIAMINE)

PURPOSE

The Committee considered the scheduling of phenylenediamines and toluenediamines used in eyelash/brow tints.

BACKGROUND

The February and June 2004 NDPSC Meetings considered the outcomes of investigations into incorrectly packed and labelled eyelash/brow tints containing phenylenediamines/toluenediamine. The October 2004 NDPSC Meeting subsequently noted outcomes of a **XXXXXXXX** review of chemicals in hair dyes and a report on skin and eye irritancy for phenylenediamines/toluenediamine and agreed to foreshadow an amendment to the Appendix C entry for phenylenediamines to include a prohibition on use for eyelash/brow tinting. The Committee also agreed to foreshadow the inclusion of a new Appendix C entry for toluenediamine to prohibit use in eyelash/brow tinting.

The February 2005 NDPSC Meeting agreed to foreshadow two options; (1) an amendment to the Schedule 6 entries to allow the use of appropriately labelled eyelash/brow tints in salons only; and (2) a similar amendment to allow home use of such products. The Committee also foreshadowed inclusion in Appendix C of any other phenylenediamine/toluenediamine eyelash/brow tint not covered by the Schedule 6 entry.

The June 2005 NDPSC Meeting considered the foreshadowed options. The Members noted that while phenylenediamines and toluenediamines were only moderately irritant to the skin and are not corrosive to the eye, they were clearly sensitisers. The Committee concluded, however, that the potential risk of causing a strong allergic response in a small number of individuals could be minimised through appropriate labelling. The Committee therefore agreed to:

- amend the Schedule 6 entries for phenylenediamines/toluenediamine to allow the use of eyelash/brow tints in salons and the home when appropriately labelled; and
- include in Appendix C any other phenylenediamines/toluenediamine eyelash/brow tints which would not be covered by the Schedule 6 entry.

DISCUSSION

The Committee was advised that several submissions were received regarding the following issues for phenylenediamines/toluenediamines in eyelash/brow tints:

- Mandatory label requirements for small containers;
- A question of whether salon only use was an industrial use; and
- First Aid Instructions, warning statements and Safety Directions.

In considering these issues the Committee recalled the following from the June 2005 NDPSC Meeting:

- The proposed warning statement included "..a preliminary test according to the accompanying directions..". While the Committee agreed that the wording compelled products to have directions for use, a Member enquired as to how the Committee could be satisfied as to quality of these directions. The Committee was advised that the "accompanying directions" requirement was modelled on what currently applied to hair dyes containing phenylenediamines/toluenediamine. No particular issues had arisen relating to the quality of these directions and industry appeared to be reliably self regulating. The Committee also agreed that while there was no regulator for these products, the quality of the "accompanying directions" would be a jurisdictional matter, subject to Common Law and fair trading and consumer affairs regulations.
- A Member enquired about whether there was a need to consider concentration cut-offs in the schedule entries. Members noted that eyebrow/lash tints contained significantly lower concentrations of phenylenediamines/toluenediamine than hair dye products and agreed that concentration wasn't currently an issue, particularly as the main safety concern was allergenicity.
- The Committee agreed that the labelling in the foreshadowed amendments which allowed the use of eyebrow/lash tints in salons and the home would be of sufficient strength to reduce the potential harm consistent with Schedule 6 requirements. However, the Committee had some residual concerns about eyebrow/lash tints containing phenylenediamines/toluenediamine and agreed that this would need to be watched in the future.

Mandatory label requirements for small containers

The Committee considered a submission from **XXXXXXXX** requesting a partial exemption from labelling requirements for the immediate container of small volume (≤15 mL) eyebrow/lash tints. The submission proposed an amendment to Part 2, Labels and Containers, clause 26 by adding the following:

> 'for retail packs of 15 g/mL or less (for eye tint and eyelash schedule 6 products), all SUSDP requirements are exempt on the container only, except for the signal heading, keep away from children and please read carton/leaflet carefully prior to use. These statements are to be retained.'

A Member noted that there appeared to be some confusion on behalf of industry as the exemptions under clause 26 related to indelible or embossed statements on the immediate container i.e. POISON. The Committee agreed that the submission was actually requesting an exemption from applying the Appendix E and F statements, and the statement required by the Schedule 6 entry.

The Committee noted the following from the **XXXXXXXX** submission:

- **XXXXXXXX** had no concerns with informing consumers through use of the mandatory labelling except that for small packages (i.e. 5 - 15 mL) it was impossible to comply, due to lack of labelling copy space. Even though there were exemptions in the SUSDP for small pack sizes, these were not sufficient to satisfy the space limitations.
- **XXXXXXXX** asserted that the above proposal provided a solution to labelling products in small containers without affecting safety for the consumer. The proposal would replace the mandatory labelling requirements with the above three statements for the immediate containers of small products (≤15 mL) containing Schedule 6 substances for eyelash/brow tinting. The labelling on the outer carton would continue to meet all the labelling requirements so the user would still receive all the necessary warnings and safety would not be compromised.
- For a 5 mL tube the size of the printing area was ~40mm by 35mm. **XXXXXXXX** asserted that it was impossible to fit the labelling in this space because if the requirements were fulfilled the print height would be so small as to not be legible.
- The applicant did not believe that there would be any toxicity or safety risks nor any difference in the extent and pattern of use, should less labelling be allowed.

The Secretariat advised that it requested a comment from **XXXXXXXX** on the **XXXXXXXX** submission. Members noted the following from **XXXXXXXX** comment:

- **XXXXXXXX**, in its report to the June 2005 NDPSC Meeting, had recommended a prohibition on the use of phenylenediamines/toluenediamine in eyelash/brow tints based on the toxicity of the chemicals. The Committee, however, did not accept this recommendation and decided to allow the use of phenylenediamines/toluenediamines in eyelash/brow tints on the basis that proper labelling would mitigate the risk.
- The **XXXXXXXX** submission stated that "consumers are generally aware of the natures of these products as it relates to their safety". No data was provided to support this and it appeared contrary to the view formed at the June 2005 NDPSC Meeting.
- No data was presented on the actual sizes of the products. **XXXXXXXX** assumed that both 5 and 15 mL sizes are marketed and it is unknown whether the tubes are single or multi use. **XXXXXXXX** agreed that the available space on a 5 mL tube was inadequate to fully comply with the SUSDP requirements. No data was given on the printing area dimensions for the 15 mL tube but if it is assumed it is 3 times the 5 mL tube area, in both dimensions, then the space would be ~120 mm by 105 mm. This space seemed adequate to fit all the requirements. **XXXXXXXX** presented no evidence that it could not meet the current requirements for the 15 mL packs.
- **XXXXXXXX** also noted that the applicant's suggested amendment was not restricted to eyelash/brow tints containing phenylenediamines/toluenediamine but would allow the exemption for all eyelash/brow tints containing Schedule 6 ingredients.

- **XXXXXXXX** was concerned about the carton and package insert being separated from the immediate container (if a full set of labels was not included on the immediate container). For a single use tube this may not be an issue but for a multiple use tube such separation would mean that the warnings and safety directions may not be available for later uses.

The Committee recalled that it allowed eyebrow/lash tints containing phenylenediamines/toluenediamine in Schedule 6 because the labelling would be of sufficient strength to reduce the potential harm consistent with Schedule 6 requirements. The Committee also noted that it was possible for all the required warning statements to be fitted on the immediate container for small volume products, noting precedence in the market of some eye drop products that employed fold out labels to address space issues. The Members also agreed that the request to remove warning statements from immediate containers, for small volumes, with a view to relying on the outer packaging undermined the intention of the Committee in only allow these products where the warnings were fully conveyed to the user, particular as there was a concern about separation of the product from the outer packaging. Additionally, the end point of concern, sensitisation, was not dose dependent.

The Members therefore agreed that all mandated labelling should continue to be applied to eyebrow/lash tints containing phenylenediamines/toluenediamine.

Industrial use

The Committee considered an email **XXXXXXXX** advising **XXXXXXXX** of labelling requirements for eyelash/brow tints containing phenylenediamines/toluenediamine. Members also considered a second email **XXXXXXXX**, in part addressing whether salon use was an industrial use. The following points were noted:

- **XXXXXXXX** had discussed labelling issues with **XXXXXXXX** for a tinting product for national distribution to beauty salons for use by professionals only.
- During that discussion it was noted that application of Part 2, Labels and Containers, Paragraph 13, exempted poisons packed and sold solely for dispensary, industrial, laboratory or manufacturing purposes from the SUSDP's labelling requirements if they were labelled in accordance with the NOHSC's (now called the Australian Safety and Compensation Council - ASCC) code of practice. The issue under consideration was whether professional use in beauty salons was industrial use.
- The email noted that the OED defined "industrial" as "of industry or industries" and "industry" as "..habitual employment in useful work; branch of trade or manufacture". It appeared, therefore, that there was already an exemption from the SUSDP's labelling requirements for these products if the ASCC's requirements were met.

Members noted that the main warning label for these products was stipulated in Schedule 6 as a reverse schedule entry. The Committee agreed that this statement was both a labelling requirement and a scheduling condition. The parent entry for eyebrow/lash tints

containing phenylenediamines/toluenediamine was Appendix C and it was only where the scheduling condition was met (i.e. presence of the Schedule 6 warning statement) that the product became Schedule 6. The Committee confirmed that this would apply whether the use was domestic or industrial. However, the additional statements in Appendix E and F would not apply for industrial use if the ASCC's requirements were met.

A number of Members were concerned that ASCC labelling was focused on worker safety and that there was a potential health and safety gap if the general public were being exposed to a substance in an industrial setting. Members also recalled that labelling, including Appendix E and F labelling, was previously held up as a means of addressing the problem of apparently poor and conflicting training material for the beauty industry for use of these products. Some Members felt that the current SUSDP label, including Appendix E and F statements, may provide direction to the operator who would then be responsible for protecting the consumer health.

Other Members noted that beauty salons are workplaces and therefore there was a requirement to have material safety data sheets (MSDS) for all products in use. Additionally, the point was made that the consumer would not normally be given access to the packaging or labels in a salon use situation (as distinct from products available for retail sale through a salon, which Members agreed would not be an industrial use). A Member asserted that the real issue was about the standard of education and training materials for the beauty salon industry.

The Committee questioned where in the ASCC framework (set up to protect the worker) would there be instructions to a beauty salon worker to inform the public health risk to the consumer before they applied the product. The **XXXXXXXX** Member agreed to direct **XXXXXXXX** to refer the issue of industrial "salon" usage of toluenediamine/ phenylenediamines in eyebrow/lash tints to ASCC, drawing particular attention to the issue of capturing consumer safety in a framework set up to protect the worker.

The **XXXXXXXX** Member noted that currently a consolidated booklet of MSDS's was being prepared for the beauty industry on hair dyes and agreed, on behalf of the Committee, to investigate the warnings and concerns conveyed. Another Member noted that workers in the beauty industry had a responsibility to get informed about the safety of the products they were applying to the general public.

First Aid Instructions, warning statements and Safety Directions.

The Secretariat received an enquiry from **XXXXXXXX** seeking clarification of the first aid instructions required for eyebrow/lash tints containing phenylenediamines/ toluenediamine. Members noted:

- The entry for phenylenediamines in Schedule 6 had several components - hair dye, photographic, water testing and eyebrow/lash tints. **XXXXXXXX** suggested, and **XXXXXXXX** confirmed, that this meant that hair dye and eyebrow/lash tinting are separate uses and/or preparations.

- In Appendix E and F there were also two entries; one related to hair dyes and the other "in preparations other than hair dyes". The June 2005 Meeting had confirmed that eyebrow/lash tints were captured by “other preparations”, not “hair dyes”.
- **XXXXXXXX** noted that the first aid instructions for “other preparations” included S1 “If skin or hair contact occurs, remove contaminated clothing and flush skin and hair with running water”. **XXXXXXXX** asserted that as the purpose of the tints was to dye eyelashes/brows it was impossible to avoid contact with hair. Furthermore, **XXXXXXXX** asserted that it was unlikely that removal of contaminated clothing was appropriate for the eyelash/brow tints as only a small portion was used. **XXXXXXXX** also noted that manufacturers could not 'substitute' the statement for hair dyes as this specifically mentioned not to "use this product for dyeing eyelash or eyebrows; to do so may be injurious to the eye".
- Although **XXXXXXXX** agreed that certain warnings were required to ensure the safe use of the product, **XXXXXXXX** believed that the removal of "hair contact " and "contaminated clothing" was appropriate. **XXXXXXXX** proposed the following first aid instruction:
    - “If product gets into eyes wash out immediately with water for at least 15 minutes. If skin contact occurs remove contaminated clothing and wash skin thoroughly with water. If swallowed do NOT induce vomiting. For advice, contact Poisons Information Centre (AUSTRALIA Ph 13 1126; NEW ZEALAND Ph 0800 764 766) or a doctor at once as urgent hospital treatment likely to be needed”.

The Committee also noted that the second email **XXXXXXXX** asserted that First aid instructions G1 and G3, and Safety Direction 8 relating to inhalation should not apply to these products.

Members noted that the actual wording of Safety Directions and First Aid Instructions in Appendix E and F were not stipulations, they were guidance statements to aid in standardisation. The Committee agreed that there was no need to include new categories in Appendix E and F to account for all variations resulting from different formulations and that the introduction to both appendices gave enough flexibility and scope for **XXXXXXXX** to make the requested changes. The Committee confirmed that:

- It was the responsibility of the manufacturer, packer and supplier to ensure that the user was given sufficient information to be able to use it correctly and safely.
- Scheduled substances must be labelled with appropriate warning statements and/or safety directions. The selection of warning statements and safety directions will depend on the formulation and use of the product. Appendix E and F were prepared as guides for this purpose.
- The wording of statements specified in Appendix E or F may be varied provided that the intent was not changed. Additional statements may also be added to ensure that

the user of a product was sufficiently advised of its harmful nature and how to avoid any deleterious effects.

OUTCOME

The Committee agreed that:

- as the main risk was sensitisation, which in this case did not demonstrate a clear dose response, strong label warnings were required before such products could be available as Schedule 6; and
- as there was a risk of separation of an outer pack from the immediate container, it was appropriate that all mandatory labelling continued to be applied to the immediate container, regardless of pack size.

The Committee also

- noted that the warning statement for these products stipulated in the Schedule 6 entry was both a labelling requirement and scheduling condition; and
- confirmed that this statement would need to be applied, whether the use was domestic or industrial, or the product default to Appendix C. However, the additional statements in Appendix E and F would not be required for industrial use if the product were labelled in accordance with the ASCC's code of practice.
- further confirmed that the introduction to both Appendix E and F provided sufficient flexibility to allow for variation of product use and formulation.

5.2 SUSDP, PART 5

5.2.1 [ITEM DELETED]

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

6.1 CYDIA POMONELLA GRANULOSIS VIRUS

PURPOSE

The Committee considered the scheduling of *Cydia pomonella* Granulosis virus.

BACKGROUND

[Section deleted**]**

DECISION 2006/47 - 4

The Committee agreed that, due to its low toxicity, *Cydia pomonella* Granulosis Virus be included in Appendix B of the SUSDP. The Committee further agreed to broaden the existing Appendix B entry for Baculovirus *Cydia pomonella* (Codling Moth Granulosis Virus) so that all *Cydia pomonella* viruses, including for insecticide uses other than for the control of codling moth, would be captured by the entry. In this regard, the Committee noted that any insecticide use of *Cydia pomonella* would still be the subject of assessment and approval by the APVMA, including consideration by the Office of Chemical Safety.

APPENDIX B – Amendment

BACULOVIRUS CYDIA POMONELLA (Codling Moth Granulosis Virus) - Amend entry to read:

SUBSTANCE	DATE OF ENTRY	REASON FOR LISTING	AREA OF USE
BACULOVIRUS CYDIA POMONELLA	June 2006	a	1.2

6.2 SULFURYL FLUORIDE

PURPOSE

The Committee considered the scheduling of sulfuryl fluoride.

BACKGROUND

[Section Deleted**]**

DISCUSSION

[Section deleted**]**

Based on a consideration of its toxicological profile, **XXXXXXXX** suggested that the NDPSC may consider sulfuryl fluoride appropriate for inclusion in Schedule 6 of the SUSDP.

The Committee also noted that Schedule 6 of the SUSDP includes the parent entry for fluorides. The Committee confirmed that sulfuryl fluoride would be within the scope of this entry. Given the nature of sulfuryl fluoride and its use (an agricultural fumigant with potential OH&S implications), the Committee considered that it may be more appropriate to include a specific entry for sulfuryl fluoride in Schedule 6.

A member noted that the health hazards associated with sulfuryl fluoride included respiratory injury, including changes in the lungs following repeated exposure and possible CNS effects. The toxicity of sulfuryl fluoride was distinct from fluoride ion poisoning and therefore the member considered that it was appropriate to include a specific scheduling entry for sulfuryl fluoride. The member considered Schedule 6 was appropriate on toxicological grounds.

The **XXXXXXXX** representative confirmed that the draft product label showed sulfuryl fluoride was intended for professional use. **[**Section deleted**]**

Members were generally of the view that fumigation products based on sulfuryl fluoride should be limited to professional use, though also noting that sulfuryl fluoride had a good safety record over 40 years of use.

The **XXXXXXXX** member noted that sulfuryl fluoride had possible use as a replacement to methyl bromide. Another member noted that in respect to the application before the Committee, the proposed packaging was large compressed gas cylinders. This suggested that non-professional use was not being considered at this stage.

The **XXXXXXXX** representative noted that, having regard to the concerns of the Committee in regard to possible non-professional use, the Agvet Code had provisions that could make sulfuryl fluoride a Restricted Chemical Product.

DECISION 2006/47 - 5

The Committee confirmed that the toxicity of sulfuryl fluoride was consistent with a Schedule 6 poison but agreed that additional controls to ensure only professional use were required. The **XXXXXXXX** proposal to include sulfuryl fluoride as a Restricted Chemical Product was agreed by the Committee as being essential.

The Committee agreed that, based upon its moderate acute toxicity, low to moderate inhalation toxicity, and intended APVMA classification as a Restricted Chemical Product, sulfuryl fluoride be specifically included in Schedule 6 of the SUSDP.

Schedule 6 - New entry

SULFURYL FLUORIDE

6.3 PROSULFOCARB

PURPOSE

The Committee considered the scheduling of prosulfocarb.

BACKGROUND

[Section deleted**]**

DISCUSSION

[Section deleted**]**

A Committee member noted that as the application was for approval of an active ingredient but, as that there were some aspects of the toxicological conclusions which may have a bearing on the scheduling of product(s) based upon prosulfocarb as the active ingredient, it would be desirable that no cut-off value be considered until such time as an application for the scheduling of a product was before the Committee.

DECISION 2006/47 - 6

The Committee agreed to include prosulfocarb in Schedule 6 of the SUSDP.

Schedule 6 - New entry

PROSULFOCARB.

6.4 TRENBOLONE ACETATE/OESTRADIOL/TYLOSIN TARTRATE

PURPOSE

The Committee considered the scheduling of tylosin for infection control when included in a growth and finishing implant for steers and heifers.

BACKGROUND

[Section deleted**]**

DISCUSSION

The Committee noted that consideration of this scheduling proposal may need to await completion of the tylosin review by the APVMA and advice from Expert Advisory Group on Antimicrobial Resistance (EAGAR) which is to be sought by the APVMA. The NDPSC recalled the Joint Expert Technical Advisory Committee on Antibiotic Resistance Recommendation 6 “That all antibiotics for use in humans and animals (including fish) be classified as S4 (prescription only)”.

[Section deleted**]**

APVMA discussed the proposed scheduling of the tylosin implant and referred to the ongoing assessment. The APVMA also noted that the application had not yet been assessed by EAGAR.

The Committee agreed that this recent advice from the APVMA further suggested that the NDPSC should defer consideration of the scheduling of tylosin for infection control when included in a growth and finishing implant for steers and heifers until the APVMA assessment has been completed and related matters that might arise from that assessment had been resolved.

OUTCOME

The Committee agreed to defer further consideration of tylosin for inclusion in implant preparations for infection control until the APVMA had completed its assessment of tylosin and the views of EAGAR had been sought by the APVMA.

6.5 ACETYL ISOVALERYLTYLOSIN TARTRATE

PURPOSE

The Committee considered the scheduling of acetyl isovaleryltylosin tartrate.

BACKGROUND

[Section deleted**]**

The OCS advised that at this stage only the parent compound is to be scheduled. No cut-off values are proposed at this time to accommodate the inclusion of acetyl isovaleryltylosin tartrate in end-use products.

The APVMA confirmed that the macrolide review covers only products containing tylosin, kitasamycin and oleandomycin with growth promotant uses or where the administration duration and dose level are the same, or very similar to those for the purposes of growth promotion (in accordance with recommendations 1 and 2 of the JETACAR Report). The APVMA also noted that **[**sentence deleted**]**.

The APVMA has also advised that they have sought the views of EAGAR on this substance but were yet to receive a response.

DISCUSSION

[Section deleted**]**

Based on its intended use and the need for professional veterinary advice and management, the **XXXXXXXX** suggested that the Committee might wish to consider it

appropriate to include acetyl isovaleryltylosin tartrate in Schedule 4 of the SUSDP with no cut-off to Schedule 5.

The **XXXXXXXX** representative and expert reviewer confirmed the need and desirability of veterinary supervision in relation to the use of this substance. Label use instructions would specifically note that the product was not for prophylactic use.

DECISION 2006/47 - 7

Having regard to the need for veterinary supervision, the Committee agreed to include acetyl isovaleryltylosin in Schedule 4 of the SUSDP.

Schedule 4 – New Entry

ACETYL ISOVALERYLTYLOSIN

6.6 ACETAMIPRID

PURPOSE

The Committee considered the scheduling of acetamiprid.

BACKGROUND

At its June 2002 meeting of the NDPSC, the Committee received data in support of TGAC approval for acetamiprid and the registration of a new product **XXXXXXXX**. At that time, acetamiprid was a new systemic insecticide and **[**sentence deleted**]**. It was noted that acetamiprid was related to imidacloprid which was included in Schedules 5 and 6, thiacloprid which was included in Schedule 6 and nitenpyram which had both a Schedule 6 and exempt status.

[Section deleted**]**

DISCUSSION

[Section deleted**]**

Based on the low toxicity of acetamiprid at the concentration used in **XXXXXXXX**, **XXXXXXXX** suggested that the Committee consider that acetamiprid be exempted from poisons scheduling at a concentration of 10 g/L (1%).

DECISION 2006/47 – 8

The Committee agreed that, based on low toxicity, acetamiprid in preparations of one percent or less of acetamiprid be exempt from scheduling.

Schedule 6 – Amendment

ACETAMIPRID **except** in preparations containing 1 per cent or less of acetamiprid.

6.7 METFLUMAZONE/AMITRAZ

PURPOSE

The Committee considered the scheduling of metaflumizone.

BACKGROUND

This item was listed for discussion and included in the pre-meeting Gazette Notice. However, in the interim, the item was withdrawn.

OUTCOME

As there was no information for the Committee to consider, the Committee agreed to defer consideration of the scheduling of metflumazone until such time as information was presented that would allow the NDPSC to make a scheduling decision.

6.8 TULATHROMYCIN

PURPOSE

The Committee considered the scheduling of tulathromycin.

BACKGROUND

[Section deleted**]**

Tulathromycin is a semi-synthetic macrolide antimicrobial. Tulathromycin and other macrolide antibiotics (eg erythromycin, clarithromycin) inhibit bacterial protein synthesis resulting in bacterial death. The registrant has submitted studies to support the establishment of an ADI, ARfD and scheduling.

DISCUSSION

[Section deleted**]**

Based on the low acute toxicity of tulathromycin and its intended use as a therapeutic agent requiring professional veterinary advice and management, the **XXXXXXXX** suggested that the NDPSC consider including tulathromycin in Schedule 4 of the SUSDP with no cut-off to schedule 5.

[Section deleted**]**

The **XXXXXXXX** representative noted that because of the importance of macrolide antibiotics in human and animal health, tulathromycin had been referred to EAGAR **[**Section deleted**]**.

DECISION 2006/47 - 9

The Committee agreed that tulathromycin be included in Schedule 4 of the SUSDP having regard to its low acute toxicity and its intended use as a therapeutic agent under the supervision of a veterinarian.

Schedule 4 – New Entry

TULATHROMYCIN

6.9 INDOXACARB

PURPOSE

The Committee considered the scheduling of indoxacarb.

BACKGROUND

[Section deleted**]**

Indoxacarb is an oxadiazone insecticide for use in the control of insect pests and is currently included in Schedule 6 of the SUSDP.

DISCUSSION

The Committee noted that the ISO approved name “indoxacarb” applies only to the insecticidally active S-enantiomer, which is also known as DPX-KN128. The R-enantiomer, DPX-KN127, while not insecticidally active, has mammalian toxicity like the S-enantiomer. The R- and S- enantiomers can be regarded as approximately equivalent in terms of mammalian toxicity.

[Section deleted**]**

The **XXXXXXXX** suggested that the NDPSC should consider a cut-off at 1% to Schedule 5 for this product, with a requirement that the syringe presentation include a child-resistant closure.

It was also noted, that in 2000 when the NDPSC first considered the active indoxacarb it was not readily appreciated that the name "indoxacarb" which had been approved by the International Organization for Standardization (ISO) referred only to the insecticidally active S-enantiomer and not the racemic mixture. Unfortunately the term 'indoxacarb' is now frequently used when referring to mixtures containing differing proportions of the R and S enantiomers.

The toxicology database which supported approval of the active was composed of studies in which the test animals were dosed with an indoxacarb mixture in which the ratio of R to S enantiomers was either 50:50 or 25:75. A number of 'bridging' studies in test animals were provided to demonstrate that any difference in toxicological endpoints or sensitivity between the two enantiomer mixtures was unlikely to be great.

The current application before the NDPSC sought a cut-off for indoxacarb **[**section deleted**]**.

The Committee specifically considered the proposed child resistant packaging which was necessary because the product was packed in corn syrup which could be attractive to children. The **XXXXXXXX** representative advised that they intended to give close attention to the packaging as part of the registration process. At present it was considered by the **XXXXXXXX** that the proposed child resistant packaging did not conform to the Australian Standard.

DECISION 2006/47 - 10

The Committee agreed to amend the entry for indoxacarb to reflect that it is a mixture of the R and S enantiomers.

The Committee further agreed to include indoxacarb in Schedule 5 of the SUSDP when included in preparations containing 1 per cent or less of indoxacarb and when packed in child resistant packaging.

Schedule 6 - Amendment

INDOXACARB (Includes the R and S enantiomers) **except** when included in Schedule 5.

Schedule 5 – New Entry

INDOXACARB (Includes the R and S enantiomers) in preparations containing 1 per cent or less of indoxacarb when packed in child-resistant packaging.

6.10 SULFENTRAZONE

PURPOSE

The Committee considered the scheduling of sulfentrazone.

BACKGROUND

[Section deleted**]**

DECISION 2006/47 - 11

The Committee agreed to include Sulfentrazone in Schedule 7 of the SUSDP having regard to its toxicity and, in particular, its developmental and reproductive toxicity.

Schedule 7 - New entry

SULFENTRAZONE.

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

No items were considered.

8. OTHER MATTERS FOR CONSIDERATION

8.1 PAINT FOR CHILDREN'S PLAY EQUIPMENT AND THE DEFINITION OF TOY

PURPOSE

The Committee considered whether children's play equipment was captured by the SUSDP definition of "toy".

BACKGROUND

The SUSDP definition of "toy" under Part 1, Interpretation, is:

"Toy" means an object or number of objects manufactured, designed, labelled or marketed as a plaything for a child or children up to the age of fourteen years.

The SUSDP currently applies certain restrictions to paint for children's toys, including the following entry in Appendix I, Uniform Paint Standard:

4. A person must not manufacture, sell, supply or use a paint for application to toys unless the paint complies with the specification for coating materials contained in Part 3 of Australian Standard 1647 for Childrens Toys (Safety Requirements).

DISCUSSION

XXXXXXXX advised the Meeting of an issue with a particular swing set for children, the paint for which contained lead at a level in excess of the specification for coating materials contained in Part 3 of Australian Standard 1647 for Childrens Toys (Safety Requirements). However, the Member advised that there was some dispute with the company in question as they contended that children's play equipment was not a toy.

The Members noted the current definition in the SUSDP for "toy" and agreed that children's play equipment was captured by this definition. It was further agreed that the definition remained appropriate and there was no need to add an addition reference to children's play equipment such as swing sets.

OUTCOME

The Committee agreed that children's play equipment was captured by the current SUSDP definition for toy and hence Paragraph 4 of Appendix I (Uniform Paint Standard) applied to any paint for use on children's play equipment.

9. INFORMATION ITEMS (AG/VET, INDUSTRIAL & DOMESTIC CHEMICALS)

9.1 NAPHTHALENE

PURPOSE

The Committee considered a report of haemolytic anaemia in a child exposed to naphthalene.

BACKGROUND

Naphthalene, the most abundant single constituent of coal tar (~11%), is used as a starting material for a variety of industrial chemicals, dyes, resins, solvents, lubricants and fuel components. Naphthalene is also a moth repellent and insecticide.

The October 2003 NDPSC Meeting considered an application to vary the labelling requirements for a naphthalene product to be used as a moth repellent in wardrobes, clothes drawers and for the protection of books and other paper or cloth based material in storage. The Committee concluded that, based on the available data, the existing scheduling for naphthalene remained appropriate. The Committee also considered adding the following warning statement to Appendix F:

- Do not use on the clothing of infants or in the bedrooms of young children.

The Committee agreed to defer their consideration of this matter to the February 2004 Meeting to allow consideration of more information on exposure studies referred to in the submission evaluation.

At the February 2004 NDSPC Meeting the Committee again considered the Appendix F warning statement above. The Committee agreed that the Schedule 6 entry for all users for naphthalene remained appropriate. Furthermore, the Committee supported the addition of warning statement 105 to alert users of the potential hazard naphthalene products present to young children - those being three years of age or less.

DISCUSSION

The Committee considered a report from **XXXXXXXX** of a child with haemolytic anaemia that may have resulted from exposure to naphthalene, forwarded by **XXXXXXXX**. **XXXXXXXX** also provided a copy of his letter to **XXXXXXXX**. Members particularly noted:

- The infant suffered haemolytic anaemia at 4 weeks of age that required a transfusion. **XXXXXXXX** advised that the infant appeared to have no predisposition to haemolytic anaemia. It was thought that the haemolytic anaemia was due to oxidative haemolysis after naphthalene flake exposure.
- The history of exposure was storage of household furniture within a container with naphthalene flakes on the floor until 8 months prior to the above incident. Additionally, more recent storage of a cot in a shed with scattered naphthalene flakes had occurred. **XXXXXXXX** advised that the quantity of naphthalene used was very large.
- **XXXXXXXX** asserted that haemolytic anaemia caused by naphthalene exposure was a real and avoidable problem for newborns and proposed that there should be a warning on the product that it should 'not be used near clothing or furniture that babies will be exposed to'. **XXXXXXXX** was advised by the Secretariat of warning statement 105 "Do not use on the bedding or clothing of infants or in the bedrooms of children 3 years of age or less" and agreed that this sufficiently conveyed the warning about exposure of naphthalene to young children. He remained concerned that the parents had asserted that no such warning was on the naphthalene flake product.

The Committee also noted the following points from the February 2004 NDPSC Meeting:

- Naphthalene is readily absorbed when inhaled, or administered orally or dermally, and readily passes the placenta into the foetus. The lowest lethal doses reported in humans are 100 mg/kg bw in a child and 29 and 74 mg/kg in adults.
- The majority of naphthalene poisonings occur in children and are characterised by haemolytic anaemia preceded by non-specific symptoms such as headache, anorexia, vomiting and diarrhoea.

- In 1990, 2400 cases of accidental naphthalene ingestion were reported to 72 PICs in the USA, 90% in children under 6. If a lethal naphthalene exposure has been achieved, rapid progression to coma and convulsions will occur with death from renal failure in adults, or kernicterus in young infants which may lead to permanent neurological damage. Hepatic centrilobular necrosis may also occur. Newborns are unable to conjugate naphthalene metabolites effectively and are consequently more susceptible to haemolysis. Dermal absorption is facilitated both by their thinner skin and by application of baby oil.
- Jaundice and haemolysis has been reported in infants dressed in clothes treated with naphthalene mothballs. The principal route of exposure has been suggested to be either, or both, dermal and/or inhalational.
- The original recommendations made by **XXXXXXXX** to not use on the clothing of infants (who are largely immobile and appear to be more sensitive to naphthalene toxicity) or in the bedrooms of young children (where they are likely to remain in a closed room for 8 to 10 hours and are likely to have greater accessibility to locations where naphthalene balls or flakes are used) recognized both the extended exposure periods of these groups and the apparent higher sensitivity of infants. The recommendation also recognized the potential for children to suffer significant morbidity from ingestion of small amounts of naphthalene which some find attractive.

OUTCOME

The Committee confirmed that the Schedule 6 entry for all users of naphthalene remained appropriate. Furthermore, the Committee agreed that warning statement 105 must remain a requirement for naphthalene products to alert users of the potential hazard naphthalene presents to young children.

PHARMACEUTICALS

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

10.1 POTASSIUM CHLORIDE

PURPOSE

The Committee considered post-meeting comment in relation to the decision to amend the scheduling of potassium chloride which was made at the February 2006 NDPSC Meeting.

BACKGROUND

Potassium chloride slow-release tablets have been supplied in Australia since 1967. At the May 1982 NDPSC Meeting, the Committee agreed that electrolyte balance control in patients at risk required proper supervision but made no recommendations for scheduling. 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. This decision was confirmed at the February 1986 Meeting.

At the October 2005 NDPSC Meeting, the Committee discussed a **XXXXXXXX** Report into the death of a child from an overdose of slow release potassium chloride. **XXXXXXXX** recommended that slow release potassium chloride products be included in Schedule 4. Members noted that potassium chloride had a wide range of uses and there was therefore 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.

At the February 2006 NDPSC meeting, the Committee considered the merits of a lower scheduling for high dose oral potassium chloride products other than the recommended Schedule 4. The Committee noted that the current unscheduled status of slow release potassium chloride products technically allowed them to be available through retail outlets. A Member noted that Schedule 2 would be in line with the current New Zealand entry for slow release preparations. The New Zealand Member confirmed this but acknowledged that this classification was probably not consistent with the safety profile of high dose potassium chloride and that it should be Schedule 4. Additionally, a Member noted that if the slow release potassium chloride product involved in the death of the child had been Schedule 2 the child would still have been at the same risk, given the fact that the product was bought from a pharmacy. The Committee therefore agreed to a Schedule 4 entry for potassium chloride. The Committee considered limiting the S4 entry to slow-release potassium chloride but instead agreed to a broader “oral preparations for therapeutic use”.

The decision of the Committee at the February 2006 Meeting (Decision 2006/46-27) was:

- To include oral potassium chloride (>100 mg per dosage unit) for therapeutic use in Schedule 4 on the grounds that its toxicity profile required professional oversight.
- To exempt oral potassium chloride preparations containing >100 mg per dosage unit for oral rehydration therapy and for enteral feeding.
- To recommend to **XXXXXXXX** that, in order to minimise any potential harm to children, child-resistant closures be mandatory for the scheduled potassium chloride products.

DISCUSSION

Members noted post-meeting submissions received from **XXXXXXXX**, **XXXXXXXX** and **XXXXXXXX**.

- The following points were highlighted in **XXXXXXXX** submission:
    - **XXXXXXXX** supported the actions taken to restrict the use of single active slow release potassium chloride in the community.
    - **XXXXXXXX** proposed that the scheduling entry should exempt complementary medicines containing incidental potassium chloride when labelled with a "Keep Out of Reach of Children" warning. It is noted that the proposed Schedule 4 entry for potassium chloride (with the upper limit of 100 mg per dosage for exemption of scheduling) would pick up all glucosamine sulphate-potassium chloride complex forms in the market place, of which there are a substantial number. **XXXXXXXX** maintained that these glucosamine products are used as a safe alternative in treatment of osteoarthritis with a recommended daily dosage of up to 1500 mg. **XXXXXXXX** stated they believed that to include glucosamine sulphate-potassium chloride complex in S4 would deprive the community of access to a valuable safe complementary medicine.
    - **XXXXXXXX** requested an opportunity to discuss this matter directly with the Chair of the Committee before legislative provisions are enacted, should this proposed amendment to the scheduling decision not be accepted.
- **XXXXXXXX** also recommended an amendment to the wording of the S4 entry to ensure that existing Listed glucosamine products in a potassium chloride (as excipient, up to 20%) complex are excluded from an S4 classification.
- **XXXXXXXX** recommended that the most effective means to reduce the risk of accidental overdose by children would be with mandatory child resistant closures (CRCs). **XXXXXXXX** made the point that to include a substance in Schedule 4 does not exclude a child accessing said substance, whereas a CRC would. **XXXXXXXX** refers to Therapeutic Goods Order 65 and states that this order would be the most useful mechanism to ensure children do not access such products. [*Secretariat note: TGO 65 is the Order which enforces use of CRCs*].

[Sentence deleted**]** was also noted. **XXXXXXXX** highlighted the following points:

- Almost half (184/ 399 or 46.1%) of the total number of glucosamine-containing products would become S4 poisons as a result of the February 2006 NDPSC decision. Of the products which contain glucosamine complexed with potassium chloride, 86.7% would become S4 poisons (see the summary table below).

Total products containing any form of oral glucosamine*	399	% of All Products	% of KCl containing products
Products containing glucosamine sulphate & KCl**	213	53.1%	100%
KCl > 100 mg / dose unit	**184**	**46.1%**	**86.7%**
KCl < 100 mg / dose unit	28	7.0%	13.2%
KCl amount unspecified	1		

* Note: Multiple pack sizes are treated as a single product.

** Note: Other glucosamine products are based on its hydrochloride salt.

- An analysis of the Adverse Drug Reactions Unit (ADRU) database revealed only one report of hyperkalemia (among 471 adverse drug reactions associated with glucosamine reported till May 2006) which was associated with a glucosamine sulfate product (containing 247 mg of potassium chloride). The recommended daily dose of this product was two capsules daily (total dose = 494mg potassium chloride). The Adverse Drug Reactions Advisory Committee (ADRAC) gave the report a causality rating of 'probable' because the event was correlated in time with the introduction of glucosamine. It should be noted that the subject was aged 80 yo, had congestive heart failure and was on other medications (frusemide, ramipril) which may also interfere with blood potassium levels. Hence, the available information provided no compelling evidence that the potassium chloride component of these products is associated with the adverse events reported. The Committee noted, given the fact that glucosamine is used in the treatment of osteoarthritis, it is not unlikely that individuals who might take such complimentary medicines suffer a number of co-morbidities and therefore might also be taking prescription medicines that affect blood potassium levels.
- A further 3 Listed multi-vitamin/mineral products would be affected by the proposed scheduling decision as the unit dose of potassium chloride exceeds 100mg.
- Given the widespread use of various glucosamine products in Australia, the proposed scheduling of potassium chloride would obviously have a major impact on marketing of, and consumer access to, these products. In **XXXXXXXX**'s opinion, this would represent an unacceptable situation in the absence of adverse drug reaction data implicating a casual link with the potassium chloride component.
- **XXXXXXXX** and **XXXXXXXX** conducted a comprehensive safety review of glucosamine in April 2004. This review concluded that there was no justification for any regulatory intervention on these products. The review did not look specifically for potassium chloride related adverse events.

- In **XXXXXXXX** view, the Committee should consider providing an exemption for complementary medicine products, or reconsider the threshold for S4 scheduling of potassium chloride-containing products.

The Committee was informed that a short meeting between members of the Secretariat and **XXXXXXXX** had taken place to discuss rewording the scheduling entry without inadvertently capturing the large group of complementary medicines. A number of reworded options for the Schedule 4 entry for potassium chloride that might no longer unintentionally capture complementary medicines containing glucosamine sulphate-potassium chloride complex were put forward and discussed. **XXXXXXXX** ruled out the addition of the words "slow release" to the proposed entry because, while there is currently no slow release formulation containing glucosamine sulphate potassium chloride complex on the ARTG, wording such as this might stifle future innovation for these complementary medicines. Adding the phrase "when used as an excipient" was also ruled out because the term "excipient" is not clearly defined and, given that the complex as a whole is therapeutically active, potassium chloride could not be considered an excipient. **XXXXXXXX** felt that options which included the phrase "when present as a single active" or similar were the most appropriate.

Members discussed the possibility of introducing child-resistant packaging (CRC) for potassium-containing complementary medicine products. The Committee did acknowledge that CRCs would trigger an alert to consumers that the contents of the container are not harmless. It was further acknowledge that some consumers may find the addition of CRCs on such products an imposition but this alone would not be a justification to exclude the use of CRCs. Regardless, the Committee agreed that the issue of whether or not a product required a CRC is separate to scheduling issues and should therefore be dealt with as part of the registration process.

The Committee reiterated that, even though slow-release potassium chloride products have been in the market for many years without being scheduled, when the NDPSC scheduling guidelines are applied, such products appropriately should be placed in Schedule 4.

In considering the data that **XXXXXXXX** presented justifying the exemption of glucosamine complexed products, the Committee remained extremely concerned about allowing such an exemption. The Committee felt that, rather than provide any assurance of safety, the ADRU data which listed one case report of hyperkalaemia only served to highlight the potential problem that existed with these complimentary medicine products. Indeed, hyperkalaemia is often asymptomatic and thus relying solely on adverse event reporting is in no way an appropriate risk-based approach to the issue. In short, the Committee felt that there was no empirical toxicological data before them which demonstrated clearly that the amount of potassium in the complexed glucosamine products would not be as fatal as a single-active slow-release potassium chloride preparation, should a child ingest a large amount. Given that products listed in

XXXXXXXX had up to 1.8gm of potassium chloride per unit, the Committee felt that their concerns were warranted.

DECISION 2006/47 – 12 (Variation of Decision 2006/46-27)

The Committee's concerns regarding the potential for any therapeutic product containing substantial amounts of potassium per unit dose to result in an inadvertent overdose similar to that which **XXXXXXXX** firmly remained, despite the assurances that **XXXXXXXX** gave using ADRU post marketing surveillance data. For this reason, the Committee concluded that toxicological data must be presented to them before they would consider exempting such products from scheduling. Such data would need to clearly demonstrate that products, such as glucosamine complexed products which contain substantial amounts of potassium per unit dose, cannot result in high serum potassium levels. In order to allow all stakeholders time to provide such data, the Committee agreed to vary its February decision so that only slow release preparations would be captured by the new Schedule 4 entry.

Schedule 4 – NEW ENTRY

POTASSIUM CHLORIDE in slow-release oral preparations for human therapeutic use **except** when containing 100 mg or less of potassium chloride per dosage unit.

OUTCOME

The Committee further agreed to foreshadow a decision to alter the wording of the Schedule 4 entry for potassium chloride to that which was originally agreed to at the February 2006 Meeting.

POTASSIUM CHLORIDE – amend entry to read:

POTASSIUM CHLORIDE in oral preparations for human therapeutic use **except**:

(a) when containing 100 mg or less of potassium chloride per dosage unit;

(b) in preparations for oral rehydration therapy; or

(c) in preparations for enteral feeding.

10.2 ORLISTAT

PURPOSE

The Committee considered post-meeting comments in relation to the Appendix H inclusion of orlistat, a decision made at the February 2006 NDPSC Meeting (Decision 2006/46-29).

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 and physical exercise 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** capsules containing orlistat 120 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.

Separate submissions to reschedule orlistat for the treatment of obesity from S4 to S3 were considered at both the June 2002 and February 2003 NDPSC meetings. The February 2003 submission also sought to have orlistat included in Appendix H. On both these occasions, the Committee decided that the information submitted by the sponsor did not provide adequate evidence to address the Committee's concerns in relation to its safety profile, to the necessity for medical assessment to determine a patient's suitability for treatment with orlistat, and to the view that therapeutic intervention should not be the first-line treatment for obesity.

The October 2003 NDPSC meeting considered a third new submission to reschedule orlistat for the treatment of obesity from S4 to S3 without inclusion in Appendix H. The NDPSC agreed to reschedule orlistat from S4 to S3 for the treatment of obesity on the basis that the sponsor had provided adequate evidence addressing the Committee's previous concerns.

Both the February 2005 and June 2005 NDPSC Meetings considered two separate proposals 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. Furthermore, 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. The Committee was also of the view 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

position that consumers should be encouraged to undertake appropriate lifestyle changes as a first-line option to achieve safe, long-term weight loss.

At the February 2006 NDPSC Meeting, the Committee considered a new application from **XXXXXXXX**. The Committee noted additional information provided by the sponsor including post-marketing surveillance study, media survey and consumer/market research, as well as the fact that experience has been gained by pharmacists in screening and consulting patients on suitability of orlistat for other clinical conditions. The Committee also believed that the newly amended TGAC which has been strengthened with regards to the advertising of weight loss products shall ensure responsible and appropriate banded advertising of the orlistat product **XXXXXXXX** by the sponsor. The Committee hence agreed to include orlistat in Appendix H on the grounds of potential public health benefit (Decision 2006/46-29).

DISCUSSION

Members noted post-meeting submissions received from **XXXXXXXX**, **XXXXXXXX**. All correspondents fully support the NDPSC's decision to allow branded advertising of orlistat, with the following points highlighted:

- There is potential public health benefit for orlistat used in weight loss.
- Pharmacists are gaining experience everyday in weight management and in the use of orlistat, with **XXXXXXXX** active support.
- Brand advertising for orlistat will allow consumers to make a more informed choice, and to develop realistic expectations on weight loss.
- Brand advertising will facilitate pharmacist supply of orlistat.

Members also noted a submission from **XXXXXXXX**. **XXXXXXXX** commended the Committee for its decision and pointed out that with the new decision on branded advertising of orlistat the important role that pharmacists play in the weight management category and the potential public health benefit will be maximised, and consumers who seek advice on weight loss and weight loss medication options will be fully and appropriately informed.

DECISION 2006/47 – 13 (Confirmation of Decision 2006/46-29)

The Committee confirmed the scheduling decision for orlistat made at the February 2006 NDPSC (Decision 2006/46-29) which was to include orlistat in Appendix H on the grounds of potential public health benefit.

Appendix H – New entry

Orlistat.

10.3 IBUPROFEN

PURPOSE

The Committee considered the post-meeting comment in relation to scheduling amendment for ibuprofen in divided oral doses of 400 mg.

BACKGROUND

Ibuprofen, a propionic acid derivative, is a non-steroidal anti- inflammatory drug (NSAID). Ibuprofen is used in the management of mild to moderate pain and inflammation in conditions such as dysmenorrhoea, headache including migraine, post-operative pain, dental pain, musculoskeletal and joint disorders such as ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis including juvenile idiopathic arthritis, peri-articular disorders such as bursitis and tenosynovitis, and soft-tissue disorders such as sprains and strains. It is also used to reduce fever.

Ibuprofen was first included in Schedule 4 of the SUSDP in February 1973. At the May 1989 meeting, ibuprofen in packs of 24 or less tablets or capsules for the relief of dysmenorrhoea or of pain associated with inflammation was rescheduled to Schedule 3. The Schedule 3 entry was amended over several meetings since and in May 1995, ibuprofen when the only therapeutically active substance in divided preparations for oral use containing 200 mg or less of ibuprofen per dosage unit in a pack containing 50 or less dosage units and labelled with a recommended daily dose of not more than 1200 mg, was rescheduled from S3 to S2.

The June 2003 NDPSC Meeting agreed to exempt divided preparations containing 200 mg or less of ibuprofen per dosage unit in packs containing 25 or less dosage units when labelled with a recommended maximum daily dose of 1200 mg of ibuprofen and compliant with the mandatory label requirements from scheduling. The Committee agreed that exempting certain low dose ibuprofen oral preparations in small pack sizes from the requirements of scheduling was unlikely to lead to any public health concerns, and that it would provide consumers with an additional choice of simple analgesic product available at general outlets.

At the February 2006 NDPSC meeting, the Committee considered an application from **XXXXXXXX** seeking reclassification from S4 to S2 of divided doses of ibuprofen 400 mg in oral preparations. The Committee agreed to include 400 mg ibuprofen per dose unit in packs of not more than 50 dose units and labelled not for the treatment of children aged less than 12 years in Schedule 3 of the SUSDP (Decision 2006/46-26). Whilst the Committee remained reassured of the safety of OTC low dose ibuprofen in small pack sizes when taken as directed, members considered pharmacist involvement at the point-of-sale essential to minimise consumer confusion over the increased strength per dose unit of the proposed product and ensure appropriate use. The Committee also considered the inclusion of ibuprofen 400 mg in Appendix H. However, members did not support

the Appendix H listing for this product on the basis that direct-to-consumer advertising of high dose ibuprofen was unlikely to have any public health benefits.

DISCUSSION

Members noted a post-meeting submission from **XXXXXXXX** with the following points highlighted:

- Whilst **XXXXXXXX** is prepared to accept the Committee's recommendation, they feel that Schedule 2 is the appropriate schedule **XXXXXXXX**.
- **XXXXXXXX** indicates that they provided data to support the safety profile of ibuprofen in the OTC setting with a maximum daily dose of 1200 mg for mild to moderate pain. Therefore, it is important to include this maximum daily dose in the S3 entry. The following wording is hence suggested: "IBUPROFEN in divided preparations containing 400 mg or less ibuprofen, in packs of not more than 50 dosage units, with a maximum daily dose not exceeding 1200 mg, and labelled not for the treatment of children under 12 years of age **except** when included in or expressly excluded from Schedule 2."
- **XXXXXXXX** also reiterated their concerns expressed in the pre-meeting response to the evaluator's report with respect to the use of the term severe pain. They argued that the Record of Reasons does not clarify what constitutes "severe" pain.

Members agreed that **XXXXXXXX** had made a valid point about the 1200 mg maximum daily dose, and inclusion of this dose restriction would also provide consistency with other OTC entries for ibuprofen. The Committee felt that it is important to make consumers aware of the recommended minimum effective dose (200 mg) and the maximum daily dose (1200 mg). The Committee hence agreed to amend the decision by adding the words "with a maximum daily dose not exceeding 1200 mg" into the S3 entry for ibuprofen. It was discussed that similar words should also occur in the product label.

Upon review of the Record of Reason for the February 2006 Meeting, members determined that the term "severe" pain related to severe symptoms (compared to mild) of the proposed S3/S2 indications, i.e. migraine, headache, cold and flu. This term was used to distinguish the need for a 400 mg dose of ibuprofen over a 200 mg dose. The original evaluator's report specifically references migraine pain of "severe" baseline pain intensity and quotes the conclusion from a trial (Codispoti et al, 2001) that it was only in these migraine cases that a 400 mg dose of ibuprofen was significantly superior to placebo whilst a 200 mg dose was not. This was clearly illustrated in the Record of Reasons by the statement: "… given that the lower end of the effective dose range (200-400 mg) could not be achieved with this product (400 mg tablets), it should only be used by individuals who require a 400 mg dose, either because they have **severe symptoms** or because they have failed to respond to 200 mg. The selection of a 400 mg unit dose product rather than a 200 mg unit dose product may therefore be a decision that would be better made with pharmacist's advice and counselling than without it." The use of word

"severe" should therefore not be misinterpreted to infer indications other than those allowed for OTC use.

DECISION 2006/47- 14 (Variation of Decision 2006/46-26)

The Committee confirmed the scheduling decision for ibuprofen 400 mg (Decision 2006/46-26) with revision of the wording to include a daily dose limit of 1200 mg in the Schedule 3 entry. Inclusion in Appendix H was not supported on the basis that direct-to-consumer advertising of high dose ibuprofen was unlikely to have any public health benefits.

Schedule 4 - Amendment

IBUPROFEN **except:**

(a) when included in or expressly excluded from Schedule 2 or 3; or

(b) in preparations for dermal use.

Schedule 3 – New entry

IBUPROFEN in divided preparations, each containing 400 mg or less of ibuprofen, in packs of not more than 50 dosage units when labelled:

(a) with a recommended daily dose of 1200 mg or less of ibuprofen; and

(b) not for the treatment of children under 12 years of age

except when included in or expressly excluded from Schedule 2.

10.4 KETOTIFEN

PURPOSE

The Committee considered post-meeting comment in relation to the rescheduling decision made at the February 2006 NDPSC Meeting to reschedule ketotifen in topical eye preparations containing 0.025% or less of ketotifen from Schedule 4 to Schedule 3.

BACKGROUND

Ketotifen has the antihistamine properties in addition to a stabilising action on mast cells analogous to that of sodium cromoglicate. It is used in the prophylactic management of

asthma and is also used in the treatment of allergic conditions such as rhinitis and conjunctivitis.

At the February 2006 NDPSC Meeting, **XXXXXXXX** sought to obtain a Schedule 3 classification as well as Appendix H inclusion for ketotifen 0.025% for ophthalmic use. The Committee agreed to reschedule ketotifen in topical eye preparations containing 0.025 percent or less of ketotifen from Schedule 4 to Schedule 3 on the basis that the product fulfilled criteria for S3 listing. It was noted that such an approach would also result in harmonisation with New Zealand. The Committee further agreed on the basis of potential public health benefit, to include ketotifen in Appendix H of the SUSDP with the standard implementation date of 1 September 2006 (Decision 2006/46-24).

DISCUSSION

Members noted post-meeting comment from **XXXXXXXX** in relation to the following statement in the Record of Reasons for the February 2006 NDPSC meeting:

> "It is pointed out that **all** other products used to treat SAC are included in S2 of the SUSDP, e.g. other H1-receptor antagonists (levocabastine hydrochloride, antazoline salts and pheniramine maleate) and mast cell stabilisers (sodium cromoglycate and lodoxamide)."

XXXXXXXX pointed out that olopatadine, the active ingredient in **XXXXXXXX**, which is an H1-receptor antagonist and mast-cell stabiliser, is in Schedule 4 only. The product is indicated for the treatment of the signs and symptoms of seasonal allergic conjunctivitis (SAC), and is most commonly prescribed by ophthalmologists for SAC.

Members noted that the above statement was present as one of the dot points abstracted from the scheduling application. It had been brought to the Committee's attention that not all medicines used in treatment of SAC appear in Schedule 2 of the SUSDP.

DECISION 2006/47 - 15 (Confirmation of Decision 2006/46-24)

The Committee confirmed the scheduling decision for ketotifen (Decision 2006/46-24) which was to reschedule ketotifen in topical eye preparations containing 0.025 percent or less of ketotifen from Schedule 4 to Schedule 3 and to include ketotifen in Appendix H of the SUSDP with the standard implementation date of 1 September 2006.

Schedule 4 – Amendment

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

Schedule 3 – New Entry

KETOTIFEN for ophthalmic use in preparations containing 0.025 per cent or less of ketotifen.

APPENDIX H New Entry

Ketotifen.

11. OTHER OUTSTANDING MATTERS FROM PREVIOUS MEETINGS

11.1 FRACTIONATED PLASMA PRODUCTS

PURPOSE

The Committee considered the foreshadowed decision to exempt fractionated plasma products and comparable recombinant products from scheduling requirements through inclusion in Appendix A of the SUSDP.

BACKGROUND

Considering the adequate controls that exist at Commonwealth and State/ Territory level, the Committee has had a standing policy not to schedule blood products. The Committee considered the recommendations arising from the Review of the Australian Blood Banking and Plasma Product Sector at the February 2005 Meeting and was satisfied that appropriate regulatory mechanisms were in place to warrant the exemption of blood products from scheduling requirements and agreed to foreshadow the inclusion of blood products in Appendix A of the SUSDP.

XXXXXXXX provided advice in May 2005, stating 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). **XXXXXXXX** stated that historically, **XXXXXXXX** manufactured most plasma derived product and this was distributed by the **XXXXXXXX** but in more recent times, foreign manufactured product is commercially available directly from sponsors and this situation is set to 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.

At the June 2005 Meeting, the Committee concluded that hospitals and health services have policies and guidelines in place to ensure best practise in the supply and use of whole 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 (effective 1 January 2006) but to foreshadow the consideration of the scheduling of plasma fractionated and comparable recombinant product at the October 2005 Meeting.

At the October 2005 Meeting, the Committee agreed not to include fractionated plasma products and comparable recombinant products in Appendix A but to instead seek input from the **XXXXXXXX** on the possible ramifications of scheduling such products and to consider this input, along with other public submissions, at the February 2006 Meeting.

At the February 2006 Meeting, the Committee agreed that advice should be sought from **XXXXXXXX** as to how scheduling of fractionated plasma and recombinant blood products might fit into current control frameworks. As a starting point, the **XXXXXXXX** should be provided with the list of products that had been supplied to the Committee by the **XXXXXXXX**. **[**Sentence deleted**]**

XXXXXXXX wrote to the Chair in May expressing concerns in relation to the possible scheduling of fractionated plasma products. The concerns that were aired at the most recent **XXXXXXXX** were summarised as follows:

- There has been an apparent lack of detailed consultation with the blood sector, especially in relation to the key differences in the delivery of blood products through the supply chain compared to the delivery of most pharmaceuticals;
- **XXXXXXXX** had made a submission to the NDPSC previously suggesting a 12 month consultation period to ensure that all issues and concerns are adequately canvassed;
- **XXXXXXXX** itself has a crucial role under the National Blood Agreement to ensure such proposed changes to the way blood products are managed do not disrupt the blood supply or cause unwarranted costs to be imposed on the blood sector; and
- **XXXXXXXX** believes that it is not clear what the scheduling status of some blood products (apparently) is and whether or not the appropriate regulatory oversight (under the schedule) was being applied.

XXXXXXXX requested that:

- The NDPSC agrees to a 12 month consultation period on the possible scheduling of blood products to allow the blood sector adequate time to raise and discuss all concerns and issues;
- The NDPSC agree to **XXXXXXXX** making a submission to the NDPSC within this 12 month period, noting that **XXXXXXXX** intends to establish a working party to develop its submission, including a consultation process with stakeholders.

In the response to **XXXXXXXX**, the following points were made:

- All the concerns raised by **XXXXXXXX** were noted, particularly the request for a 12 month consultation period and these concerns would be brought to the attention of the full NDPSC at the June 2006 Meeting.
- **XXXXXXXX** was encouraged to have the **XXXXXXXX** communicate their concerns to their NDPSC counterparts in order to ensure that their concerns were adequately represented at the June 2006 Meeting.

XXXXXXXX provided a pre-Meeting submission where the following points were made:

- A consistent approach be taken for exemption/ scheduling of blood products, regardless of their method of manufacture. That is to say, recombinant be treated the same as plasma-derived product.
- A consistent approach be adopted for all plasma products. **XXXXXXXX** noted that immunoglobulins are currently listed as S4 but no other plasma derived or recombinant product was currently scheduled.
- **XXXXXXXX** also suggested, given the complexity of the situation, that a 12 month consultation period involving key stakeholders be initiated.
- **XXXXXXXX** felt that, as all these products are sterile injectables and fully evaluated by TGA prior to marketing, a case-by-case approach would not be appropriate but these products should all be treated the same.

The Committee recalled that the decision to schedule immunoglobulins was made at the November 1990 Meeting in relation to clarifying the entry for antigens which simply read as "ANTIGENS for human therapeutic use" at that time. At that time, the Committee decided to amend this entry to only include parenteral (c.f. oral) antigens and to also include all other immunological agents, including immunoglobulins. At this meeting, immunoglobulins were defined as "preparations containing antibodies against infectious micro-organisms obtained from human material, often plasma". The Committee conceded that this definition may not be appropriate for all of immunoglobulins available in Australia today, as not all immunoglobulins contain antibodies against infectious micro-organisms.

The Committee noted that advice had been sought from **XXXXXXXX** regarding a list of products supplied through the National Blood Supply Chain which the **XXXXXXXX** considered to be either fractionated blood products or recombinant products. A brief response was provided via email on 16 June 2006 in which **XXXXXXXX** agreed in principle to exempting fractionated product & recombinant product, should mechanisms ensuring appropriate oversight of transport, storage and traceability are in place. **XXXXXXXX** also stated that immunoglobulins must be scheduled/ exempted in the same way that all other fractionated products are. That is to say, if others are exempted, immunoglobulins should be too.

One Member summarised by saying that these products are for the treatment of diseases requiring medical supervision and for that reason might be assumed to be Prescription Only Medicines, are administered to individual patients as though they are Prescription Only Medicines and yet the current scheduling system does not take into account the distribution system that exists for these products. That is to say, should the consultation period that **XXXXXXXX** have agreed to take carriage of take place, it would reveal one way or the other, whether scheduling is warranted to ensure proper medical supervision

over the supply of these products or, alternatively, that the mechanisms which are already in place are enough to ensure safe distribution and supply of these products.

OUTCOME

The Committee agreed to defer this item to allow time for **XXXXXXXX** to establish a working party and carry out a consultation process involving all relevant stakeholders. It is apparent from the submissions received that wider stakeholder consultation is necessary to avoid unwarranted restrictions placed on the supply and availability of fractionated/recombinant blood products through scheduling and the Committee needs to be reassured that existing controls on these products are indeed adequate. The Committee will await the submission from **XXXXXXXX** which will be provided at the end of the consultation period.

11.2 OCTOCOG ALFA

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) **XXXXXXXX**. The proposed indication was "for use in haemophilia A for prevention and control of haemorrhagic episodes. Patients with haemophilia A may be treated with **XXXXXXXX** as peri operative management. **XXXXXXXX** is not indicated in von Willebrand's disease".

Octocog alfa (rch) was designated as an Orphan Drug for the proposed indication.

XXXXXXXX is produced from **XXXXXXXX** under conditions which are free from the use of animal derived protein.

Compared to **XXXXXXXX** existing recombinant Factor VIII (Recombinate), the cell cultures used for the production of **XXXXXXXX** do not contain bovine proteins, and the formulation does not contain human albumin as a stabiliser. This eliminated potential contamination by adventitious agents derived from human or animal materials or excipients. The purification scheme included immuno-affinity columns, and a solvent/detergent treatment for viral inactivation.

[Section deleted**]**

The Committee noted at the May 2001 NDPSC Meeting that **XXXXXXXX** and **XXXXXXXX** are sterile, stable, purified recombinant human antihaemophilic Factor VIII concentrates **[**sentence deleted**]**.

The Committee agreed in May 2001 that its policy of leaving blood products for therapeutic use unscheduled remained appropriate. That policy is currently being reconsidered by the Committee with a view to including an entry in Appendix A for fractionated plasma products and equivalent recombinant products.

The Committee noted that, while octocog alfa is listed as a Prescription Medicine in New Zealand, generic Factor VIII is listed as General Sale. It is assumed that the generic listing refers to plasma-derived product only.

OUTCOME

The Committee agreed to defer consideration of this matter until completion of the consultation period suggested by **XXXXXXXX**, in which **XXXXXXXX** will form a working party, consult key stakeholders and report back to the NDPSC.

11.3 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 thromboembolic 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**, indicated for the treatment of purpura fulminans and coumarin-induced skin necrosis in patients with severe congenital protein C deficiency.

[Sentence deleted**]**

OUTCOME

The Committee agreed to defer consideration of this matter until completion of the twelve month consultation period suggested by **XXXXXXXX**, in which **XXXXXXXX** will form a working party, consult key stakeholders and report back to the NDPSC.

11.4 CETIRIZINE

PURPOSE

The Committee considered removal of cetirizine for oral use from Appendix K and Appendix F Part 3 of the SUSDP.

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.

Cetirizine was first approved as a prescription medicine in May 1993, and included in Appendix K based on the incidence of drowsiness/somnolence associated with doses of cetirizine from 5 to 20 mg per day during phase III efficacy/safety clinical trials. A decision to reschedule cetirizine tablets from Schedule 4 to Schedule 3 was made at the May 1997 Meeting, and so did with oral liquid formulations at the February 1998 Meeting. At the February 1999 Meeting, the Committee supported a recommendation from the Trans Tasman Harmonisation Working Party that, on grounds of harmonisation, cetirizine in preparations for oral use be rescheduled from Schedule 3 to Schedule 2.

At the October 2005 NDPSC meeting as the balance of current evidence indicated that cetirizine was 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 (Decision 2005/45-19). The Committee further agreed to refer the issue of warning statement requirements for all non-sedating antihistamines to the Medicine Evaluation Committee (MEC) to check for consistency with New Zealand.

Having considered post-Meeting comment from various stakeholders at the February 2006 Meeting, the Committee agreed to set aside Decision 2005/45-19 and retain cetirizine in Appendix K and Appendix F, Part 3 of the SUSDP. It was advised that the December 2005 MEC Meeting was unwilling to recommend removal from RASML of the requirement to include a 'drowsiness' warning on the label of products containing cetirizine based on data provided to MEC. Whilst the Committee accepted that the data submitted by the applicant and the evaluation report may have supported the contention that 10mg cetirizine is relatively unlikely to cause drowsiness, the approved maximum recommended daily dosage for existing cetirizine products in S2 was up to 20mg a day. The Committee noted the proposal by the applicant to limit the maximum recommended daily dosage for its S2 cetirizine products to 10mg. The Committee also noted that as of 1 May 2006, the transfer of all mandatory label advisory statements for medicines from the SUSDP to the *Required Advisory Statements for Medicine Labels* (RASML) would take effect at which time Appendix F of the SUSDP would cease to be the reference document for medicine label requirements. The Committee agreed to seek further advice from the MEC as to the status of this proposed application.

An article by Mann et al. ("Sedation with "non-sedating" antihistamines: four prescription event monitoring studies in general practice." *British Medical Journal* Vol 320:1184-1187, 2000) was submitted to the Committee by **XXXXXXXX** as part of their post-Meeting submission. This was a meta analysis of data from prescription event monitoring studies intended to show relative sedation rates between loratadine, acrivastine, fexofenadine and cetirizine. This article was referred to MEC and their advice was sought as to the potential implications this article might have for label requirements for cetirizine and other so-called second generation antihistamines. The Committee also agreed to review the inclusion of cetirizine in Appendix K of the SUSDP at the June 2006 Meeting, provided advice is received from MEC by that time.

DISCUSSION

Members noted Minute from the OTC Medicines Section (OTCMS) regarding an application to amend the entries in the RASML for cetirizine. The OTCMS confirmed that **XXXXXXXX**, applied in March 2006 to remove the current drowsiness label warning statement and replace it with the statement required in New Zealand "*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** has also applied to have this same label warning statement apply to all second generation antihistamines. As per standard public consultation process, submissions for this application have been received, **[**sentence deleted**]**. These data are currently being evaluated and will be considered at the August 2006 MEC Meeting. The NDPSC Secretariat will be notified of the outcome of the MEC's deliberations when the ratified minutes become available in early December.

Members noted post-meeting comment for the February 2006 Meeting submitted by **XXXXXXXX** in which they expressed disagreement with the following statement in the Record of Reasons: "…*the data submitted by the applicant and the evaluation report may support the contention that 10mg cetirizine was comparable to 10mg loratadine…*". **XXXXXXXX** argued, as they did in both their September 2005 and December 2005 submissions, that the overall body of scientific evidence provides compelling support that, at a dose of 10 mg, loratadine causes little or no drowsiness, no impairment of cognitive or psychomotor performance and no impairment in ability to drive/ operate machinery. In comparison, doses of 5mg-20mg of cetirizine have been associated with CNS effects. **XXXXXXXX** believes that objective and subjective data convincingly show loratadine 10mg to have a different sedation profile to cetirizine 10mg.

Members also noted pre-Meeting comment submitted by **XXXXXXXX**. **XXXXXXXX** support the essence of the initial decision to remove cetirizine from Appendix K, and believe that the concerns raised at the February Meeting can be addressed by amending the wording of the entry. Their arguments are as follows:

- Appendix K relates to dispensed medicines only. Thus, cetirizine sold as an OTC medicine at a recommended dose of 10mg daily should not be captured by an Appendix K entry.

- Cetirizine does not possess the sedating properties associated with other compounds listed in Appendix K. **XXXXXXXX** maintain that all other antihistamines listed in Appendix K are S3 and thus, as per the review undertaken by the Medicines Classification Committee (MCC) of New Zealand, cetirizine should be grouped with other non-sedating antihistamines.
- It is well established that cetirizine has minimal CNS depressant effect. **XXXXXXXX** quote the TGA-approved PI where it is stated under "Pharmacology": "*Studies in normal volunteers using objective measurements (e.g. sleep latency time, mental alertness and simulated driving performance) showed that cetirizine at doses up to 20 mg induced minimal CNS depressant effects*".
- The proposal to remove cetirizine at a recommended dose of 10mg daily from Appendix K was based on appropriate evidence. That is to say that the Committee's decision to remove cetirizine from Appendix K was supported by results of appropriate objective & subjective tests in healthy subjects. **XXXXXXXX** state that the information on CNS impairment potential, as stated in the PI for cetirizine, was based on the following:

    (a) Cetirizine is an active metabolite of hydroxyzine (a first generation sedating antihistamine) and drowsiness warning labels were included in Phase III trials. **XXXXXXXX** maintains that this may have biased trial participants to expect drowsiness.

    (b) Allergy itself is associated with drowsiness.

    (c) Results of placebo-controlled trials may be biased due to cetirizine's effectiveness.

- The commonly recommended dose for cetirizine is 10mg daily. **XXXXXXXX** states that 20mg daily is only referred to in two places: in the PI's Dosage & Administration section, where it is stated that 10mg should be the starting dose and only increased to 20mg if response is insufficient and also on the label of a product which is soon to be amended (**XXXXXXXX** include a copy of the amended label).
- Some drowsiness is associated with all second generation antihistamines. **XXXXXXXX** make reference to the article by Mann et al. (2000) and maintains that the article concludes that although a higher incidence was reported with cetirizine and acrivastine, no difference was seen in the incidence of accident and injury between the four antihistamines. [Secretariat note: the following statement is made in the conclusion of the article: "*The number of reports of sedation with all four antihistamines was low. However, the adjusted odds ratios suggest that cetirizine was 3.5 times more likely and acrivastine 2.8 times more likely to result in reports of sedation than loratadine; there was no significant difference between loratadine and fexofenadine. Sedation might result in an increased risk of accident and injury, but we found no such difference between the antihistamines.*"]. **XXXXXXXX** also quote results from a recent on-line market survey in which survey participants associated non-drowsiness with cetirizine, loratadine and fexofenadine approximately equally

and go on to conclude that the data suggests OTC customers do not perceive second generation antihistamines as being different, in terms of non-drowsiness.

Members noted **XXXXXXXX**'s recommendation, as shown in their initial application presented at the October 2005 Meeting, to amend the Appendix K entry for cetirizine to read "cetirizine except when included in Schedule 2" and also by changing the S2 entry for cetirizine to read "Cetirizine in preparations for oral use when labelled with a recommended daily dose of not more than 10mg".

Members also noted a pre-meeting submission from **XXXXXXXX** who believe that cetirizine should be deleted from Appendix K, since Appendix K should only relate to dispensed medicines, and all cetirizine products are available OTC. In regards to cetirizine's inclusion in Appendix F Part 3, **XXXXXXXX** point out that the RASML document came into effect as of 1 May 2006 and a current submission is known to be submitted to the MEC to alter the RASML entry for cetirizine. Therefore it would be prudent to await the outcomes of the MEC's deliberations on this matter.

Members recalled the extensive discussions at both meetings in October 2005 and February 2006 in relation to the Appendix K and Appendix F Part 3 entries for cetirizine. Although evidence provided by the sponsor indicated that 10 mg cetirizine showed minimal sedative effect, the sedation potential increase with the dose, and the approved maximum recommended daily dosage for existing cetirizine products was up to 20 mg per day. Furthermore, the advice from the MEC to the February 2006 meeting indicated that the MEC was unwilling to recommend removal from RASML of the requirement to include a 'drowsiness' warning on the label of products containing cetirizine based on data provided to date.

Members discussed the possibility of replacing the current drowsiness label warning statement, as recommended by some pharmaceutical companies, with the one required in New Zealand, i.e. "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". It was pointed out by a member that since the sedation effect of cetirizine was dose-related, the wording of label statement should be based on the recommended daily dose and maximum dose limit in Product Information. The Committee concluded that this is now a RASML issue which should be considered by the MEC.

At the February 2006 meeting, the Committee had sought further advice from the MEC on the label requirements for cetirizine and other so-called second generation antihistamines, as well as the potential efficacy issue affected by the proposal to reduce the maximum daily dosage for S2 oral preparations containing cetirizine from 20 mg to 10 mg. Members were aware that these issues together with other relevant issues would be considered at the August 2006 MEC meeting, and the outcome of the MEC's deliberations would be available to the Committee by December 2006. The Committee agreed to then reconsider the issue based on the MEC's recommendation, together with other public submissions.

OUTCOME

The Committee agreed to await further consideration of the sedation warning statements for cetirizine, until the deliberations of the MEC in regards to the submission to alter the Required Advisory Statements for Medicine Labels entry for cetirizine are known.

11.5 ACONITUM SPP

PURPOSE

The Committee considered the scheduling of Aconitum spp for use in children.

BACKGROUND

The October 2005 NDPSC meeting considered a recommendation from MCC to harmonise with New Zealand. In Australia, Aconitum spp was in Schedule 4 (S4) while in New Zealand, the primary entry was in Part I (S4) and certain oral and dermal preparations were classified as General Sale and Pharmacy Only medicines. The June 2005 MCC minutes indicated that MCC recently reclassified Aconitum spp to allow continued access to complementary products already on the market. Following the October 2005 NDPSC meeting, OCM was asked to comment on the proposal to harmonise the scheduling of Aconitum spp with New Zealand.

Prior to the February 2006 NDPSC meeting, the MCC Secretary provided a copy of the assessment report on **XXXXXXXX** proposal to reschedule Aconitum spp and to revise the cut-offs specified in the New Zealand schedule entries such that they were expressed in terms of the total alkaloid content rather than the amount of plant material in the preparations. There were no products registered on New Zealand's SMARTI database but there were numerous homeopathic products listed on the ARTG containing Aconitum spp. However, according to the assessment report, the only aconite-containing product(s) being sold as General Sale medicines in New Zealand were homoeopathic liquids or powders containing Aconite 4X (i.e. a 0.01% tincture) for internal administration, which contained a maximum of 0.000015% alkaloids, equivalent to 0.15 micrograms per 1ml (15 drop) dose. The cut-offs adopted in New Zealand were based on pack sizes of such products, i.e. 30ml or 100ml being available, which contained a maximum total amount of 4.5 micrograms or 15 micrograms (0.015mg) alkaloids in each pack size respectively. MCC noted this was less than 1% of the lowest reported fatal adult dose of 2mg.

The February 2006 NDPSC meeting noted the advice from OCM which greed with the principle of the MCC proposed scheduling for Aconitum species. OCM indicated that it was initially concerned that the proposed limit of 0.02 % for the total alkaloids was too high, as severe poisoning had been reported after ingestion of as little as 0.2 mg of the toxic alkaloid aconitine [Tai et al., (1992), as cited by IPCS (2005)]. However, a brief literature search conducted by the OCM appeared to support the limit of 0.02% for total alkaloids, as proposed by the MCC. On this basis, the Committee confirmed its foreshadowed decision to harmonise with the New Zealand entry for Aconitum spp and

rescheduled from S4 to S2, preparations for oral use in packs each containing 0.2 mg or less of total alkaloids and preparations for dermal use containing 0.02 % or less of total alkaloids in packs each containing 0.2 mg or less of total alkaloids. Furthermore, the Committee also agreed to harmonise with New Zealand's General Sale medicines containing Aconitum spp and exempted oral and dermal preparations in packs each containing 0.02 mg of total alkaloids.

Whilst the February 2006 NDPSC meeting agreed to harmonise with New Zealand on the scheduling of Aconitum spp, it was noted that the issue of safe use in children was not addressed in the advice or information provided to the Committee. Members discussed the need to include an age restriction on medicines on the basis that the maximum pack size allowed in the S2 entry was the same as the level cited by OCM in its submission to NDPSC at which severe poisoning was reported, i.e. after ingestion of as little as 0.2 mg of the toxic alkaloid aconitine, presumably in an adult. Members agreed that this matter could be effectively dealt with at registration when products became available but the Committee nonetheless agreed to seek comment from OCM on the safety of aconite preparations in children for reassurance and asked that OCM's advice be tabled for consideration at the June 2006 meeting.

DISCUSSION

Members noted that the foreshadowed consideration of Aconitum spp and in particular, its use in children, was included in the pre-meeting gazette notice to allow new information to be submitted to the Committee to assist resolve the safety concern regarding the therapeutic use of Aconitum spp in children. Members noted that pre-meeting submissions were received from **XXXXXXXX** and **XXXXXXXX**. **XXXXXXXX** did not offer any comment but asked for the right to comment on any decision and **XXXXXXXX** proposed that the words "or less" be added to the entries to clarify the pack sizes allowed for exempt preparations.

The Committee noted the comment received from OCM which supported the February 2006 NDPSC meeting decision to harmonise the scheduling of *Aconitum spp* with New Zealand. OCM also suggested that the S2 and S4 entries be amended to clarify that the exemption from scheduling applied to all preparations containing 0.02 milligrams or less of Aconitum spp alkaloids per pack.

The Committee was advised that OCM was unable to provide the advice sought in regards to the safety of Aconitum spp for the treatment of children in time for the meeting and that no other such information or data was provided for the Committee's consideration in the pre-meeting submissions received.

A member recalled that the pack size limit adopted in New Zealand for General Sale preparations was equivalent to 1% of the LD_{50} for Aconitum spp alkaloids and therefore theoretically, even if a whole pack was consumed, there should be no significant toxicity expected, even in children. On this basis, the member suggested that the Committee

should focus its discussions on the issue of appropriate dose level of Aconitum spp alkaloids for children.

Given the inherent toxicity profile of Aconitum spp alkaloids, members remained concerned over the lack of evidence to support the safety of Aconitum spp preparations for treating children and agreed that the pattern of use and appropriate therapeutic dose level were also poorly understood by the Committee. On this basis, the Committee considered that a prudent approach was warranted in this case on public health grounds and agreed to limit the use of OTC Aconitum spp preparations to adults only until evidence became available to support a broader application of this herbal substance.

DECISION 2006/47 – 16 (VARIATION TO DECISION 2006/46-1)

The Committee agreed to vary Decision 2006/46-1, which was made at the February 2006 meeting, to partly harmonise with the New Zealand scheduling of Aconitum spp for therapeutic use. The Committee was of the opinion that unscheduled preparations with a maximum pack size equivalent to 1% of the lethal dose was unlikely to result in safety issues when used by adults but the Committee remained concerned over the lack of data to support the safety of using such products in younger individuals, particularly children. The Committee agreed that until such time that evidence became available, preparations containing Aconitum spp alkaloids greater than 0.02 mg per pack should be subject to evaluation at the registration process and that products intended for use in children and adolescents should be included in S4.

The Committee also agreed to clarify that products with a pack size equal or less than 0.02 mg of alkaloids of Aconitum spp would be exempt from the requirements of scheduling when the SUSDP amendments came into effect.

Schedule 2 – New entry

ACONITUM spp for therapeutic use in adults:

(a) in preparations for oral use in packs each containing 0.2 mg or less of total alkaloids **except** in packs containing 0.02 mg or less 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 mg or less of total alkaloids **except** in packs containing 0.02 mg or less of total alkaloids.

Schedule 4 – Amendment

ACONITUM - amend entry to read:

ACONITUM spp **except**:

(a) when included in Schedule 2;

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

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

11.6 SCHOENOCAULON OFFICINALE (SABADILLA)

PURPOSE

The Committee considered the MCC proposal to harmonise the scheduling of *Schoenocaulon Officinale* (Sabadilla) with New Zealand.

BACKGROUND

The October 2005 NDPSC meeting noted that the MCC June 2005 meeting recommended that Australia harmonise with the New Zealand scheduling of sabadilla which was reclassified to permit the continued sale of complementary products that were already on the market. The Committee agreed to foreshadow consideration of the matter at the February 2006 NDPSC meeting and sought comment from OCM on the proposal.

The February 2006 NDPSC meeting noted that the OCM agreed with the principle of the MCC proposed scheduling being based on the total alkaloids (the known toxic component) of *Schoenocaulon officinale*. However, OCM also highlighted that the **XXXXXXXX** submission provided for the reclassification of sabadilla was inadequate to support an informed opinion on appropriate safety levels for the alkaloids of sabadilla. In particular, the OCM questioned how the Lethal Dose of 180 mg was determined and, also, questioned the justification of 5-20 grains as a 'therapeutic dose'. The OCM concluded that as a NOEL did not appear to be available a safe long term intake could not be determined and that in the absence of a suitable safety evaluation being undertaken for *Schoenocaulon officinale*, the OCM could not provide an informed comment on the limits applied for the proposed scheduling of this substance.

A search of the SMARTI database yielded one prescription medicine sponsored by **XXXXXXXX** containing multiple ingredients including sabadilla at 6x. OCM had also advised that there were 8 homoeopathic medicines listed on the ARTG with *Schoenocaulon officinale* as an ingredient (in potencies ranging from 2 X to 6 X in multi-ingredient formulations). No information on sabadilla's clinical use was available from **XXXXXXXX** submission and OCM's advice did not include information on the approved indications in Australia.

The February 2006 meeting noted OCM's advice and agreed to defer consideration of the harmonisation proposal to the June 2006 meeting to allow OCM adequate time to conduct a safety review to determine safe and appropriate concentration and/or pack size limits that could be applied to S2 and exempt sabadilla preparations in Australia.

DISCUSSION

The Committee noted that **XXXXXXXX** submission to the June 2006 meeting proposed the following:

- Appendix G exemption be adopted for preparations containing 10 mg or less per litre or per kilogram of the alkaloids of *Schoenocaulon officinale* (sabadilla); and
- The recommended daily dose cut-off for *Schoenocaulon officinal*e (sabadilla) of 1 mg of the dry herbal material specified in the *Therapeutic Goods Regulations* (the Regs), Schedule 4, Part 4, Division 2 be removed on the basis of the Permitted Daily Exposure (PDE) value for sabadilla alkaloids of 2.4 mg/day.

XXXXXXXX submitted the following evidence to support the above proposals:

New information from the **XXXXXXXX** report

- The new toxicological data report on Sabadilla 10% tincture from **XXXXXXXX** showed LD_{50} levels for sabadilla of 4000 to 5000 milligrams/kg which were consistent with the LD_{50} levels cited in other literature reviewed recently. **XXXXXXXX** indicated that these values are considerably higher compared to the conservative LD_{50} of 300 milligrams/kg sabadilla on which their original submissions to New Zealand were based. The following information was included in **XXXXXXXX** report (TP-Sabadilla-September-2005):
    - Highest total alkaloid content in the dried ripe seeds of *Schoenocaulon officinale* (sabadilla) = 6%.
    - PDE is 2.4 milligrams alkaloids/day.
    - LD_{50} of 4000 milligrams/kg would correspond to 240 milligrams alkaloids/kg using the alkaloid concentration of 6%.
    - Single dose toxicity - lowest published lethal dose of veratrine is 143mg/kg for human (oral administration). [*Secretariat's note: The crude extract specified in **XXXXXXXX** is called veratrine or sabadilla, and contains cevadine, veratridine, cevadilline, sabadine, and cevine*]
    - Maternal NOEL = 50 milligrams/kg/day in rats using sabadilla seed powder with 4.83% alkaloids.
    - The reported lethal dose in humans is 10g for an adult (assumed to contain 6% alkaloids).

Evidence of levels of use from the **XXXXXXXX** report

- The Commission D (German Homoeopathic Commission) monograph, whilst indicating a "D2" (2x) potency for use in oral products (liquid dilutions, pilules, etc.), recommends the "D3" (3x) potency and above may be used for children younger than 12 years.
- The report's conclusion is that the "D3" (3x) potency "can be assessed as being safe for oral use" in relation to the maximum daily dose. A 3x is equivalent to 1 gram/L/kg of sabadilla.

Proposed Schedule Exemption

- The proposed Appendix G exemption would allow the availability of sabadilla products with 4x potency (100 milligrams/L/kg of sabadilla) containing up to 6 milligrams alkaloids/L/kg. The largest pack size on the market of 100mL of a sabadilla 4x potency would contain 10 milligrams sabadilla, equivalent to 600 micrograms of alkaloids, well below the PDE of 2.4 milligrams alkaloids/day if the whole bottle was consumed.
- The lowest published lethal dose of veratrine is 143mg/kg for human (oral administration) and therefore, a lethal dose for a 10kg-child would be 1.43 grams which is well above a 100mL pack size of 1 milligram or 600 micrograms of alkaloids.
- This schedule exemption would allow homoeopathic products that are currently general sale medicines on the New Zealand market to continue as general sale medicines under the Australian New Zealand Therapeutic Products Authority.

Recommended Daily Dose Cut-off of **XXXXXXXX** Products

- All products on the market have a recommended daily dose of sabadilla alkaloids well below the PDE of 2.4 milligrams alkaloids/day based on the largest pack size of 100 mL containing 1 milligram sabadilla alkaloids. A 1-mL dose of this product would contain 10 micrograms sabadilla alkaloids and a maximum daily dose of up to 10 doses would equate to 100 micrograms sabadilla alkaloids.
- 1 milligram of sabadilla could contain up to 60 micrograms sabadilla alkaloids, well below the PDE of 2.4 milligram alkaloids/day. The PDE corresponds to 40 mg sabadilla as a daily dose, using 6% alkaloids as the highest alkaloid concentration of sabadilla.

Therapeutic Dose

- **XXXXXXXX** agreed with OCM that the basis for the 5-20 grains as a 'therapeutic dose' was unclear. **XXXXXXXX** indicated that it was difficult at the time to find adequate therapeutic information on Sabadilla and that the information provided to MCC was based on published literature *[pg. 698, A Modern Herbal, by Mrs M, Grieve, published by Peregrine Books]* which showed that there was a large difference between the historical therapeutic use and the proposed cut-off points.

XXXXXXXX and **XXXXXXXX** did not comment on the harmonisation proposal but asked for the right to comment on any decision.

The Committee noted that advice from OCM was received and it stated that a safety evaluation of *Schoenocaulon officinal*e (Sabadilla) was unlikely to be undertaken at the present time, particularly as:

- An ingredient restriction rule applies for *Schoenocaulon officinal*e (Sabadilla) limiting the maximum daily dose to 1 mg equivalent of the dry herb;
- Sabadilla has a long history of safe use in the homeopathic tradition. There are currently any number of homeopathic products available on the market, where the concentration of Sabadilla is more dilute than 1000-fold dilution of the mother tincture. There is only one adverse reaction potentially implicating Sabadilla in the ADR database which could not be conclusively attributed to Sabadilla.
- The primary safety concern appears to relate to the alkaloid content. The theoretical LD_{50} for total sabadilla alkaloids is 240 mg/kg, based on studies on the use of Sabadilla dust as a pesticide. The study by Reigart and Roberts suggested that commercial Sabadilla is usually less than 0.5% and this would equate to a theoretical LD_{50} of 20 mg/kg.
- There have been no known adverse reactions in Australia to products labelled with the maximum recommended daily intake of 1mg of the dried herb equivalent. However, OCM did not object to the proposed concentration cut-off of 10 mg/kg for the alkaloids of sabadilla, as suggested by **XXXXXXXX**.

The Committee considered and discussed the following issues:

- Australia had been asked to harmonise with the New Zealand scheduling for sabadilla but the MCC harmonisation recommendation appeared to be no longer relevant based on **XXXXXXXX** new reclassification proposal. Members noted that the existing New Zealand classification was based on the pack size limits for exempt preparations on Sabadilla containing 6% maximum alkaloids with an estimated LD_{50} of 300 mg/kg Sabadilla which equated to 18 mg/kg alkaloids of Sabadilla (equivalent to 180 mg for a 10-kg child). The maximum pack size allowed for exempt preparations in New Zealand of 1.8 mg equated to 1% of the lethal dose for a 10-kg child. It was highlighted however that the maximum recommended daily dose specified for General Sale sabadilla preparations in New Zealand of 0.6 mg total alkaloids was 10x greater than what was currently allowed by the TGA for such preparations (6% of 1 mg dried herb = 0.06 mg total alkaloids). A member advised that the MCC considered this maximum recommended daily dose appropriate based on the safety information reviewed at the time and that the Pharmacy Only entry was included in New Zealand on the request of **XXXXXXXX** to allow the sale of mother tinctures in pharmacies.
- Members noted that the Commission D (German Homoeopathic Commission) monograph quoted in **XXXXXXXX** submission recommended a safe maximum daily dose level for oral use including in children younger than 12 years of up to $\leq$1 g/kg/L (3x or higher dilutions) of sabadilla or $\leq$60 mg/kg/L of alkaloids. It was also noted that the lowest published lethal dose for veratrine was 143 mg/kg for humans (oral administration) and therefore, a lethal dose for a 10kg-child would be 1.43 grams. Members considered the safety margin provided in the proposed exemption from

scheduling for preparations containing up to 10 mg per kilogram or litre of sabadilla alkaloids adequate and should not lead to safety concerns. Additionally, the Committee felt that **XXXXXXXX** had adequately addressed the safety aspects of its scheduling proposal.

- The Committee noted the summary table of **XXXXXXXX** products containing Sabadilla and Aconitum spp. for supply to Australia and/or New Zealand which showed that all products listed contained less than 10 mg/kg or L total alkaloids of *Schoenocaulon officinale* and that the recommended daily dosages complied with the current TGA restriction of 1 mg equivalent of the dry herb.

The Committee was advised that Appendix G of the existing SUSDP may be incorporated into the Schedules of the new SUSMP and that it may be appropriate to incorporate any future exemptions for dilute preparations into the Schedule entries.

DECISION 2006/47 - 17

The Committee agreed to exempt preparations containing 10 mg or less per kilogram or 10 mg or less per litre of the alkaloids of *Schoenocaulon officinale* (sabadilla). The Committee based its decision on the evidence provided which supported the safety of exempting such preparations and advice in relation to sabadilla's long history of safe use in the homeopathic tradition in Australia.

In regards to the proposal to delete the maximum daily dosage requirement of 1 mg equivalent of the dry sabadilla herb specified in the Regs, the Committee considered this a matter for the OCM and agreed that the proposal be accordingly referred to this Office for consideration.

Schedule 4 - Amendment

SCHOENOCAULON OFFICINALE (sabadilla) **except** in preparations containing 10 mg/kg or 10 mg/L or less of total alkaloids of *Schoenocaulon officinale*.

11.7 [ITEM DELETED]

11.8 IBUPROFEN

PURPOSE

The Committee considered the foreshadowed decision from the February 2006 NDPSC Meeting – the amendment of Schedule 2 ibuprofen entry to the exemptions for divided solid-dose products in relation to labelling for use in children aged 6 years or less.

BACKGROUND

In response to the recommendations of the *Review of Non-Prescription Analgesic – An Update*, released by the Medicines Evaluation Committee (MEC) in April 2003, the June 2003 NDPSC Meeting commenced a review of label requirements for non-prescription analgesics including NSAIDs, which took several meetings to finalise.

The June and October 2003 NDPSC Meetings agreed to exempt appropriately labelled small packs of oral ibuprofen 200mg from the requirements of scheduling. The October 2005 NDPSC Meeting amended the Schedule 2 entry for ibuprofen to transfer the warning statements to the *Required Advisory Statements for Medicine Labels* (RASML).

At the February 2006 NDPSC Meeting, the Committee noted a submission from MEC. This submission was prompted by an issue raised in the October 2005 MEC consideration of a chewable tablet containing 100 mg ibuprofen which was intended for use in children aged 2 to 12. The proposed labelling presented the tablets as unscheduled, as the product complied with the conditions and labelling requirements for the Schedule 2 ibuprofen exemption, including the statement "Unless your doctor has told you to, don't use [this product / name of product] in children 6 years of age or less".

In considering this issue Members noted the inconsistencies between the scheduling of products containing ibuprofen and paracetamol, i.e. that solid dose products containing ibuprofen were exempt from scheduling, with no age limit, provided the relevant label warnings were included and the product met the other specified requirements, whereas paracetamol products labelled for use in children aged 6 years or under were in Schedule 2. Members discussed MEC's advice regarding amending the Schedule 2 entry for ibuprofen to deny exemptions for solid-dose products if they were labelled for use in children aged 6 years or under. Some Members expressed the view that this would be a significant change for ibuprofen scheduling, and needed to be discussed separately, and should not be automatically included just for consistency with paracetamol. A Member indicated that there were a number of existing ibuprofen products in the market which might be affected by the potential change.

Accordingly, the Committee agreed to foreshadow a decision to amend the ibuprofen Schedule 2 entry to tighten the exemptions for solid-dose products so as to explicitly omit those labelled for use in children aged 6 years or under, which would become consistent with paracetamol scheduling.

DISCUSSION

Members ware advised that submissions received from both **XXXXXXXX** and **XXXXXXXX** support the foreshadowed decision, with the following comments:

- **XXXXXXXX** agrees that there was never any intention to allow the sale of unscheduled ibuprofen, let alone solid-dose preparations, labelled for children under the age of 6 years. **XXXXXXXX** agrees with the proposal to amend the entry for unscheduled ibuprofen medicines to clearly indicate that the medicine is not intended for use in children in this age group.

- **XXXXXXXX** notes that the *Required Advisory Statements for Medicine Labels* (RASML) is currently consistent with the SUSDP labelling requirements, even though the statements are numbered differently. If the NDPSC proposed change is endorsed, there will also be a need for the TGA to amend RASML in a timely manner so that consistency between it and the SUSDP is maintained.
- **XXXXXXXX** appreciates that it was an oversight in the schedule entry which has resulted in the unintended exemption of solid-dose ibuprofen in young children.
- **XXXXXXXX** asserts that an evidence based approach should be the basis for defining an appropriate lower age limit for exempt solid-dose ibuprofen preparations and requested that the Committee provide details as to the factors influencing any final recommendations. It is further asserted that there was an opportunity to determine, based on the general body of evidence, a suitable lower age limit. [Secretariat's note: no such evidence was provided in the **XXXXXXXX** comment].
- **XXXXXXXX** also noted that a specific area of concern may be the potential choking hazard posed for young children and asserted that data indicated that this was largely a concern for children under 3 who are still developing the ability to chew and swallow effectively, through muscular and dentition development in addition to experience.

Members recalled the following points in MEC's advice (from the minutes of the October 2005 MEC Meeting and the subsequent minute from MEC to NDPSC):

- **[**Section deleted**]**.
- The concern was that the tablet could pose a choking hazard to young children who may accidentally inhale the tablet instead of chewing it. It was suggested that if a chewable tablet product was only available from pharmacies, a pharmacist could at least ask purchasers whether the child can chew a tablet.
- Another concern is the inconsistency between the scheduling of products containing ibuprofen and paracetamol (the latter requires products labelled for use in children 6 or under to be Schedule 2).
- MEC recommended amending the Schedule 2 ibuprofen entry to remove the exemption for solid-dose products for use in children 6 or under.

Members noted that currently the RASML statements required on ibuprofen products for exclusion from scheduling includes statement 131 "*Unless a doctor has told you to, don't use [this product/insert name of product] in children 6 years of age or less*". While warning not to use the product in children under 6 the presence of the statement allowed divided preparations to be exempt from scheduling as long as they were compliant with the other conditions and labelling requirements. It suggested the Committee may not have specifically considered the prospect of tablet products for young children, i.e. the potential choking hazard, when making the initial decision to exempt divided preparations of ibuprofen from scheduling.

Regarding the query on the evidence based approach for defining an appropriate lower age limit for exempt solid-dose ibuprofen preparations, Members were advised that there is no accurate toxicology data or scientific calculation available for defining such an age limit for solid-dose ibuprofen, and formulation-related potential choking hazard for young children (generally defined as under 7 years old) was the major concern for this type of products according to MEC's advice. This consideration will lead to the consistency between ibuprofen and paracetamol scheduling.

The Committee noted that the wording of the pre-meeting gazette notice (Ibuprofen - Consideration of an amendment to the Schedule 2 entry for ibuprofen to remove the exemption for solid-dose products labelled for use in children aged 6 years or under) inadvertently implied that the current Schedule 2 entry for ibuprofen contained an exemption for solid-dose products labelled for use in children aged 6 years or under. It intended to address the current exemption from scheduling, with no age limit, provided the relevant label warnings were included. The foreshadowed amendment to the ibuprofen Schedule 2 entry included a new condition for qualifying for the scheduling exemption - "*not labelled for the treatment of children 6 years of age or less*". This condition conveyed the same intent as RASML statement 131 but was more strongly worded and actively constrained products of this type to Schedule 2.

DECISION 2006/47 - 18

The Committee agrees:

- to confirm the foreshadowed decision to amend the schedule 2 entry for ibuprofen to explicitly state that divided preparations labelled for use in children aged 6 years or under do not qualify for exemption from scheduling.
- to recommend to RASML that required statement 131 was no longer applicable.
- to advise MEC of the outcome.

Schedule 2 – Amendment

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;

(iv) not labelled for the treatment of children 6 years of age or less; and

(v) complies with the requirements of the Required Advisory Statements for Medicine Labels.

11.9 FLUPENTHIXOL

PURPOSE

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

BACKGROUND

Flupenthixol is a thioxanthene antipsychotic used mainly in the treatment of schizophrenia and other psychoses, but also for its antidepressant qualities. Flupenthixol can be administered orally or by deep intramuscular injection.

[Section deleted**]**

At its April 1994 meeting, the NDPSC noted the **[**sentence deleted**]**. The NDPSC recommended that flupenthixol decanoate be added to Schedule 4 of the SUSDP. At this time, the Committee did not consider flupenthixol's inclusion in Appendix K of the SUSDP.

DISCUSSION

The Committee noted that at the February 2006 NDPSC meeting, they had considered advice that was sought from **XXXXXXXX** regarding amisulpride. **[**Section deleted.**]**

As flupenthixol was not included in Appendix K, the Committee agreed to foreshadow the inclusion of flupenthixol in Appendix K for the June 2006 Meeting.

The Committee noted the following information from the approved Product Information for flupenthixol

- Pharmacological actions: in low to moderate doses (up to 100mg/2weeks) flupenthixol is non-sedating, while a sedative effect may be expected when higher doses are administered.
- Precautions: although flupenthixol is a relatively non-sedating drug, sedation may occur in some patients. Therefore, ambulatory patients should be warned about engaging in activities such as driving a car or operating machinery.
- Interactions with other medicines: flupenthixol may enhance the sedative effects of alcohol and the effects of barbiturates and other CNS depressants (including opioid analgesics).
- Adverse effects: CNS effects reported with flupenthixol include drowsiness, somnolence and fatigue.
- Overdosage: may cause somnolence or coma.

The Committee also noted that the Australian Pharmaceutical Formulary and Handbook (17th Edition) instructs that ancillary label 1 should be attached to flupenthixol upon dispensing. Label 1 states: "This medicine may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery."

The Committee also noted that the Consumer Medicine Information on **XXXXXXXX**, obtained from the MIMS Online website, states that "**XXXXXXXX** generally does not cause drowsiness, however drowsiness may occur in some patients."

The Committee were advised that no public submissions were received in response to the gazette notice.

A Member suggested that the information provided by **XXXXXXXX**, the PI and the CMI on the sedation potential of flupenthixol was sufficient to include flupenthixol in Appendix K. It was also noted that, as many similar antipsychotic drugs are already included in Appendix K, it would seem appropriate to include flupenthixol in that appendix for the sake of consistency.

DECISION 2006/47 – 19

The Committee agreed to include flupenthixol in Appendix K of the SUSDP. This decision was based on advice from **XXXXXXXX** as well as statements from the PI and CMI.

Appendix K - New entry

Flupenthixol

11.10 CLOTRIMAZOLE, CICLOPIROX AND AMOROLFINE – CLARIFYING SCHEDULE ENTRIES IN RELATION TO APPLICATION TO NAILS

PURPOSE

The Committee considered the scheduling of clotrimazole (11.10.1), ciclopirox (11.10.2) and amorolfine (11.10.3) when used for application to nails.

BACKGROUND

Specific backgrounds for clotrimazole, ciclopirox and amorolfine are set out under items 11.10.1, 11.10.2 and 11.10.3.

The August 1999 NDPSC Meeting agreed to include the definition of "Dermal Use" (application to the skin primarily for localised effect) in the SUSDP following a recommendation by the trans-Tasman Harmonisation Working Party (TTHWP). 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.

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. Members agreed that there was a need to provide clarity to stakeholders in terms of which definition covered 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 an antifungal treatment tincture for nail infections containing miconazole. The Committee concluded that as the Schedule 2 entry for miconazole used dermal, and as the definition of "Dermal Use" in the SUSDP refers to skin with no reference to nail, products like this could be captured by Schedule 4, an outcome which appeared unintended. The Committee agreed to foreshadow the following amendment to the Schedule 2 miconazole entry to allow application to nail:

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

The October 2005 NDPSC Meeting agreed, in order to clarify the scheduling of miconazole for use on nail and in the absence of any public health concerns, to confirm the above foreshadowed decision. The Committee also confirmed that while nail was covered by the current definitions of "External" and "Topical Use":

- nail was 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.

DISCUSSION

The Committee was advised that following the October 2005 NDPSC Meeting the Secretariat notified **XXXXXXXX** of the interpretation that "Dermal Use" did not cover application to nail, and requested that any inadvertent rescheduling of products as a result of this decision by brought to Committee's attention. A response from **XXXXXXXX** advised of a number of products, currently marketed as Schedule 2 or 3, which would be Schedule 4 as a consequence of the interpretation that "Dermal Use" did not cover application to nail. These included miconazole (addressed at the October 2005 NDPSC Meeting), clotrimazole (11.10.1) and ciclopirox (11.10.2). Additionally, amorolfine (11.10.3) was identified as being used in products for the treatment of nail and, while there was no inadvertent rescheduling issue for this substance, there was an opportunity to reword for consistency.

Members recalled that a number of arguments against considering nail to be dermal were considered at the June and October 2005 NDPSC Meetings, including:

- Pharmacokinetically there was 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.
- There may 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**, are specifically indicated not for infections involving nail – implying that some manufacturers viewed nail and skin as distinct.
- If nails were included in the "Dermal Use" definition then this in effect robbed the Committee of a definition for skin only.

Members also recalled the following points from the discussions at the June and October 2005 NDPSC Meetings regarding broadening entries using dermal to some other wording that would include nail:

- Changing an entry from 'dermal' to 'topical' or 'external' may imply that the poison can be applied to the ears, eyes or nose which may not be appropriate and would also require amendments to many Schedule 2 entries. Adding a specific reference to nail in an individual entry (as was done to resolve the miconazole issue at the October 2005 NDPSC Meeting) could also require amendments to some Schedule 2 entries.
- 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 were not the only products that the SUSDP covered. 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.

OUTCOME

The Committee confirmed the current definition of "Dermal Use" and that for medicines applied to the nail it was preferable to specify in the schedule entry a statement to the effect of "for application to nail".

11.10.1 CLOTRIMAZOLE

PURPOSE

The Committee considered the scheduling of clotrimazole where the substance was used for application to nails.

BACKGROUND

The background to the issue of definition of 'Dermal Use' and application to nails was detailed above (11.10).

Clotrimazole is an antimycotic drug belonging to the imidazole group of drugs, effective against a large number of fungal species. Its major application is for the treatment of tinea pedis and tinea cruris. Clotrimazole is also effective against a range of external candida infections.

The August 1977 NDPSC Meeting included clotrimazole in Schedule 4. The February 1985 NDPSC Meeting agreed to a request to reschedule 1% clotrimazole for the treatment of fungal infections of the skin to Schedule 3. The May 1990 NDPSC Meeting included 'topical' in the following Schedule 3 entry for clotrimazole to preclude a possible interpretation of the existing wording to include internal treatment:

CLOTRIMAZOLE for human use in topical preparations containing 1 per cent or less of clotrimazole, for the treatment of fungal infections of the skin.

The November 1990 NDPSC Meeting agreed to move the Schedule 3 entry above to Schedule 2. The entry was then reworded at the November 1996 NDPSC Meeting, to maintain consistency with the ketoconazole entry, to "for human use in dermal preparations". No explicit consideration appeared to have been made regarding application to nails.

The July 2005 NDPSC Meeting agreed that, in order to harmonise with New Zealand, the scheduling of a number of topical antifungals, including clotrimazole, be amended to allow exemptions when for the treatment of tinea pedis.

DISCUSSION

The Members noted that the **XXXXXXXX** response advised of the following clotrimazole products, considered Schedule 2 to now, which could be captured in Schedule 4:

- **XXXXXXXX** – ARTG indications include treatment of candidal skin infections including nail infections.
- **XXXXXXXX** – ARTG indications include candidal skin infections including nail infections.

Members recalled that at the November 1990 NDPSC Meeting Members noted that:

- Following topical use there was little systemic absorption of clotrimazole.
- There were very few adverse effects that occur commonly.
- Skin sensitivity develops on rare occasions.

Members also noted a submission from **XXXXXXXX** supporting moves to clarify scheduling entries for antifungal substances which were also indicated for the treatment of nails, as was done for miconazole.

DECISION 2006/47 - 20

The Committee confirmed that it had intended that applications of clotrimazole to the nail be Schedule 2 and agreed to amend the Schedule 2 clotrimazole entry to explicitly include a statement "application to the nails".

Schedule 2 – Amendment

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

11.10.2 CICLOPIROX

PURPOSE

The Committee considered the scheduling of ciclopirox where the substance was used for application to nails.

BACKGROUND

The background to the issue of definition of "Dermal Use" and application to nails was detailed above (11.10).

Ciclopirox is a broad spectrum antimycotic agent with some antibacterial activity used therapeutically as an antifungal agent. It is effective against pathogenic dematophytes and yeasts, and is used in the treatment of mild dermatoses.

The February 2001 NDPSC Meeting agreed to adopt a recommendation from the TTHWP to include ciclopirox in Schedule 2 (≤1%) and Schedule 3 for dermal use with a Schedule 4 parent entry.

The February 2002 NDPSC Meeting agreed to amend the Schedule 2 cut-off for ciclopirox dermal preparations to 2%. The wording of this entry was slightly amended at the October 2002 NDPSC. At that Meeting the Committee noted that there was one product **XXXXXXXX** containing ciclopirox for topical use. The Committee agreed at this time that the amendment (dermal preparations containing 2 per cent or less) would have no regulatory impact on this product (the issue of whether nails were captured by the definition of dermal did not appear to have been considered).

DISCUSSION

The Members noted that the **XXXXXXXX** response advised of the following ciclopirox product, considered Schedule 3 to now, which could be captured in Schedule 4:

- **XXXXXXXX** – ARTG indication is "For the topical treatment of mild to moderate onychomycosis, without lunular involvement, due to dermatophytes. Indicated for the treatment of fingernails and toenails".

The Committee was advised that both the Schedule 2 and 3 ciclopirox entries referred to 'dermal use' and that no nail product was currently captured by the Schedule 2 entry.

Members also noted a submission from **XXXXXXXX** supporting moves to clarify scheduling entries for antifungal substances which were also indicated for the treatment of nails, as was done for miconazole.

DECISION 2006/47 - 21

The Committee confirmed that it was intended that applications of ciclopirox to the nail be Schedule 3 and agreed to amend the Schedule 3 entry to explicitly include a statement "application to the nails". The Committee also agreed:

- that it was appropriate to extend the current 2% cut-off to schedule 2 for dermal use to include applications to the nail; and
- to amend the Schedule 2 entry to explicitly include "for application to the nails".

Schedule 2 – Amendment

CICLOPIROX in preparations for dermal use and for application to the nails containing 2 per cent or less of ciclopirox.

Schedule 3 – Amendment

CICLOPIROX in preparations for dermal use and for application to the nails **except** when included in Schedule 2.

11.10.3 AMOROLFINE

PURPOSE

The Committee considered the scheduling of clotrimazole including application to nails.

BACKGROUND

The background to the issue of definition of "Dermal Use" and application to nails was detailed above (item 11.10).

Amorolfine is a morpholine derivative with antifungal activity. It appears to act by interfering with the synthesis of sterols essential for the functioning of fungal cell membranes. Amorolfine is active in vitro against a wide variety of pathogenic and opportunistic fungi including dermatophytes, *Blastomyces dermatitidis*, Candida spp., *Histoplasma capsulatum*, and *Sporothrix schenckii*. It also has variable activity against Aspergillus spp. However, despite its *in vitro* activity, amorolfine is inactive when given systemically and this limits its use to topical application for superficial infections.

The February 1995 NDPSC Meeting agreed to include amorolfine in Schedule 4 following **XXXXXXXX** recommendation for approval of amorolfine for the treatment of dermatomycoses caused by dermatophytes, and cutaneous candidiasis.

The February 1998 NDPSC Meeting considered a rescheduling request from Schedule 4 to Schedule 2 for topical preparations containing 5% or less of amorolfine for the treatment of infections of the nail. The product before the Committee at this time, **XXXXXXXX**, contained 5% amorolfine and was for the treatment of **XXXXXXXX**. The Members did not support rescheduling.

Following receipt of post-meeting comment on this decision the Committee reconsidered the issue at the May and August 1998 NDPSC Meetings. The Committee agreed that on the information provided the potential for adverse effects associated with long term use of the substance was sufficiently low to support rescheduling to Schedule 3 for topical preparations containing 5% or less of amorolfine.

The August 1999 NDPSC Meeting considered a recommendation from the TTHWP to harmonise the amorolfine entries with New Zealand by introducing a Schedule 2 entry for topical preparations containing 0.25% or less of amorolfine. This was prompted through the existence in New Zealand, in addition to the 5% lacquer for nails, of a 0.25% cream for use in tinea pedis. The Committee supported a Schedule 2 entry for topical

preparations with 0.25% or less of amorolfine. There was no indication that this was to apply specifically to nails or any non-dermal surface. The Committee also agreed to include amorolfine in Appendix H.

The October 2005 NDPSC Meeting noted that there were no significant safety issues identified from Australian adverse reaction reports associated with the use of amorolfine topical cream products on the nails or on the foot. It was further noted that the June 2005 NDPSC meeting agreed to exempt from the requirements of scheduling certain antifungal agents indicated for the treatment of tinea pedis to harmonise with New Zealand but these did not include amorolfine. On the basis of the substance's safety profile, the Committee agreed to foreshadow a decision to harmonise the scheduling of amorolfine with New Zealand at the February 2006 meeting through inclusion of such an exemption. At the February 2006 NDPSC Meeting the Committee confirmed the foreshadowed decision on the grounds of harmonisation.

DISCUSSION

The Members noted that the **XXXXXXXX** response advised of the following product, containing amorolfine, registered as Schedule 3:

- **XXXXXXXX** nail lacquer (**XXXXXXXX** amorolfine, as hydrochloride).

This product was not affected by the determination that 'dermal' did not include nail as the Schedule 3 entry referred to 'topical use'. However, the Committee considered replacing 'topical use' with 'dermal use and for application to the nails' for consistency with other anti-fungals for application to nails.

The Committee was advised of the following two applications of amorolfine:

- For the treatment of nail infections caused by dermatophytes, yeasts, and moulds a lacquer containing the equivalent of 5% amorolfine is painted onto the affected nail once or sometimes twice weekly until the nail has regenerated. Treatment generally needs to be continued for 6 to 12 months. The single product currently registered in Australia is of this form. A product is also available in New Zealand.
- For skin infections, including dermatophyte infections, a cream containing the equivalent of 0.25% amorolfine can be applied once daily for at least 2 to 3 weeks (up to 6 weeks for foot infections) and continued for 3 to 5 days after clinical cure is achieved. A cream of this type was in use in New Zealand but registration has been discontinued.

Members also considered a submission from **XXXXXXXX** supporting moves to clarify scheduling entries for antifungal substances which were also indicated for the treatment of nails, as was done for miconazole.

The Committee noted that rewording the amorolfine entries for consistency with clotrimazole, ciclopirox and miconazole could potential represent a narrowing the

permitted use of this substance. The Members therefore agreed that an amendment for consistency was not appropriate in this case.

OUTCOME

The Committee confirmed the current wording in the schedule entries for amorolfine, noting a minor editorial amendment dealt with under item 21.1.2.2.

11.11 CODEINE – FURTHER CONSIDERATION OF THE SCHEDULING OF LIQUID PREPARATIONS CONTAINING CODEINE AS A SINGLE ACTIVE INGREDIENT

PURPOSE

The Committee further considered the scheduling of codeine linctus.

BACKGROUND

Australia is a signatory to the *United Nations Single Convention on Narcotic Drugs, 1961* (the Convention). As such, Australia is obliged to carry out the Convention's provisions within its own territory. One of the Convention's provisions is the list of narcotic drugs under international control. Part 2 of this list includes preparations of narcotic drugs exempted from Schedule II to Schedule III of the Convention. The first item in this part includes preparations of a number of substances, including codeine "when compounded with one or more other ingredients and containing not more than 100 milligrams of the drug per dosage unit and with a concentration of not more than 2.5 per cent in undivided preparations". Where this exemption does not apply, codeine preparations are subject to Schedule II of the Convention. Thus, as per the intention of the Convention (which bases its exemption less on the potential for harm to an individual and more on the potential for illicit diversion), all single (active) ingredient undivided preparations of codeine are not exempted from any provision of the Convention.

At the February 1968 and November 1969 PSC Meetings, a proposal was considered to include a Schedule 4 entry for codeine along the lines set out in the above exemption from Schedule II of the Convention. The Committee agreed that phrasing of this exemption to be placed word for word into the Schedule 4 entries for all of the opiates that were available in Australia at the time. The Schedule 4 entry for codeine was re-worded at the August and November 1979 Meeting to introduce a more stringent specification of the amount of codeine allowable per dosage unit (from an upper limit of 2.5% to 1%). The wording is the same in the current S4 entry.

The Committee also introduced a Schedule 2 entry and a Schedule 3 entry for codeine, the wording of which evolved over time, but which consistently required the codeine to be compounded with one or more other therapeutically active substances.

At the February 2006 NDPSC Meeting, the Committee confirmed the current scheduling of codeine and agreed that the interpretation of the current entry requires that any single active preparation of codeine, including liquid preparations, be classified as a Schedule 8 medicine. The Committee also requested that the TGA, sponsors of codeine linctus, and the Australian Pharmaceutical Formulary (APF) be approached to confirm that codeine linctus products were regarded as single active products.

DISCUSSION

The Members noted that advice was sought from sponsors to verify the scheduling status of codeine linctus products and to confirm that they are regarded as single-active products. **[**Sentence deleted**]** To date, only **XXXXXXXX** and **XXXXXXXX** had provided a response. In their responses, they stated that their codeine linctus products contained codeine phosphate as the single active ingredient, but were regarded to be Schedule 4 Prescription Only Medicines. One sponsor further stated that this scheduling status was given at the time of grandfathering.

The Members also noted that, given that sponsors of proprietary codeine linctus products generally use the APF formula, advice was also sought from the APF Editorial Board. The request was for confirmation that codeine linctus comprises only codeine as the active ingredient. Advice was received from the APF, stating that the Pharmaceutical Society of Australia advises that codeine linctus contains codeine phosphate as a single active ingredient and all other ingredients are considered to be excipients.

The Members noted that advice was also sought from the Drug Safety and Evaluation Branch (DSEB) regarding the status of codeine linctus products currently on the Australian Register of Therapeutic Goods (ARTG). A list has been provided by DSEB confirming the single-active status of codeine linctus products. However, there are some discrepancies in relation to the listed scheduling status of these products given that they are clearly described on the ARTG as single active preparations. This has been brought to the attention of DSEB and discussions on this matter are continuing.

The Members noted that, as confirmed by the APF, codeine linctus products are indeed single active and therefore Schedule 8 drugs. Members pointed out that many manufacturers and pharmacists are unaware of this, and as a result some codeine linctus products are incorrectly labelled as S4. Members discussed the need to confirm the S8 status of codeine linctus products, and agreed that the TGA, manufacturers and pharmacies should be made aware of the scheduling status of these products.

OUTCOME

The Committee agreed to confirm the Schedule 8 status of single-active codeine linctus products.

11.12 AZELASTINE HYDROCHLORIDE

PURPOSE

The Committee noted advice from the OTC Medicines Section relating to pack size, length of treatment and any age limitations imposed on azelastine topical eye preparations containing 0.05 per cent or less of azelastine.

BACKGROUND

Azelastine hydrochloride is an antihistamine H1 receptor antagonist initially developed as a tablet formulation for the prophylaxis and treatment of allergic rhinitis and bronchial asthma. It has been marketed as tablets and granules in Japan since 1987, and an intranasal formulation was subsequently developed for seasonal and perennial allergic rhinitis. In May 2000 the NDPSC supported the inclusion of azelastine in preparations for nasal use in S2.

The ADEC recommended the approval of azelastine hydrochloride **XXXXXXXX** at its February 2005 meeting for the 'treatment and prevention of the symptoms of seasonal and non-seasonal (perennial) allergic conjunctivitis in adults and children 4 years and older', with subsequent approval by the TGA. In October 2005, the sponsor requested that the NDPSC consider the rescheduling of this product from S4 to S2 based on evidence from overseas countries where it is available as a non-prescription product, and that a number of other ocular products registered in Australia for allergic conjunctivitis are S2 items.

The eye drop formulation was registered in 1998, in the EU/UK initially for seasonal allergic conjunctivitis in adults and children aged 12 years and in children aged 4 years and over from 1999. Azelastine eye drops are currently licensed in more than 50 countries worldwide including New Zealand and the US. An OTC switch from prescription only status was granted in 2002 in Denmark, and subsequently in the UK, Germany and Switzerland.

DISCUSSION

The Committee recalled that, at the February 2006 NDPSC Meeting, it had concurred with an external evaluator's report and agreed that azelastine in eye preparations containing 0.05 per cent or less of azelastine be included in Schedule 3 of the SUSDP. The Committee also agreed to include azelastine in Appendix H of the SUSDP on the basis of public health benefit (Decision 2006/46-25).

The Committee also noted that it had agreed to seek advice from the OTC Medicines Section on the need to limit pack size based on overseas experience of pack sizes up to 6mL, length of treatment as well as any age limitation.

The Committee also recalled that in post-Meeting correspondence, the Secretariat sought advice from the OTC Medicines Section (OTCMS) in April 2006. The advice related to pack size, length of treatment and any age limitations imposed on **XXXXXXXX**.

The Committee noted the response received from the OTCMS, which explained that they had not yet received an application from **XXXXXXXX** for the S3 product. The OTCMS was prepared to look at the issues raised by the NDPSC when the application was received, and to advise the Committee if the MEC recommended any restrictions or limitations in relation to pack size, length of treatment and age for inclusion in the SUSDP. It was suggested that, if the relevant information was required before the committee made a final decision on the rescheduling application, the Committee could consider looking at the relevant **XXXXXXXX** minutes and evaluation reports or referring the issue back to the applicant with a specific request for the information together with a report from a suitably qualified expert.

OUTCOME

The Committee noted the advice given by the OTC Medicines Section relating to pack size, length of treatment and any age limitations imposed on azelastine topical eye preparations containing 0.05% or less of azelastine.

12. PROPOSED CHANGES/ADDITIONS TO THE STANDARD FOR THE UNIFORM SCHEDULING OF DRUGS AND POISONS.

12.1 SUSDP, PART 4

12.1.1 MOMETASONE FUROATE

PURPOSE

The Committee considered an application to reschedule topical mometasone furoate 0.1% from Schedule 4 to Schedule 3 and to include mometasone furoate in Appendix H of the *Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP).

BACKGROUND

Mometasone furoate is a corticosteroid used topically for its glucocorticoid activity in the treatment of various skin disorders. It is usually employed as a cream, ointment, or lotion containing 0.1%. When applied topically, particularly to large areas, when the skin is broken, or under occlusive dressings, or when given intranasally, corticosteroids may be absorbed in sufficient amounts to cause systemic effects. That said, mometasone undergoes extensive first-pass hepatic metabolism and so short term use is generally without consequence.

At its160th Meeting in August 1992, the Australian Drug Evaluation Committee (ADEC) recommended approval for mometasone furoate for treatment of inflammatory and pruritic manifestations of corticosteroid responsive dermatoses, including psoriasis and atopic dermatitis. The lotion was also recommended for approval for treatment of psoriasis of the scalp and seborrhoeic dermatitis. The Committee then recommended a Schedule 4 entry for mometasone furoate at the DPSSC 68th Meeting in February 1993. This entry was amended to the parent compound mometasone from a TTHWP recommendation in August 1999.

While mometasone has been down-scheduled to S2 in aqueous nasal sprays for prophylaxis or treatment of allergic rhinitis, it has remained S4 for topically use (i.e. on the skin).

DISCUSSION

Members noted an application from **XXXXXXXX** to down-schedule topical mometasone furoate 0.1% from Schedule 4 to Schedule 3 and to include mometasone furoate in Appendix H, and the data submitted contain the following arguments:

- Mometasone furoate topical preparations have been available for many years on prescription with intranasal preparations being available without a prescription since 1999.
- Similar corticosteroid preparations have been reclassified to non-prescription status in Australia and elsewhere. Hydrocortisone is Schedule 2 here (and equivalent in New Zealand) and both clobetasone and alclometasone are Schedule 3. Some hydrocortisone preparations are GSL in the UK, with restrictions.
- While mometasone is prescription-only in other countries, many of these countries do not have a classification similar to Schedule 3.
- Mometasone furoate 0.1% compares favourably to betamethasone diproprionate, is more effective than hydrocortisone salts, betamethasone valerate and clobetasone. It has a better safety profile than betamethasone and an equivalent side-effect profile to hydrocortisone 1% and clobetasone 0.05%.
- There is no potential for abuse and little potential for harm from inappropriate use with labelling, pharmacist counselling and pack size restrictions.
- Most side effects are transient and mild. More serious side effects are usually only seen in chronic use over large body areas.
- Administration of nasal, oral or topical mometasone furoate has not produced any clinically significant decrease in serum cortisol levels & no symptoms of hypothalamic-pituitary-adrenal (HPA) axis suppression were observed in any patients treated topically up to 21 days. Available safety data shows that despite mometasone's moderate potency, there is a marked disassociation of potency from increased risk of side effects including dermal atrophy.

- While there have been reports of cutaneous atrophy after more than 3 weeks continuous therapy with several of the topical corticosteroids, studies with mometasone furoate 0.1% show that up to 3 weeks therapy leads to minimal side-effects occurring.
- Labelling will caution patients from using on skin infections (eg cold sores, shingles, chicken pox, thrush, tinea, ringworm & acne), in or around the eyes or groin or under occlusive dressing unless advised by a doctor to do so.

Members noted the evaluation report which raised the following points:

- The proposed labelling is for once-daily application for up to four weeks in adults and children over the age of two years for relief from inflamed and itchy skin conditions due to psoriasis, dermatitis and eczema. Included are warning statements required for topical corticosteroid preparations (see report for full list). CMI & approved PI will be consistent with current S4 product PI.
- Mometasone furoate has been available in Europe and the USA since 1987 and Australia since 1993. However, the evaluator points out that the corticosteroids which the sponsor lists as currently available without prescription in Australia (hydrocortisone, hydrocortisone acetate, clobetasone and alclometasone) are class 1 to class 2 (i.e. mild to moderate) corticosteroids whereas mometasone is a class 3 (potent) corticosteroid.
- The sponsor provided clinical trial data demonstrating efficacy of topical formulations for psoriasis, dermatitis & other paediatric & adult dermatoses when using for three to eight weeks.
- With over fifteen years of clinical use, adverse effects (AEs) include expected events of stinging, burning, pruritus, folliculitis, dryness, tenderness and skin atrophy. These AEs are clearly stated in the draft PI and are listed under warnings in draft CMI. Clinical trials in health male volunteers did not produce any clinical decrease in serum cortisols or symptoms of HPA axis suppression for up to 21 days topically or 36 days intranasally.
- Mometasone demonstrated only a low potential for overt skin atrophy even though it demonstrated clinical and statistical superiority over hydrocortisone in the treatment of psoriasis.
- The Adverse Drug Reactions Advisory Committee (ADRAC) reports back to 1990 show 162 reports where mometasone was suspected possible, probable or certain association. The majority of AEs were skin and subcutaneous tissue disorders The most prevalent skin disorders were dermatitis (9 reports), rosacea (11 reports), acne (5 reports), rash and urticaria (11 reports) and skin depigmentation (8 reports), consistent with the expected adverse event profile for this product as identified in the PI/CMI.
- The evaluator considered that the request for down-scheduling for the stated indication is appropriate; it is for common conditions which would be easily identified by the consumer, with appropriate counselling from the pharmacist. Abuse

potential is nil and harm risk is low for short term (up to four weeks) use. There is also a low risk of masking a serious disease. Appropriate warnings appear in the proposed CMI.

- Mometasone is Category B3; no studies have identified corticosteroids as teratogenic. There are statements in the proposed PI that topical corticosteroids should not be used by pregnant women in large amounts for prolonged periods. Caution in lactation also listed in proposed PI/ CMI.
- As mometasone would be the most potent topical corticosteroid available OTC, the evaluator does not recommend Appendix H inclusion as close monitoring of safety would be prudent before promoting it more broadly through advertising.

Members noted the sponsor's pre-Meeting response to the evaluator's report. The sponsor stated that while they felt the evaluator was being overly cautious in not recommending Appendix H inclusion, they would be prepared to re-apply for Appendix H listing after the first year of OTC use.

Members also noted the submission from **XXXXXXXX** which does not support an S3 listing for mometasone. **XXXXXXXX** maintains that, while pharmacists would be able to properly advise on and prescribe potent corticosteroids such as mometasone, it is more appropriate that pharmacists have access to moderate corticosteroids first. [*Secretariat note: both alclometasone and clobetasone are currently S3 for topical use*]. It is also stated that professional protocols and educational packages should be made available to pharmacists prior to down-scheduling.

The submission from **XXXXXXXX** opposing an S3 listing or Appendix H inclusion for mometasone was also noted. **XXXXXXXX** expressed concern that mometasone would be the first OTC potent corticosteroid and thus the safety of OTC use of potent corticosteroids is as yet unestablished.

The Committee also noted the submission from **XXXXXXXX** not supporting either the S3 listing or the Appendix H inclusion of mometasone. **XXXXXXXX** believe that while acute inflammatory eruptions, including allergic dermatitis and eczema, are generally responsive to mild (eg hydrocortisone) or moderate (eg clobetasone) corticosteroids, chronic, thickened or hyperkeratotic dermatoses would require potent or very potent corticosteroids. The latter conditions require ongoing medical supervision and so are not appropriate for self-medication. Both mild (hydrocortisone and hydrocortisone acetate) and moderate (alclometasone and clobetasone) are already available without prescription in Australia. **XXXXXXXX** discussed the risk factors for topical corticosteroids and suggest that, despite labelling restrictions, there is still potential for a potent corticosteroid such as mometasone to be inappropriately used and, in some cases, abused. **XXXXXXXX** recommended that opinion on this matter be sought from the Australasian College of Dermatologists (ACD). The Committee felt that, on further discussion, such action would be unnecessary.

Members were advised that **XXXXXXXX** sought clarification over the potentially ambiguous use of the word "topical" in the gazettal notice. "Topical use" is defined in Part 1 of the SUSDP as 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. Thus, use of the word "topical" could, in this instance, refer to either an intranasal preparation or a dermal preparation. **XXXXXXXX** had no further pre-Meeting comment in relation to this rescheduling application but reserved their right to provide post-Meeting comment.

[Section deleted**]**

A member pointed out that, although the moderately potent corticosteroids alclometasone and clobetasone are Schedule 3, neither of these substances is available as marketed OTC preparations (these substances were both rescheduled as a result of trans-Tasman harmonisation). Thus, the member reiterated the importance of appropriate pharmacist education prior to an S3 launch of dermal OTC preparations containing mometasone.

Another member raised the issue of the correlation between potency and side-effect profile: the data presented clearly indicated that the side-effect profile of mometasone warrants an S3 listing. That is to say that the theoretical concerns regarding the use of a potent corticosteroid are not realised in clinical practise as it is clear that mometasone does not cause adrenal suppression in short term dermal use.

Members agreed that mometasone furoate has safely been marketing in the US and Europe for almost 20 years, and in Australia for approximately 15 years. Members accepted the evidence provided by the sponsor and the opinion by the evaluator that, compared to other corticosteroids, mometasone furoate topical formulations showed high efficacy and low or equivalent potential adverse effects. Members also considered other S3 criteria for the 0.1% topical preparations of mometasone furoate, i.e. the indications easily identified by consumers, with appropriate counselling from the pharmacist, minimal abuse potential, low harm risks for short term use (up to 4 weeks) and a low risk of masking a serious disease. The Committee hence considered the down scheduling for the 0.1% topical preparations of mometasone furoate appropriate.

The Committee felt that Appendix H inclusion was not appropriate at this stage and that market experience for mometasone as an OTC product would need to be garnered before promoting this potent topical corticosteroid more broadly through direct-to-consumer advertising.

DECISION 2006/47 - 22

The Committee agreed to reschedule topical mometasone furoate 0.1% preparations from Schedule 4 to Schedule 3 on the basis of that the evidence provided by the sponsor adequately meets the criteria for Schedule 3 inclusion, and the concern in relation to inappropriate use of this potent corticosteroid would be waylaid through appropriate pharmacist eduction prior to product launch. The Appendix H inclusion is not supported

by the Committee at this stage due to a lack of OTC experience for this potent corticosteroid.

Schedule 3 – NEW ENTRY

MOMETASONE as the only therapeutically active substance in preparations for dermal use containing 0.1 per cent or less of mometasone in packs containing 30 g or less of the preparation.

Schedule 4 - AMENDMENT

MOMETASONE – amend entry to read:

MOMETASONE **except** when included in Schedule 2 or 3.

12.1.2 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 is a corticosteroid with both glucocorticoid and to a lesser extent mineralocorticoid activity. As cortisol it is the most important of the predominantly glucocorticoid steroids secreted by the adrenal cortex. Hydrocortisone is used, usually with a more potent mineralocorticoid, for replacement therapy in adrenocortical insufficiency. It may also be used for its glucocorticoid properties in other conditions for which corticosteroid therapy is indicated but drugs with fewer mineralocorticoid effects tend to be preferred for the long-term systemic therapy of auto-immune and inflammatory disease.

For topical application in the treatment of various skin disorders hydrocortisone and the acetate, buteprate, butyrate, and valerate esters are normally employed in creams, ointments, or lotions. Concentrations usually used have ranged from 0.1 to 2.5%. Although it is considered that hydrocortisone has fewer side-effects on the skin and is less liable to cause adrenal suppression than the more potent topical corticosteroids, it should be borne in mind, that this property may be considerably modified both by the type of formulation or vehicle used and by the type of esterification present; other factors that may also influence the degree of absorption include the site of application, use of an

occlusive dressing, the degree of skin damage, and the size of the area to which the preparation is applied.

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 SUSP, permitting the advertisement of hydrocortisone for rectal use.

The Committee considered a rescheduling application from **XXXXXXXX** for the abovementioned indication at the October 2005 Meeting. At that meeting, the Committee agreed that the scheduling of hydrocortisone should not be amended for two reasons. Firstly, the Committee had concerns 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 Committee also had concerns that the safety data presented by **XXXXXXXX** with the rescheduling application did not truly 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.

The Committee was informed that **XXXXXXXX** had submitted a new application seeking approval to reschedule the current Schedule 3 entry for hydrocortisone 0.5% for rectal use when combined with a local anaesthetic, to Schedule 2. This present application intended to demonstrate how the proposal complied with the NDPSC criteria for down-scheduling from S3 to S2 in addition to addressing the specific items raised by the Committee during their previous deliberations. The major points of the submission were as follows:

- Haemorrhoids and other anorectal conditions are currently regarded as conditions that are appropriate for self diagnosis and in the event of inadequate relief of symptoms, patients will be encouraged to seek advice from their doctor
- The sponsor claimed that **XXXXXXXX** is at least as safe and effective as other S2 treatments for haemorrhoids and, as prescribing is limited to seven days, if self misdiagnosis occurs, medical attention will be received (as symptoms will not be relieved) and this minimises the chance of AEs.
- The sponsor pointed out that significant post-marketing data are available, given that hydrocortisone and cinchocaine HCl have been marketed internationally since 1966. Post-marketing safety data have not revealed new findings.

- 0.5% hydrocortisone in packs of 30gm or less as a single active or when combined with an antifungal are already available as S2.
- **XXXXXXXX** committed to undertaking educational initiatives on anorectal disorders and treatment options for pharmacy assistants.

NDPSC Evaluation report

The Committee noted that the NDPSC evaluation report raised the following points:

- The sponsor summarised current scheduling status elsewhere. The point is made that rescheduling would be sought in New Zealand, should the NDPSC make a positive recommendation. In the UK, hydrocortisone with cinchocaine is POM although hydrocortisone with lidocaine was switched from Pharmacy Only to General Sales in 2004 for the symptomatic relief of anal and perianal irritation and pain associated with external haemorrhoids. **XXXXXXXX** (containing hydrocortisone) is a Prescription Product. The sponsor also pointed out that that hydrocortisone + cinchocaine ointment/ suppositories are registered in 55 countries.
- The sponsor pointed out that the same warning statements that currently appear on OTC haemorrhoid treatments will also be applied to **XXXXXXXX** labelling and package inserts.
- The evaluator agreed with the sponsor's point that use of topical and/ or anal preparations for haemorrhoids and other anorectal conditions without a pharmacist's supervision is warranted as they are self-limiting disorders which are appropriate for self-diagnosis, with initial diagnosis often having been confirmed by a medical practitioner.
- One of the reasons stated for not down scheduling at the October 2005 Meeting was concern over the use of such preparations on infected skin, thereby masking or exacerbating the condition. The sponsor pointed out that the risk of such an event is as likely as it is with currently available S2 products containing hydrocortisone (eg 0.5% hydrocortisone cream or 0.5% hydrocortisone + miconazole nitrate cream), although these products are not used rectally. The sponsor stated that they would consider the inclusion of additional warnings such as the following:
    - *"hydrocortisone may mask or exacerbate signs of infection. If a favourable response does not occur promptly that the use of this product should be discontinued and medical advice sought."*
- The sponsor proposed such warnings be placed on the CMI and/ or packaging. The evaluator agreed that such a warning statement would be appropriate.
- In regards to efficacy, the sponsor pointed to an open-label, multicentre general practice study where symptoms of second degree haemorrhoids were relieved (ref: Smith & Moodie *Current Medical Research and Opinion* 1988; 11: 34-40). The sponsor stated that there are no known drug-drug interactions and no documented

cases suggesting resistance. Due to low toxicity, chances of misuse or abuse are minimal.

- PSURs from 14 May 1995 to 25 May 2004 were included in **XXXXXXXX**. **XXXXXXXX** was an updated PSUR from 12 November 2003 to 25 May 2005 and this revealed no new trends or increased AE rates although, as with the previous submission, this report does not differentiate between route of administration or length of therapy. **XXXXXXXX** showed ADRAC reports with 16 reports to date with such AEs as pruritus ani, application site reaction, pyrexia, hypersensitivity, upper respiratory tract infection, urticaria, pruritus, rash, arrhythmia and myocarditis, most of these being minor, local reactions, easily identifiable by the patient. **XXXXXXXX** listed ADRAC reports for S2 preparations for anorectal condition but the evaluator noted that none of these preparations contain a corticosteroid.
- In conclusion, whilst the evaluator concurred with the Committee's concerns stated at the October 2005 Meeting, there appeared to be no particular or disturbing safety issues that have presented while this product has been available as an S3. The evaluator therefore considered it reasonable, from the public health perspective, that patients who don't receive relief from other OTC treatments may benefit from a low potency corticosteroid. The evaluator reiterated that the warning statements referring patients to doctors should symptoms not be promptly relieved must be made in either CMI or product labelling. With these provisos, the evaluator recommended down scheduling.

Pre-Meeting response from Sponsor

The sponsor was provided a copy of the evaluation report and the Committee noted the following points that were raised in the sponsor's pre-Meeting response:

- The sponsor concurred with the evaluator's recommendation to down schedule.
- The sponsor also concurred with the evaluator's observation that the use of rectal preparations without the supervision of a pharmacist for the treatment of haemorrhoids and other anorectal conditions is appropriate as these are self diagnosable conditions. Down scheduling would increase access to treatment options for those who find no relief from currently available S2 treatments.
- **XXXXXXXX** was in agreement with the evaluator's suggestion to include additional information in the CMI to advise patients of the potential for masking or exacerbation of infection and to seek medical advice should there not be prompt relief of symptoms. The following statement was proposed to be added to the current CMI:

  *"***XXXXXXXX** *may hide signs of infection."*

  The following statement already appears in the "How long to use it" section"

  "You should check with your doctor if you need to use it for more than 7 days."

  The following statement already appears on the carton labelling:

  "CAUTION: do not use for more than 7 days unless a doctor has told you to."

- A copy of the proposed amended CMI was included with proposed additional text underlined.

Pre-Meeting submissions

XXXXXXXX provided a pre-Meeting submission. They pointed out that both benign and malignant conditions share symptoms that can be masked by topical anal preparations, so there should be a relatively low threshold for referral and by maintaining hydrocortisone-containing preparations as S3, it will ensure that patient-pharmacist interaction will take place before such products are supplied. **XXXXXXXX** made the further point that down scheduling provides no substantial benefit to the consumer but would result in an increased risk of indiscriminate use of such products on potentially non-benign conditions

XXXXXXXX also provided a pre-Meeting submission. **XXXXXXXX** did not support this proposed down scheduling. They stated that prolonged use can thin tissues, result in systemic absorption and/ or mask symptoms of a more serious condition. They stated in conclusion that conditions for which this substance would be used required monitoring by a health professional and referral where necessary.

One member questioned the validity of the idea that haemorrhoids and other anorectal conditions are self-diagnosable and maintained that while an individual may know that something was wrong, they would not necessarily know that they had haemorrhoids. Furthermore, the argument that down scheduling this product would increase the number of S2 treatment options available is not necessarily a logical one as it is premised on people “shopping around” for effective haemorrhoid treatments and such action could be avoided if they were to seek advice from a pharmacist as to appropriate available treatments. Because of the nature of the condition being treated, a member suggested that it is appropriate that potential users of this product should always speak to a pharmacist.

The point was again raised that that, in some States, the ointment would remain behind the counter, should it be down scheduled to S2. In practical terms, this completely diminishes any argument regarding improved consumer access that might occur with down scheduling. Given that the suppositories must be refrigerated, again there would be no improved access with down scheduling because the consumer, in all likelihood, would need to request the product from a pharmacy assistant.

There was discussion regarding the fact that the safety profile of this product since being down scheduled from S4 to an S3 medicine would suggest it would be appropriately scheduled as an S2 medicine. One member put forward that the favourable safety profile while in S3 may be only due to the fact that pharmacists are intervening and therefore the product should appropriately remain in S3.

OUTCOME

The Committee agreed that the current scheduling of hydrocortisone and hydrocortisone acetate remained appropriate. Specifically, it was felt that the sponsor has again not

adequately justified exactly what advantage there would be to the consumer, should this product be down scheduled and therefore accessed without mandatory intervention of the pharmacist.

12.1.3 SUMATRIPTAN

PURPOSE

The Committee considered a proposal to include oral preparations of sumatriptan 50 mg in packs of 2 tablets for the treatment of migraine attacks in Schedule 3 (S3) and Appendix H of the SUSDP.

BACKGROUND

Sumatriptan is a selective serotonin agonist that acts at 5-hydroxytryptamine$_{1B/1D}$ receptor subtype (5-HT$_{1B/1D}$) receptors. Activation of 5-HT$_{1B}$ receptors produces vasoconstriction of cranial arteries while activation of 5-HT$_{1D}$ receptors on nociceptive trigeminal nerve afferents reduces the release of vasoactive neuropeptides and inhibits transmission via second-order neurons of the trigeminocervical complex. These actions correlate with relief of migraine headache.

Sumatriptan was first considered by the Committee at the August 1992 meeting. The Committee noted that the 157th ADEC meeting recommended approval for the registration of sumatriptan for the acute relief of migraine. The DPSSC included sumatriptan in S4 of the SUSDP. Sumatriptan tablets **XXXXXXXX** were first marketed in Australia in 1992.

At the June 2005 NDPSC Meeting, the Committee considered a proposal to include 2 tablets x 50mg or less of sumatriptan in Schedule 3. At that meeting, the Committee agreed that sumatriptan should remain a Schedule 4 substance because migraine is a condition that requires clinical diagnosis. In addition, the Committee felt that there was no evidence of a suitable, validated diagnostic tool for pharmacists to accurately diagnose migraine. The Committee also had concerns about the safety profile of sumatriptan, particularly its cardiovascular and cerebrovascular side effects, and the high prevalence of diagnosed and undiagnosed cardiovascular disease in the community and the Committee therefore felt this mandated the use of sumatriptan in the setting of medically supervised initiation and monitoring of therapy.

The Committee noted that all other 5-HT$_1$ agonists such as naratriptan and zolmitriptan are also classified as S4.

XXXXXXXX

The Committee was informed that **XXXXXXXX** had provided an updated dossier for reconsideration of the revised scheduling of sumatriptan. The data included in the dossier

has taken into account the June 2005 NDPSC Record of Reasons and in particular provides:

- Updated safety data including exposure data to enable consideration of the incidence of AEs in the context of a widely-used medicine.
- An updated version of the Migraine Questionnaire, as well as data from three studies to demonstrate its validation.
- A revised pharmacist education program developed in dialogue with professional pharmacy bodies.
- Revised information pertaining to the Appendix H listing, suggesting that inclusion in Appendix H take place after sumatriptan is rescheduled to allow time for pharmacist education and training to take place.

NDPSC Evaluation report

The Committee noted that the NDPSC evaluation report recommended that sumatriptan remain in S4. The following points were highlighted in the report:

- On 11 November 2005, the Medicines and Health Care Products Regulatory Agency (MHRA) reported that the Commission on Human Medicines (CHM) had approved both an application from **XXXXXXXX** to reclassify sumatriptan 50mg tablets and an application by **XXXXXXXX** to reclassify zolmitriptan 2.5mg tablets. The following conditions applied to the approval:

  (a) The PI should state that it is the patient's responsibility to inform their GP they are self medicating with a triptan.

  (b) Both companies should agree on a common Summary of Product Characteristics and harmonise the organisation of the PI.

  (c) A real-life monitoring study of pharmacists' recommendations should be carried out after the launch.

- A similar application to reclassify naratriptan 2.5mg tablets as pharmacy medicine was submitted by **XXXXXXXX** in March 2005 to Germany and this was approved on 21 December 2005.
- An expert report, authored by **XXXXXXXX** evaluates triptan cardiovascular safety by reference to retrospective epidemiological studies reference in the original evaluation report (Hall et al. Neurology 2004; 62: 563-568 & Velentgas et al Headache 2004; 44: 642-651). The first study (n = 63,575) garnered information from a general practice research database in the UK and showed no significant difference in frequency of cardiovascular disease amongst migraineurs treated with triptans compared to migraineurs not treated with triptans. The second study (n = 130,411), from a US health insurance database, demonstrated a suggestion of increased myocardial infarction rate ratio for recent triptan use, though this increase was not

statically significant nor was there an increase in all cause mortality with current or recent triptan use. These issues regarding the second study were raised in the initial evaluation report.

- The same authors referred to a **XXXXXXXX** study (n = 456). Patients were surveyed by 11 GPs and 18 pharmacists. Of the 156 patients deemed suitable for triptan therapy, 26 were deemed unsuitable by GPs which equates to nearly one in five patients recommended triptans by pharmacists inappropriately. While the authors stated the importance of clear diagnosis of migraine headache with thorough cerebral and cardiac risk stratification before commencing triptan therapy, they concluded that triptans available through pharmacists with the proposed questionnaire would appear unlikely to substantially increase the overall risk of cardiovascular events for these patients.
- The evaluator raised concern that the authors did not make reference to **XXXXXXXX** database referred to in the original evaluation where two-thirds of reports suggestive of myocardial ischaemia were from patients with no history of cardiac disease. The evaluator also pointed out that the authors made no declaration of conflict.
- The evaluator felt that the key point of the sponsor justifying down-scheduling is premised on the fact that simple analgesics are used in the initial treatment of migraine so pharmacists are now already intervening. The evaluator reiterated what was said in the previous evaluation, that triptans, due to their safety profile, cannot be described as simple analgesics and indeed the aforementioned **XXXXXXXX** study inferred a potential 20% increase in over-diagnosis of migraine in true non migraine sufferers.
- Efficacy of sumatriptan is well established and the evaluator is of the opinion that most placebo-controlled and comparator-controlled studies against sumatriptan with simpler analgesics demonstrate that sumatriptan has comparable or only slightly better efficacy compared to simple analgesics. The evaluator stated that the updated PSURs and ADRAC database information raised no new concerns from the original evaluation.
- The evaluator felt that the **XXXXXXXX** Migraine Treatment Questionnaire (intended for use by pharmacists in assisting diagnosis) has significant deficiencies. The example is used that the questionnaire does not incorporate currently established guidelines for treatment of acute migrainous attack, as per Therapeutic Guideline – Neurology 2002.
- **[**Section deleted**]**
- In conclusion, the evaluator stated that, due to rare but serious AEs, particularly with cardiovascular events and drug interactions, the incomplete questionnaire and concern over the current PBS-listed authority-required indication (“migraine attacks in patients receiving or who have failed to respond to oral therapy with ergotamine and other appropriate agents or in whom these patients are contraindicated”), this application to down-schedule should be rejected. A more comprehensive algorithm

and the need for tailoring of treatment to individual patients with more frequent attacks suggests close monitoring by a medical practitioner is required.

Pre-Meeting response from Sponsor

XXXXXXXX provided a six page response to the evaluator's report. In it they stated that the current submission specifically addressed issues raised in the June 2005 Record of Reasons. The sponsor expressed concern that much of the new data in this submission had been either overlooked or misinterpreted. Their rationale for this assertion was as follows:

- In reference to the **XXXXXXXX** database, the evaluator pointed out that two-thirds of the reports had no history. The sponsor clarified by saying that spontaneous reporting of AEs is often incomplete and so the correct interpretation of this observation is that CV risk factors were not documented in two-thirds of cases.
- Concerning the lack of disclosure of conflict-of-interest, the sponsor explained that the authors of the Expert Report **XXXXXXXX** were provided commercial-in-confidence information by **XXXXXXXX** and renumerated for their time. The sponsor pointed out that this is standard practise. The point was raised in the discussion that a more pertinent conflict is whether there was a past or present ongoing relationship between sponsor and author and this issue was not addressed.
- Contrary to the inference made in the evaluation report, **XXXXXXXX** was not assuming sumatriptan to be in the same class as simple analgesics; sumatriptan should only be used when a clear diagnosis of migraine has been made. The point the sponsor was making is that, as pharmacist discuss simple analgesic therapy in the treatment of migraine with patients, they are already managing migraine sufferers. Indeed, the sponsor referred to research showing migraineurs being as likely to consult their pharmacist as they are their GP. It was discussed that the comparison here may not be reasonable, given that the safety profile, mode of action and so on for triptans compared to simple analgesics are so completely different.
- In regards to consistency with current clinical standards, **XXXXXXXX** stated that use of OTC sumatriptan would remove the need to supply combination analgesics such as those with codeine and this is in line with National Prescribing Service (NPS) recommendations.
- The sponsor felt that the evaluation report seemed to cast some doubt over the superior efficacy of sumatriptan. The sponsor highlighted the comparison study between 1gm effervescent aspirin and encapsulated 50mg sumatriptan and puts forward that efficacy may be underestimated when a comparator product is encapsulated and the test product is not. **XXXXXXXX** with data from a patient preference study showing that the majority of patients (70%) preferred triptan over non triptan therapy ($p<0.001$) and greater efficacy was the main reason (62%) for choosing so.
- The sponsor felt that the position of the Migraine Treatment Questionnaire as a tool within a wider Pharmacy Protocol has been overlooked, thereby diminishing its

usefulness. These protocols have been developed with initial input by the **XXXXXXXX** and the **XXXXXXXX** and are entirely consistent with currently established guidelines for the management of migraine. The Committee expressed concern that the questionnaire didn't elaborate in strong enough terms the role of non-pharmacological therapy as first-line treatment of migraine such as lying down in a quiet room etc.

- The sponsor also contested the evaluator's point that the Migraine Treatment Questionnaire does not reflect current clinical guidelines as to when prophylaxis should be considered. The NPS guidelines quote more than 3 migraines per month; the questionnaire quotes more than 4 per month. More importantly, both the **XXXXXXXX** and medical consensus state that introducing prophylaxis should not solely depend on the frequency of migraine attacks. The sponsor reiterated that the questionnaire's purpose is to determine which migraine sufferers can be managed with OTC sumatriptan and which should be referred to their doctor. The sponsor further reiterated that this document is a work in progress. The Committee believed that suffering even one or two migraine attacks per month on a *regular* basis may be enough to warrant regular prophylactic treatment.
- The suggestion in the evaluation report that triptan therapy should only be considered once ergotamine therapy has failed is refuted by the sponsor. The sponsor suggests this interpretation may have been garnered from the wording of the PBS listing but this in no way reflects NPS guideline recommendations. Indeed, the sponsor made the statement that ergotamines are now rarely prescribed in Australia.
- In regards to the evaluator's reference to the PBS listing for sumatriptan, the sponsor pointed out that this is unrelated to the TGA approved indication for sumatriptan, namely for the acute relief of migraine attacks with or without aura. The PBS authority listing is unrelated to safety issues but rather pharmacoeconomic ones **[**sentence deleted**]**.
- In relation to the false positive rates, the sponsor believes the evaluator has incorrectly concluded that pharmacists over-diagnosed migraine in the studies listed **[**sentence deleted**]**. The false positive rate was the chosen endpoint to provide a measure of accuracy of the pharmacist assessment. The main concern was whether such false positives would have posed a safety concern, should sumatriptan have been supplied and the sponsor maintains that this concern was not borne out by the data. Moreover, the Australian validation study demonstrated that pharmacists identified more subjects with contraindications/ CV risks than the doctors in the study **[**sentence deleted**]**.
- In conclusion, **XXXXXXXX** felt the evaluation report had inappropriately recommended not down-scheduling, despite the fact that similar applications had been granted in the UK and Germany, based largely on the same data and pharmacists' tools.

Pre-Meeting submissions

XXXXXXXX provided a pre-Meeting submission in which they recommend that sumatriptan be down-scheduled to S3 without Appendix H inclusion. Their points were:

- Currently there are no triptans in S3 and **XXXXXXXX** believed that the development of a professional treatment protocol and education of pharmacy staff is essential to ensure that the place of sumatriptan in OTC management of migraine is understood. On this note, **XXXXXXXX** pointed out that much work is yet to be done on the Migraine Questionnaire before it can be widely distributed to pharmacists.
- **XXXXXXXX** preferred an implementation date of July 2007, should the Committee decide to down-schedule. **XXXXXXXX** felt that December, January & February are not good months for introducing newly available pharmacist-only medicines. They reiterated that the profession needs time to ensure that the majority of the pharmacy workforce is well prepared for an addition to the "OTC armamentarium" for the treatment of migraine.
- **XXXXXXXX** felt that advertising sumatriptan would be contrary to the Quality Use of Medicines (QUM) guidelines and so recommends exclusion from Appendix H. **XXXXXXXX** pointed out that the Committee have previously shown concern about the safety profile of sumatriptan and that migraine needs a thorough diagnosis. As such, brand advertising would be inappropriate.

XXXXXXXX reiterated the comments made in a pre-Meeting submission when the Committee considered down-scheduling sumatriptan in June 2005. These were:

- After initial diagnosis, migraine is a self-recognisable condition, with early initiation of therapy ensuring better treatment outcomes. Thus, pharmacists are well placed to provide professional advice and optimal treatment.
- **XXXXXXXX** aired concern over the PBS authority listing and the fact it is not first line therapy. Thus, additional considerations may be required of the Committee in this near unique down-scheduling situation.
- **XXXXXXXX** also made the point that sponsors must invest resources and work with the profession to provide appropriate materials for pharmacists. A longer lead time prior to implementation was suggested and Appendix H inclusion was opposed.

The Committee noted that **XXXXXXXX** was in favour of including sumatriptan in Schedule 3. In their submission, mention was made of known precautions/ contraindications including SSRIs and nitrates and so **XXXXXXXX** recommended change only after a set of guidelines, agreed to by professional pharmacy associations, were in place. **XXXXXXXX** did not endorse Appendix H inclusion.

The Committee also noted an email submission sent to the Secretariat on behalf of **XXXXXXXX**. Briefly, down-scheduling was supported as the efficacy of sumatriptan has been established and there isn't potential for abuse.

XXXXXXXX, one of the pharmacists involved in the development and trialling of **XXXXXXXX** Migraine Questionnaire provided a late submission commending the

materials that were used in the study and stating her confidence that, with said materials, pharmacists will have the tools and knowledge they need to appropriately manage OTC supply of sumatriptan.

[Section deleted**]**

One Committee member suggested that, should sumatriptan be down-scheduled, it would be accessed through pharmacists by the same kind of patient as those whom access salbutamol in so much as there are patients for whom sumatriptan is established safe and effective therapy and, should they require it for immediate treatment, they would benefit from not having to obtain a prescription beforehand. The Committee discussed the fact that, should a pattern of migraine be established in a particular patient, such a patient could have a prescription on-hand, in case of a migraine attack. Indeed, these patients are often advised by their doctor to always keep a spare dose of sumatriptan at home. As well as this possible avenue for ensuring immediate access to such established pattern migraineurs, the provisions within State and Territory legislation which allow an emergency three day supply of prescription medicines in certain circumstances could be used. Thus, there is no question of lack of access for these patients.

Concern was raised that certain patients may overuse sumatriptan if they find that the drug effectively treats their migraine, and this brought up the issue of chronic migraine and so-called rebound headache. Further to this and of much greater concern to the Committee was discussion over emerging evidence that sumatriptan is not entirely "migraine specific" and has been shown to relieve pain in some non migraine conditions. Indeed, there have been case reports of subarachnoid haemorrhage responding to sumatriptan in established pattern migraineurs. Recent clinical papers have put forward the biologically plausible theory that neither ergots nor triptans exclusively relieve pain associated with migraine but indeed will do so for any process that activates trigeminal fibres, including migraine, subarachnoid haemorrhage and meningitis. The Committee felt that this emerging safety concern needed to be further looked into.

The Committee recalled that, when they last considered the rescheduling of sumatriptan at the June 2005 Meeting, the **XXXXXXXX** opposed rescheduling. It was suggested that it would be highly useful for the Committee to seek a consensus expert opinion from the **XXXXXXXX** as to increasing access to consumers with pharmacists' supervision. It was further considered that the **XXXXXXXX**, should they conclude that increased access to consumers with pharmacists' supervision is appropriate, could provide valuable input into the development of the Migraine Questionnaire. Concerns were raised by the Committee that, while this questionnaire had received input already from the **XXXXXXXX** and the **XXXXXXXX**, input from **XXXXXXXX** was yet to be garnered.

OUTCOME

The Committee agreed to defer a decision on the rescheduling of sumatriptan until advice has been sought from the **XXXXXXXX** on the following issues:

- to comment on the appropriateness of triptans as Schedule 3 medicines; and
- to provide opinion on the emerging safety concerns of both triptans and ergots potentially masking the symptoms of either meningitis or subarachnoid haemorrhage; and
- to provide input on the proposed Migraine Questionnaire.

12.2 SUSDP, PART 5

No items were considered.

13. MATTERS REFERRED BY THE AUSTRALIAN DRUG EVALUATION COMMITTEE (ADEC)

13.1 NEW SUBSTANCES (NOT SEEN BEFORE BY NDPSC)

13.1.1 PLASMA-DERIVED FACTOR VIII

PURPOSE

The Committee considered the scheduling of a new medicine, plasma-derived factor VIII.

BACKGROUND

Plasma-derived factor VIII is a protein involved in blood coagulation, and is used for treating patients with haemophilia A.

The December 2005 ADEC Meeting recommended approval of a submission by **XXXXXXXX** to register **XXXXXXXX** for "treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency)".

[Sentence deleted**]**

DISCUSSION

The Committee noted that **XXXXXXXX** had in May 2006 requested a 12 month consultation period between the NDPSC and the blood sector, to allow adequate time to raise and discuss concerns and issues associated with the possible scheduling of blood products.

OUTCOME

The Committee agreed to defer consideration of this matter until completion of the twelve month consultation period suggested by **XXXXXXXX**, in which **XXXXXXXX** will form a working party, consult key stakeholders and report back to the NDPSC.

13.1.2 BORTEZOMIB

PURPOSE

The Committee considered the scheduling of a new medicine, bortezomib.

BACKGROUND

Bortezomib inhibits proteasomes, which are enzyme complexes that break down regulatory proteins of the cell cycle. The inhibition of proteasomes disrupts tumour cell turnover and induces apoptosis.

The December 2005 ADEC Meeting recommended approval of a submission by **XXXXXXXX** to register **XXXXXXXX**, for "the treatment of multiple myeloma patients who have received at least one prior therapy".

[Sentence deleted**]**

DISCUSSION

[Section deleted**]**

The Committee also noted the following from the Micromedex monograph on bortezomib:

- Bortezomib has many side effects, the most common of which include asthenia, gastrointestinal disturbances, peripheral neuropathy, fever, thrombocytopenia, neutropenia, anaemia, and orthostatic hypotension. The dose should be reduced, or treatment withdrawn, according to the degree of toxicity experienced, particularly when peripheral neuropathy, neuropathic pain, and haematological toxicity occur.
- Bortezomib should be used with caution in patients with hepatic impairment, congestive heart failure, amyloidosis, and those with risk factors for seizures.
- Care should be taken when combining bortezomib with oral antidiabetics or drugs associated with peripheral neuropathy or hypotension.

The Committee noted that no public submissions were received in response to the gazette notice.

DECISION 2006/47 – 23

The Committee agreed that bortezomib be included in Schedule 4 of the SUSDP:

- On the grounds that the condition being treated necessitates appropriate medical diagnosis and the safe use of this medicine requires patient management and monitoring by a medical professional.

- To harmonise scheduling with New Zealand.

Schedule 4 - New entry

BORTEZOMIB

13.1.3 AZACITIDINE

PURPOSE

The Committee considered the scheduling of the new medicine, azacitidine.

BACKGROUND

Azacitidine is an antimetabolite antineoplastic agent which also inhibits cellular pyrimidine synthesis, commonly used in the treatment of myelodysplastic syndrome. Myleodysplastic syndrome (MDS) represents a heterogeneous hematopoietic disorder in which mature blood cells are derived from an abnormal multipotent progenitor cell. Refractory anemia (RA) with or without ringed sideroblasts can persist for years, but RA with excess blasts (RAEBs) or RAEBs in transformation to leukemia (RAEBt) exhibit an accelerated course. Most patients with high-risk MDS die within 1 year from progressive bone marrow failure attributable to hemorrhage or infection. In 35% to 40% of patients, transformation to acute leukemia occurs, which is often refractory to present therapy.

[Section deleted**]**

DISCUSSION

The Committee recalled that under Therapeutic Goods legislation, there are a number of avenues whereby a drug can be accessed, even though it is not on the Australian Register of Therapeutic Goods (ARTG). These avenues include personal importation, the Special Access Scheme (SAS), and clinical trials. With this in mind, the Committee considered whether it was appropriate to schedule azacitidine even though no marketed product is approved for use in either Australian or New Zealand.

[Section deleted**]**

The Committee also noted the following from the Micromedex monograph on azacitidine:

- Azacitidine causes anaemia, neutropenia, and thrombocytopenia, and therefore blood counts should be monitored. It also commonly causes erythema at the injection site, fever, and gastrointestinal disturbances including nausea and vomiting, diarrhoea or constipation.

- Azacitidine is contra-indicated in patients with advanced hepatic malignancies, because of rare reports of progressive hepatic coma and death in such patents. It should be used with caution in renal impairment.
- Adverse renal effects of azacitidine include abnormalities in renal-function tests, renal tubular acidosis, and renal failure.

[Section deleted**]**

DECISION 2006/47 – 24

The Committee agreed to include azacitidine in Schedule 4 of the SUSDP on the grounds that the condition being treated necessitates appropriate medical diagnosis and the safe use of medicine.

Schedule 4 - New entry

AZACITIDINE

13.2 FOR INFORMATION (SUBSTANCES ALREADY SCHEDULED)

13.2.1 [ITEM DELETED]

13.2.2 FULVESTRANT

PURPOSE

The Committee noted the Australian Drug Evaluation Committee's consideration of a new product, **XXXXXXXX**, fulvestrant **XXXXXXXX**.

BACKGROUND

Fulvestrant is an oestrogen antagonist that down-regulates the oestrogen receptor protein and blocks the actions of oestrogen.

The February 2006 NDPSC meeting agreed to include fulvestrant in Schedule 4 (S4) of the SUSDP to harmonise with New Zealand scheduling.

At the December 2005 ADEC meeting, **XXXXXXXX** containing fulvestrant **XXXXXXXX**, was recommended for approval for the indication "the treatment of post-menopausal women with hormone receptor positive locally advanced or metastatic breast cancer, who have progressive disease following prior tamoxifen therapy".

OUTCOME

The Committee noted the recommendation of the Australian Drug Evaluation Committee to register **XXXXXXXX** fulvestrant **XXXXXXXX**, for the indication 'the treatment of

post-menopausal women with hormone receptor positive locally advanced or metastatic breast cancer, who have progressive disease following prior tamoxifen therapy".

13.2.3 ANECORTAVE ACETATE

PURPOSE

For the Committee to note the recommendation of the ADEC to register a new product, **XXXXXXXX** anecortave acetate **XXXXXXXX**.

BACKGROUND

Anecortave acetate is an inhibitor of angiogenesis. It performs this function by blocking vascular endothelial cell proliferation and the synthesis of proteolytic enzymes that cause new vessel growth.

The February 2006 NDPSC meeting agreed to include fulvestrant in Schedule 4 (S4) of the SUSDP in order to harmonise with New Zealand scheduling.

At the December 2005 ADEC meeting, **XXXXXXXX** containing anecortave acetate **XXXXXXXX**, was recommended for approval for the indication "the treatment of subfoveal choroidal neovascularisation (CNV) due to exudative age-related macular degeneration (AMD) where there is a classic component". The minutes from the December 2005 ADEC Meeting were not available to the NDPSC at its February 2006 Meeting.

OUTCOME

The Committee noted the recommendation of the Australian Drug Evaluation Committee to register **XXXXXXXX** anecortave acetate **XXXXXXXX**, for the indication "the treatment of subfoveal choroidal neovascularisation (CNV) due to exudative age-related macular degeneration (AMD) where there is a classic component.

13.2.4 ERLOTINIB

PURPOSE

The Committee noted the Australian Drug Evaluation Committee's consideration of a new product, **XXXXXXXX**, erlotinib **XXXXXXXX**.

BACKGROUND

Erlotinib targets the human epidermal growth factor receptor type 1 pathway, which is critical to cell growth in some cancers. Erlotinib therefore has the ability to block tumour cell growth.

The February 2006 NDPSC meeting agreed to include erlotinib in Schedule 4 (S4) of the SUSDP to harmonise with New Zealand scheduling. At the December 2005 ADEC meeting, **XXXXXXXX**, erlotinib **XXXXXXXX**, was recommended for approval for the indication "the treatment of patients with locally advanced or metastatic non-small cell lung cancer who have disease progression following prior chemotherapy".

OUTCOME

The Committee noted the recommendation of the Australian Drug Evaluation Committee to register **XXXXXXXX**, erlotinib **XXXXXXXX**, for the indication "the treatment of patients with locally advanced or metastatic non-small cell lung cancer who have disease progression following prior chemotherapy".

13.2.5 POSACONAZOLE

PURPOSE

The Committee noted the Australian Drug Evaluation Committee's consideration of a new product, **XXXXXXXX** containing posaconazole **XXXXXXXX**.

BACKGROUND

Posaconazole is a broad-spectrum oral antifungal that has been developed for the treatment of invasive fungal infections, many of which are resistant to all other available treatments.

The February 2006 NDPSC meeting agreed to include posaconazole in Schedule 4 (S4) of the SUSDP to harmonise with New Zealand scheduling.

At the December 2005 ADEC meeting, **XXXXXXXX** containing posaconazole **XXXXXXXX**, was recommended for approval for the indication: "treatment of the following fungal infections in patients 13 years and older:

- invasive aspergillosis in patients intolerant to, or with disease refractory to, amphotericin B, itraconazole or in limited numbers voriconazole or echinocandins;
- fusariosis, zygomycosis, coccidiodomycosis, chromoblastomycosis, and mycetoma in patients intolerant to, or with disease refractory to, other therapy".

OUTCOME

The Committee noted the recommendation of the Australian Drug Evaluation Committee to register **XXXXXXXX** containing posaconazole **XXXXXXXX**, for the above-mentioned indication.

13.2.6 ENTECAVIR

PURPOSE

The Committee noted the Australian Drug Evaluation Committee's consideration of new products, **XXXXXXXX** entecavir **XXXXXXXX** and **XXXXXXXX** containing entecavir **XXXXXXXX**.

BACKGROUND

Entecavir is a nucleoside reverse transcriptase inhibitor with selective antiviral activity against hepatitis B virus.

The February 2006 NDPSC meeting agreed to include entecavir in Schedule 4 (S4) of the SUSDP to harmonise with New Zealand scheduling.

At the February 2006 ADEC meeting, **XXXXXXXX** containing entecavir **XXXXXXXX** and **XXXXXXXX** containing entecavir **XXXXXXXX** were recommended for approval for the indication "treatment of chronic hepatitis B virus infection in adults 16 years or older with evidence of active liver inflammation in patients for a period no longer than 48 weeks."

OUTCOME

The Committee noted the recommendation of the Australian Drug Evaluation Committee to register **XXXXXXXX** containing entecavir **XXXXXXXX** and **XXXXXXXX** containing entecavir **XXXXXXXX**, for the indication "treatment of chronic hepatitis B virus infection in adults 16 years or older with evidence of active liver inflammation in patients for a period no longer than 48 weeks".

14. OTHER MATTERS FOR CONSIDERATION

14.1 CAFFEINE

PURPOSE

The Committee considered:

- the issue of potential misuse of stimulant/alerting caffeine products; and
- scheduling of single active caffeine.

BACKGROUND

Caffeine, when a single active, is currently unscheduled. However, caffeine is included in the Schedule 4 aspirin and salicylamide entries as a result of a 1977 NHMRC

recommendation that any analgesic combination including caffeine should be included in Schedule 4 due to the association of analgesic nephropathy with the use of these products.

At the November 1986 NDPSC Meeting the Committee discussed a letter raising concerns about caffeine as an additive in foods and the open sale of **XXXXXXXX** caffeine tablets. The Committee at this time considered that there was not sufficient evidence of a problem with **XXXXXXXX** tablets to warrant scheduling.

DISCUSSION

The Committee considered an enquiry from **XXXXXXXX** raising concerns about misuse of **XXXXXXXX** by her daughter. Members noted:

- The product was available OTC at local corner shops. **XXXXXXXX** contained **XXXXXXXX** of caffeine and appeared harmless when taken normally.
- **XXXXXXXX** had recently found empty packets of this product in her 16 yr old daughter's room. **XXXXXXXX** asserted that her daughter and daughter's friends:
    - Did not adhere to the recommended dosage but instead took two or three doses at a time to give them "a lift".
    - Used the product regularly and not occasionally as the packet warning stated.
    - Considered the product harmless because it was available OTC.
- **XXXXXXXX** did not consider the product harmless when taken in this way and questioned the need for this product to be sold at a corner shop instead of a pharmacy.

The Committee considered the following points from advice received from **XXXXXXXX** on the issue of caffeine, whether caffeine should be considered for scheduling and the potential regulatory impact on products if single active caffeine were scheduled:

- **XXXXXXXX** was a registered OTC product as caffeine did not meet the definition of a complementary medicine (nor was it Listable). Caffeine was only approved as a component of a Listable ingredient e.g. *Paullinia cupana* (guarana).
- There were a considerable number of herbal substances that contained caffeine which were approved for use in Listed medicines - therefore the regulatory impact of scheduling single active caffeine would be considerable. **[**Sentence deleted**]**
- Two lists were provided - one of products containing caffeine as an active and one of products containing caffeine as an excipient.
- The *Australian Guidelines for Registration of OTC Medicines* stated that - "Reservations are held about the use of caffeine as a stimulant or alerting agent in medicines. All such preparations are required to have the following adult dose:
    - 100 mg/dose maximum, which may be repeated at 3 hourly intervals. Do not exceed 600 mg in 24 hours.

- The label should state that the dose should be reduced if tea, coffee or other products containing caffeine are taken.
- The use of caffeine in weight control preparations is considered unsuitable."

- **XXXXXXXX** indicated that they had received no reports of abuse for any caffeine-containing product.
- **[**Section deleted**]**

The Committee also noted that **XXXXXXXX** had advised that caffeine did not appear to be an issue.

Members also considered a pre-meeting comment from **XXXXXXXX** which asserted that there was no case for a change to the current unscheduled status of caffeine. Members particularly noted:

- **XXXXXXXX** contains about as much caffeine as in a cup of strong coffee (compared to energy drinks like **XXXXXXXX** and **XXXXXXXX** which contain 80mg).
- They have marketed caffeine tablets for several decades and have received no reports of abuse nor heard of any reports of abuse of **XXXXXXXX** tablets. A review of their records going back to 1998 revealed 4 adverse drug reaction reports; one was for heartburn, one for an allergic reaction, and two for headache and nausea. There was also a possible ADR reported by an epileptic. None of these reports came from students and none was associated with abuse.
- As a matter of responsible company policy, the advertising of **XXXXXXXX** has been deliberately low key over many years. Neither promotion nor labelling encourages over consumption.
- Tablets containing caffeine are available over the counter, for general sale, in many countries, including the USA, UK, and New Zealand. In the US, tablets containing 200mg caffeine are permitted, while in Australia, 100mg per tablet is the maximum.
- Caffeine is found in many products such as coffee and tea, and in therapeutic products other than simple caffeine tablets, such as guarana tablets. As a result, the safety of caffeine has been extensively studied, and the view of serious authorities all around the world is that it is safe for ingestion in moderate amounts.

Members also noted the following information attributed by **XXXXXXXX** to various expert bodies:

- "..the available evidence on caffeine consumption suggests that with average intakes the pharmacological effects are minor. These effects largely disappear with long-term high intakes, with the development of tolerance. Evidence for long-term detrimental effects or life-threatening toxic effects is generally lacking." (NHMRC – "Caffeine, Cola Drinks and Children").
- "The evidence available appears to indicate that the consumption of up to 450mg of caffeine daily does not present a significant health problem to normal persons. Its

effects such as increased alertness, anxiety, respiratory stimulation and irritability may be viewed by some as desirable to some extent and undesirable by others. Regular ingestion of moderate amounts of caffeine i.e. up to 450mg daily appear(s) to be harmless for the majority of people. Pregnant and breast feeding women would be advised to restrict their intake of caffeine." (Australian Journal of Pharmacy, December 1988: 891-892).

Members note that, according to information from the Sports Dieticians Australia website, in January 2004 caffeine was removed from the 2004 World Anti-Doping Agency (WADA) Prohibited List.

The Committee also noted a submission from **XXXXXXXX** objecting to any proposal to schedule caffeine for therapeutic use, in that it would result in a market environment inconsistent across the food-medicine interface. **XXXXXXXX** noted:

- Doses of 100 mg –500 mg of caffeine were indicated for use in mental fatigue. Similarly, products containing complementary ingredients such as guarana were indicated for endurance and stamina and typically contain caffeine up to 100 mg daily dose when from a herbal source.
- Standard 2.6.4 of the *Australian Food Code (Formulated Caffeinated Beverages)* stated that products complying with the Code must contain no less than 145mg/L and no more than 320 mg/L of caffeine. Such products typically make claims for endurance and mental fatigue which are not prohibited health claims on such foods, but as such are equivalent to claims made on many therapeutic goods in pharmaceutical dose form containing caffeine.

Members also noted that the Australia New Zealand Food Authority had established an Expert Working Group to examine the wider aspects of the safety of dietary sources of caffeine. The task for the group was to examine the potential for acute toxicological/pharmacological effects at low doses, the potential for addictive effects and identification of any other caffeine-related hazards, particularly in children. This report was available at http://www.foodstandards.gov.au/_srcfiles/EWG_Dietary_caffeine.pdf.

The Committee considered a submission from **XXXXXXXX** registering an interest in this item. They provided some comments supporting consideration being given to broadening the availability of caffeine-containing therapeutic goods. The submission contained no comment on single active caffeine.

The Members also considered a submission from **XXXXXXXX** and noted:

- Caffeine is among the most widely used drugs in the world, and is contained in a wide variety of beverages and food products. It had a remarkable safety profile with a wide range of tolerable doses for most people.
- Although sometimes discussed as a dependence-producing drug, caffeine's dependence-producing effects are very mild for most people. Caffeine intake rarely increases to problematic or harmful levels.

- Concerns of teenage caffeine abuse largely appear to relate to the use of energy drinks. A can of high-caffeine energy drink generally provides about as much caffeine as a cup of coffee.

The Committee was advised that **XXXXXXXX** undertook a number of literature searches on this issue. Members particularly noted:

- A Nutrition Australia article asserting that excessive stimulation due to caffeine can have a detrimental effect not only on physical performance, but also on aspects of metabolism that influence health (such as blood pressure and heart rate).
- A MedSafe New Zealand article asserting that because of the wide variety of products containing caffeine a person may be ingesting a considerable amount without being aware of it. Caffeine overdose can cause nausea, diarrhoea, light-headedness and urinary frequency. Caffeine withdrawal even after moderate chronic intake may be associated with headache, nausea, nervousness, reduced alertness and depressed mood.
- A review article (M. Christian, Teratology, 64(1), 51-78) which noted that:
    - Caffeine-containing foods/beverages were consumed by most of the human populations of the world.
    - Animal studies demonstrated that the developmental NOEL in rodents was approximately 30 mg/kg per day and the teratogenic NOEL was 8,100 mg/kg per day. The overall conclusion was that caffeine was a chemical, among a long list of drugs and chemicals, which may have the potential to injure the embryo if used in marked excess. However, the usual range of human exposures to caffeine from food and beverages was below the threshold dose that would result in developmental/teratogenic or reproductive effects.

OUTCOME

The Committee agreed that single active caffeine did not warrant scheduling at this time give that:

- evidence for long-term detrimental or toxic effects from abuse of caffeine was generally lacking; and
- the *Australian Guidelines for Registration of OTC Medicines* requires all OTC medicines using caffeine as a stimulant or alerting agent to have an adult dose compliant with "a 100 mg/dose maximum, which may be repeated at 3 hourly intervals. Do not exceed 600 mg in 24 hours."

15. MATTERS REFERRED BY THE MEDICINES EVALUATION COMMITTEE (MEC)

No items were considered.

16. MATTERS REFERRED BY THE MEDICINES CLASSIFICATION COMMITTEE (MCC) OF NEW ZEALAND

No items were considered.

17. [ITEM DELETED]

18. MINUTES OF THE MEDICAL DEVICE EVALUATION COMMITTEE (MDEC)

No items were considered.

19 - 20. [ITEMS DELETED]

21. AMENDMENTS TO THE SUSDP

21.1 EDITORIAL CHANGES AND ERRATA

21.1.1 EDITORIAL CHANGES AND ERRATA INCLUDED IN THE SUSDP 21 CONSOLIDATION – ASPIRIN, BERGAMOT OIL, CAMPHOR, CLOTRIMAZOLE, DEXTROMETHORPHAN, ECONAZOLE, EMODEPSIDE, FLUORIDES, IBUPROFEN, LEMON OIL, LIME OIL, METHYLENE BLUE, MICONAZOLE, ORANGE OIL (BITTER), PARACETAMOL, PENNYROYAL OIL, "PYRIDOXINE, PYRIDOXAL OR PYRIDOXAMINE", SILVER, TIOCONAZOLE, TOLUENEDIAMINE, VITAMIN A AND ZINC COMPOUNDS

PURPOSE

The Committee considered editorial changes and errata addressed in the SUSDP 21 consolidation.

BACKGROUND

Amendments 1, 2 and 3 of SUSDP 20 have been consolidated to produce SUSDP 21. A number of changes where incorporated into this consolidation, including corrections to the Amendments and other errata or editorials identified by Members or the Secretariat.

DISCUSSION

The Committee noted that the following minor editorial amendments, identified by **XXXXXXXX**, **XXXXXXXX**, **XXXXXXXX** or the Secretariat, have been corrected in the SUSDP 21 consolidation:

Schedule 2

ASPIRIN – The "is" at the beginning of (c) (iii) was deleted for consistency.

DEXTROMETHORPHAN – The entry in the SUSDP 20 consolidation has remained in place since SUSDP 18/1 following a decision at the February 2003 NDPSC Meeting. The **XXXXXXXX** Member noted, however, that this entry should have been amended as a result of a decision at the June 2003 NDPSC Meeting as recorded in SUSDP 18/2. This amendment was inadvertently missed in producing the SUSDP 19 consolidation. The corrected dextromethorphan entry now reads:

DEXTROMETHORPHAN when supplied in a pack containing 600 mg or less of dextromethorphan and with a recommended daily dose of 120 mg or less of dextromethorphan.

IBUPROFEN – The word "complies" in (b)(iv) was amended to "compliant" for consistency with the other entries referencing the *Required Advisory Statements for Medicine Labels* (RASML). A missing "and" after (b)(iii) was also corrected.

PARACETAMOL – The word "complies" in (b)(ii) was amended to "compliant" for consistency. Also, the extra "each containing" in (c) from SUSDP 20/3 was deleted. Additionally, the wording "pack of not more" in (c)(ii) was replaced with "pack containing not more" for consistency.

SILVER – In SUSDP 20/3 clause (a) referred to "5 per cent" when it should have referred to "5 mg". This error was inadvertently introduced during the February 2005 NDPSC consideration of consequential amendments to the SUSDP for consistency with RASML.

Schedule 4

CLOTRIMAZOLE, ECONAZOLE, MICONAZOLE and TIOCONAZOLE – These entries in SUSDP 20/2 used the wording "Schedules 2, 3 or 6". This has been amended in line with the established usage in the SUSDP to "Schedule 2, 3 or 6".

PYRIDOXINE, PYRIDOXAL or PYRIDOXAMINE – The extra "except" inadvertently included in SUSDP 20/3 under (a) has been deleted. The **XXXXXXXX** Member also noted that (a) referred to "more than 50 mg" and (b) to "less than 50 mg". This left the Schedule of exactly 50 mg as ambiguous. Clause (b) has therefore been reworded to "50 mg or less" in the consolidation.

VITAMIN A – The entry was amended following advice from **XXXXXXXX** of a problem resulting from the translation of the vitamin A scheduling provisions from the SUSDP to the RASML.

It was noted that the pre-RASML entry limited vitamin A in non–prescription products to 5000 IU or less through (c)(i). Part (c) of the vitamin A entry at that time was:

(c) in other preparations for internal use labelled:

(i) with a recommended daily amount of 5 000 IU or less of vitamin A; and

(ii) where the preparation is labelled for adult use, in bold face letters not less than 1.5 mm high:

(A) with a statement to the following effect:

The recommended adult daily amount of vitamin A from all sources is 2 500 IU.

(B) and, at the beginning of the directions for use, with a warning statement to the following effect:

WARNING – When taken in excess of 8 000 IU vitamin A can cause birth defects. If you are pregnant, or considering becoming pregnant, do not take vitamin A supplements without consulting your doctor or pharmacist.

In SUSDP 20/3, (c)(i) and (ii) were replaced with a reference to RASML. Section 2 of the RASML sets out all the advisory statements and includes the following:

30. Recommended daily amount of is 5000 International Units or less of vitamin A.

31. The recommended adult daily amount of vitamin A from all sources is 2 500 International units.

32. WARNING – When taken in excess of 8 000 IU vitamin A can cause birth defects.

33. If you are pregnant, or considering becoming pregnant, do not take vitamin A supplements without consulting your doctor or pharmacist.

The RASML vitamin A entry initially picked up statements 30–33 above. However, this entry was changed (RASML update 1) to remove the statement 30 requirement because "it was not a warning/advisory statement and a statement of this sort was not required by the SUSDP". **XXXXXXXX** asserted that statement 30 was included in the original RASML in error.

The removal of statement 30 from the RASML requirements was not communicated to the Secretariat or NDPSC at the time. Advice to this effect was received following a

recent query to **XXXXXXXX** about whether products with > 5000 IU Vitamin A could be listed medicines i.e. exempt from Schedule 4.

The effect of the current Schedule 4 and RASML entries for vitamin A appeared to be that, provided warnings 31, 32 and 33 were on the label, there was no limit to the amount of vitamin A that could be included in a product while still qualifying for the Schedule 4 exemption. The intent of the Committee for the original (c)(i) to apply through RASML has been clarified by reintroducing (i) into the vitamin A entry.

Additionally, the Secretariat noted that the original vitamin A entry, under (c)(ii) included "where the preparation is labelled for adult use…". The restriction to adult use, while implicit under RASML statement 31, was no longer explicitly stated. The intent of the Committee has been clarified by including "in adults" in the first sentence of (c).

The vitamin A entry in the consolidation now reads:

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 in adults when:

(i) labelled with a recommended daily amount of 5 000 IU or less of vitamin A; and

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

ZINC COMPOUNDS – The spelling error in (b) from SUSDP 20/3, "not" misspelt as "mot", has been corrected.

Schedule 5

BERGAMOT, LEMON, LIME and ORANGE (BITTER) OILS - The superfluous "packed in containers and" under (f) was removed and (e) amended by inserting "other" between "in" and "preparations" and deleting "other than medicines for human therapeutic use". Clause (e) and (f) were then swapped for clarity and now read:

(e) in medicines for human therapeutic use, when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*; or

(f) in other preparations when packed in containers labelled with the statement:

Application to the skin may increase sensitivity to sunlight.

CAMPHOR – An error in (c) from SUSDP 20/3, "lavandin" inadvertently spelled "lavindin", was corrected. The entry was also amended by inserting "when" before "packed" in (a) and (b) for consistency with other entries.

EMODEPSIDE – The entry was rephrased from "…in preparations for external treatment of animals containing 2.5 per cent or less of emodepside" to read "…in preparations containing 2.5 per cent or less of emodepside for external treatment of animals".

ORANGE OIL (BITTER) - Reference to "orange oil" under (c) has been clarified to "orange oil (bitter)" in line with the rest of the entry.

Schedule 6

CAMPHOR – An error from SUSDP 20/3, "lavandin" under (e) inadvertently spelled "lavindin", was corrected. The entry was also amended by inserting "when" before "packed", for consistency with other entries, in (e) (i), (ii), (iii) and (iv).

PENNYROYAL OIL – The spelling of "d–pulegone" under (c) has been corrected. In SUSDP 20/3 it was inadvertently spelled "d–pulgone".

TOLUENEDIAMINE – The SUSDP 20/2 entry was missing the † to indicate that there was an Appendix C entry for this substance. This was corrected, and "not elsewhere specified in these Schedules" added for consistency with the phenylenediamines entry.

Schedule 7

METHYLENE BLUE – The SUSDP 20/2 entry "…for veterinary use **except** when included in Schedules 4 and 5" was corrected through replacing the "and" with "or".

Schedule 4, 5 and 6

FLUORIDES – The entries were corrected as follows:

The "in" at the beginning of (b) in the various entries was deleted for consistency with the Schedule 2 fluoride entry.

The use of (A) and (B) formatting under (d) of the various entries has been corrected to (i) and (ii), consistent with the normal formatting hierarchy applied in the SUSDP.

OUTCOME

The Committee noted the editorial changes and errata incorporated into the SUSDP 21 consolidation.

21.1.2 EDITORIAL CHANGES FOR SUSDP 21 AMENDMENT 1

21.1.2.1 SEDATING ANTIHISTAMINES: BROMPHENIRAMINE, CHLORPHENIRAMINE, DEXCHLORPHENIRAMINE, DIPHENHYDRAMINE, DIPHENYLPYRALINE, DOXYLAMINE, PHENIRAMINE, PROMETHAZINE, THENYLDIAMINE, TRIMEPRAZINE, TRIPROLIDINE

PURPOSE

The Committee considered editorial changes to the Schedule 2 sedating antihistamines entries for inclusion in SUSDP 21 Amendment 1.

BACKGROUND

The June 2005 NDPSC Meeting confirmed, on the grounds of harmonisation and taking into account the public health concerns regarding the potential risks associated with the sedative effects of the antihistamines, that the scheduling of sedating antihistamines amended at the February 2004 NDPSC Meeting remained appropriate i.e. similar to the following, with some variation for different substances:

[SUBSTANCE] when combined with one or more other therapeutically active substances in oral preparations for the treatment of symptoms of coughs, colds or influenza when:

(a) at least one of the other therapeutically active substances is a sympathomimetic decongestant; or

(b) in a day-night pack containing brompheniramine in the bed-time dose,

except in preparations for the treatment of children 2 years of age or less.

The October 2005 NDPSC Meeting considered a submission which highlighted that night-time doses of medicines containing sedating antihistamines that were not combined with a sympathomimetic decongestant were included in Schedule 3. Furthermore, there were a number of combination sedating antihistamine products on the ARTG which contained a sympathomimetic decongestant or phenylephrine with or without paracetamol. Given that such products were indicated for the symptomatic treatment of conditions other than coughs, colds or flu, they remained within Schedule 3 even if such products had addressed the Committee's concerns regarding the sedation risks of formulations containing sedating antihistamines. The Committee concurred and agreed to foreshadow an amendment to the sedating antihistamine Schedule 2 entries to remove references to indications. This would allow all combination preparations containing a sympathomimetic decongestant to be considered Schedule 2 substances, irrespective of indications. The Members also agreed to foreshadow amending the wording to clarify that the Committee's intent in regards to the statement "2 years of age or less" meant 2

years from the day of birth. The February 2006 Meeting confirmed the foreshadowed decision i.e. similar to the following, with some variation for different substances:

[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; and

(c) not labelled for the treatment of children under 2 years of age.

DISCUSSION

The **XXXXXXXX** Member advised that there was an error in the wording of the February 2006 NDPSC Decision on the Schedule 2 sedating antihistamine entries with regards to the use of "not labelled for the treatment of children under 2 years of age".

The Members confirmed that it was the Committee's intent to remove reference to "for the treatment of symptoms of coughs, colds or influenza". However, Members also agreed that their intent for the age statement had been to clarify that the then existing "2 years of age or less" actually meant 2 years from the day of birth. Members agreed that this was achieve by using "under two years of age" but noted that extending this to labelling was not the intent of the Committee. Additionally, the current wording applied the restriction to only part of the entry, rather than to the whole entry.

The Committee noted, however, that in the February decision a proposed amendment to the Schedule 2 thenyldiamine entry was based on that which existed in SUSDP 20 and inadvertently overlooked the subsequent removal of thenyldiamine from Schedule 2 in SUSDP 20 Amendment 2 (a decision from the July 2005 consideration of scheduling for those substances where there were no Schedule 2 or 3 products in the marketplace). The Committee agreed that it was not possible to amend a non-existent entry.

The Committee further noted that the wording of February 2006 Decision for diphenhydramine and promethazine was not in the usual format. The Members agreed to replace the wording in clause (a) "in primary packs of 10 doses or less ..." with "in a primary pack containing ten dosage units or less ..." for consisteny.

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The Committee agreed to editorial amendments to the entries for sedating antihistamines to ensure that preparations for the treatment of children under 2 years of age were not captured by the Schedule 2 entry, in any form, and instead reverted to the parent entry, as was the original intent. The Committee further agreed to an additional editorial amendment for the diphenhydramine and promethazine entries to reword clause (a) of

these entries into the standard format used in the SUSDP. The Members also agreed that, as it was not possible to amend a non-existent entry, to not include a Schedule 2 amendment for thenyldiamine in SUSDP 21 Amendment 1.

Schedule 2 – Amendments

BROMPHENIRAMINE, CHLORPHENIRAMINE, DEXCHLORPHENIRAMINE, DIPHENYLPYRALINE, DOXYLAMINE, TRIPROLIDINE – Amend entries 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 2 years of age.

DIPHENHYDRAMINE, PROMETHAZINE – Amend entries to read:

[SUBSTANCE] in oral preparations:

(a) in a primary pack containing ten dosage units or less, for the prevention or treatment of motion sickness; or

(b) when combined with one or more other therapeutically active substances when:

(i) at least one of the other therapeutically active substances is a sympathomimetic decongestant; or

(ii) in a day-night pack containing [substance] in the bed–time dose,

except in preparations for the treatment of children under 2 years of age.

PHENIRAMINE – amend entry to read:

PHENIRAMINE:

(a) in eye drops; or

(b) when combined with one or more other therapeutically active substances in oral preparations when:

(i) at least one of the other therapeutically active substances is a sympathomimetic decongestant; or

(ii) in a day-night pack containing pheniramine in the bed–time dose,

except in preparations for the treatment of children under 2 years of age.

TRIMEPRAZINE – amend entry to read:

TRIMEPRAZINE when combined with one or more other therapeutically active substances in solid 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 trimeprazine in the bed-time dose,

except in preparations for the treatment of children under 2 years of age.

21.1.2.2 POST–MEETING EDITORIALS – APPROVED NAME OF POISONS AND AMOROLFINE

PURPOSE

The Committee considered a number of minor editorial changes, identified out–of–session, to the entries for inclusion in SUSDP 21 Amendment 1.

BACKGROUND

At the June 2006 NDPSC Meeting the Committee noted the draft SUSDP 21 Amendment 1 and agreed to provide comment to the Secretariat out–of–session.

DISCUSSION

A number of minor editorial corrections were identified in comments from Members following the June 2006 NDPSC Meeting. The Secretariat advised Members that the following editorials were included in the SUSDP 21 Amendment 1 following recommendations from the Drafting Advisory Panel (DAP).

Approved name of a poison

The February 2006 NDPSC Meeting amended paragraph 7.(1)(k)(iii) to clarify that the name aromatic or aliphatic amines could be used for amines for use as curing agents for epoxy resins. DAP noted that this may be somewhat ambiguous, and as a consequence SUSDP 21 Amendment 1 has been amended to include the word "appropriate" i.e. "if the poison is a Schedule 5 poison referred to in column 1 of the following table the appropriate name opposite..".

Amorolfine

DAP noted that there was a redundant "for topical use" in clause (b) of the Schedule 3 amorolfine amendment , as it already appeared in the parent part of the entry.

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The Committee accepted the editorial corrections for SUSDP 21 Amendment 1 following review by the Drafting Advisory Panel.

PART 2 – LABELS AND CONTAINERS

Primary Packs and Immediate Containers – Amendment

Sub-paragraph 7.(1)(k)(iii) **–** Amend entry to read:

7. (1)(k)...

(iii) if the poison is a Schedule 5 poison referred to in column 1 of the following table the appropriate name opposite thereto in column 2 may be used as the approved name:

TABLE

Column 1	**Column 2**
Alkaline salts	Alkaline salts
Amines for use as curing agents for epoxy resins (unless separately specified in the Schedules)	Aliphatic amines or aromatic amines
Epoxy resins, liquid	Liquid epoxy resins
Hydrocarbons, liquid	Liquid hydrocarbons

Quaternary ammonium compounds	Quaternary ammonium compound(s)

SCHEDULE 3 – AMENDMENT

AMOROLFINE – amend entry to read:

AMOROLFINE for topical use **except**:

(a) when included in Schedule 2; or

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

21.1.3 ERRATA INCLUDED IN SUSDP 21 AMENDMENT 1 - CETIRIZINE

PURPOSE

The Committee considered, out-of-session, editorial changes to the cetirizine Appendix F and K entries for inclusion in SUSDP 21 Amendment 1.

BACKGROUND

The February 1999 Meeting supported a recommendation from the Trans Tasman Harmonisation Working Party that cetirizine in preparations for oral use be rescheduled from Schedule 3 to Schedule 2 (including consequential deletion of the Appendix H entry). At this time part (b) of the Appendix F entry read "oral preparations of astemizole, desloratadine, fexofenadine, loratadine or terfenadine" and the Appendix K entry was simply "Cetirizine".

The October 2005 NDPSC Meeting considered an application to remove the Appendix K and Appendix F, Part 3 requirements for a sedation warning for oral cetirizine medicines administered in daily doses of up to 10 mg. The Members agreed to remove cetirizine from Appendix K when included in Schedule 2 and also agreed to amend the wording of Appendix F for antihistamines to similarly remove the requirement for sedation warnings on the label of Schedule 2 cetirizine products. The wording of the October 2006 amendments were:

Appendix F, Part 3

Antihistamines – Amend paragraph (b) of the entry to read:

(b) oral preparations of astemizole, cetirizine, desloratadine, fexofenadine, loratadine or terfenadine;

Appendix K

Cetirizine – Amend entry to read:

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

At the February 2006 NDPSC Meeting the Committee considered post-meeting comment in relation to the October 2005 decision. The Committee also noted that as of 1 May 2006, the transfer of all mandatory label advisory statements for medicines from the SUSDP to the *Required Advisory Statements for Medicine Labels* (RASML) would take effect. The Committee therefore agreed that it would be appropriate for the application to remove cetirizine from Appendix F to be assessed by MEC. Accordingly, the Committee agreed to set-aside the October 2005 Decision and retain the inclusion of cetirizine in Appendix K and Appendix F, Part 3.

DISCUSSION

The Secretariat advised the Members, out-of-session, that the amendments proposed at the October 2005 NDPSC Meeting for the Appendix F and K cetirizine entries were inadvertently included in the consolidation of SUSDP 21, despite being set-aside at the February 2006 NDPSC Meeting.

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The Committee agreed to correct the inadvertent errata in the SUSDP 21 consolidation to the Appendix F, Part 3 and Appendix K entries for cetirizine.

Appendix F, Part 3 – Amendment

Antihistamines – Amend paragraph (b) of the entry to read:

(b) oral preparations of astemizole, desloratadine, fexofenadine, loratadine or terfenadine;

Appendix K – Amendment

Cetirizine – Amend entry to read:

Cetirizine.