Public Submissions on the Proposed Amendments to the Poisons Standard

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

A delegate of the Secretary to the Department of Health publishes herein all valid public submissions made in response to the invitation for public submission on the proposed amendments to the Poisons Standard (commonly referred to as the *Standard for the Uniform Scheduling of Medicines and Poisons* - SUSMP). These submissions were considered by the Advisory Committee on Chemicals Scheduling (ACCS) #9, the Advisory Committee on Medicines Scheduling (ACMS) #10 and the joint committee of ACCS-ACMS #7 (November 2013 meetings).

In accordance with the requirements of subsection 42ZCZL of the Regulations these submissions have had confidential information removed.

Material claimed to be commercial-in-confidence was considered against the guidelines for the use and release of confidential information set out in Chapter 6 of the Scheduling Policy Framework for Medicines and Chemicals (SPF), issued by the National Coordinating Committee on Therapeutic Goods. The SPF is accessible at www.tga.gov.au/industry/scheduling-spf.htm.

Discrete submissions have been grouped by substance. Four submitters provided submissions that related to multiple substances and these has been separately grouped.

List of Submissions

Substance	**Total number of public submissions**
1,3-Cyclohexadiene-1-carboxylic acid, 4,6,6-trimethyl-, ethyl ester	3 submissions under ‘submissions on multiple substances’
2-Amino-5-ethylphenol	2 submissions under ‘submissions on multiple substances’
2-Butanone, oxime (also known as methyl ethyl ketone oxime)	2 submissions under ‘submissions on multiple substances’
2-Furancarboxaldehyde (furfural)	3 submissions under ‘submissions on multiple substances’
2-Nitrotoluene	1 submissions under ‘submissions on multiple substances’
3,7-Dimethy-2,6-octadienal isomers (CITRAL, geranial and neral)	4 submissions under ‘submissions on multiple substances’

Substance	Total number of public submissions
Benzidine-based dyes	2 submissions under ‘submissions on multiple substances’
Aminopyralid	1 submissions under ‘submissions on multiple substances’
C11-C15-secondary, ethoxylated, oxirane and oxirane, ethyl (oxirane)	2 submissions under ‘submissions on multiple substances’
Diethylene glycol monobutyl ether	2 submissions under ‘submissions on multiple substances’
Ethylene glycol monomethyl ether	2 submissions under ‘submissions on multiple substances’
Mercaptoacetic acid	2 submissions under ‘submissions on multiple substances’
Methanol	3 submissions under ‘submissions on multiple substances’
Pentanoic acid, 3-methyl-2-oxo-, ethyl ester	2 submissions under ‘submissions on multiple substances’
Phosphonium, tributyloctyl-, chloride (1:1)	1 submissions under ‘submissions on multiple substances’
Pyridine, 2-chloro-6-(trichloromethyl)	2 submissions under ‘submissions on multiple substances’
Sulfites - i.e. Salts of sulfurous and disulfurous acids	3 submissions under ‘submissions on multiple substances’
Tetrahydrofuran	2 submissions under ‘submissions on multiple substances’
Triethanolamine	3 submissions under ‘submissions on multiple substances’
Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]-	2 submissions under ‘submissions on multiple substances’
Zinc lactate	4 submissions under ‘submissions on multiple substances’
Cosmetic use Personal care use	4 submissions under ‘submissions on multiple substances’
Ethanol, 2-(dimethylamino)-	3 submissions under ‘submissions on

Substance	Total number of public submissions
	multiple substances’
Salicylic acid	4 submissions under ‘submissions on multiple substances’
Macrogol	2 submissions (1 under ‘submissions on multiple substances’)
Esomeprazole	3 submissions (1 under ‘submissions on multiple substances’)

Submission on Multiple Substances

One submission was on 1,3-cyclohexadiene-1-carboxylic acid, 4,6,6-trimethyl-, ethyl ester, 2-amino-5-ethylphenol, 2-butanone, oxime, 2-furancarboxaldehyde (furfural), 2-nitrotoluene, 3,7-dimethy-2,6-octadienal isomers (CITRAL, geranial and neral), aminopyralid, benzidine-based dyes, C11-C15-secondary, ethoxylated, oxirane and oxirane, ethyl (oxirane), diethylene glycol monobutyl ether, ethylene glycol monomethyl ether, mercaptoacetic acid, methanol, pentanoic acid, 3-methyl-2-oxo-, ethyl ester, phosphonium, tributyloctyl-, chloride (1:1), pyridine, 2-chloro-6-(trichloromethyl), sulfites - i.e. salts of sulfurous and disulfurous acids disuldisulfurous acids, tetrahydrofuran, triethanolamine, trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]- and zinc lactate.

One submission was on 1,3-cyclohexadiene-1-carboxylic acid, 4,6,6-trimethyl-, ethyl ester, 2-amino-5-ethylphenol, 2-butanone, oxime, 2-furancarboxaldehyde (furfural), 3,7-dimethy-2,6-octadienal isomers (CITRAL, geranial and neral), benzidine-based dyes, C11-C15-secondary, ethoxylated, oxirane and oxirane, ethyl (oxirane), diethylene glycol monobutyl ether, ethylene glycol monomethyl ether, mercaptoacetic acid, methanol, pentanoic acid, sulfites - i.e. salts of sulfurous and disulfurous acids, tetrahydrofuran, triethanolamine and zinc lactate.

One submission was on 1,3-cyclohexadiene-1-carboxylic acid, 4,6,6-trimethyl-, ethyl ester, 2-amino-5-ethylphenol, 2-butanone, oxime, 2-furancarboxaldehyde (furfural), 3,7-dimethy-2,6-octadienal isomers (CITRAL, geranial and neral), methanol, pyridine, sulfites - i.e. salts of sulfurous and disulfurous acids, tetrahydrofuran, triethanolamine, trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]- and zinc lactate.

One submission was on 3,7-dimethy-2,6-octadienal isomers (CITRAL, geranial and neral), triethanolamine, cosmetic personal care use and salicylic acid.

Two submissions on cosmetic use personal care use, ethanol, 2-(dimethylamino)- and salicylic acid.

One submission on cosmetic use personal care use, ethanol and salicylic acid.

One submission on macrogol and esomeprazole.

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12th November 2012

The Secretary
Scheduling Secretariat
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Dear Sir or Madam,

Re: Invitation for public comment – ACCS and joint ACCS/ACMS Meetings, November 2013
ASMI comment – ACCS meeting

We refer to the notice inviting public comment under Regulation 42ZCZK of the Therapeutic Goods Regulations and would like to provide comment on the scheduling proposals that are to be considered by the ACCS and the joint ACCS/ACMS meetings in November 2013. The comments submitted below address matters raised in s.52E of the *Therapeutic Goods Act 1989*.

ASMI (Australian Self Medication Industry) is the peak body representing companies involved in the manufacture and distribution of consumer health care products (non-prescription medicines) in Australia. ASMI also represents related businesses providing support services to manufacturers, including advertising, public relations, legal, statistical and regulatory consultants.

ACCS Agenda – General comments

ASMI notes the many proposals for the amendment of schedule entries for various substances in the poisons standard, to be considered by the ACCS. The proposals for consideration appear to pertain mainly to the use of the chemicals in cosmetic products and some industrial chemicals, however ASMI notes that there is insufficient detail in the proposals to allow an adequate assessment of impact on the therapeutic goods industry.

Some of the proposals on the agenda appear to follow the NICNAS IMAP review process and recommendations, however we are concerned that the possible impact on ingredients entered in the ARTG for use in therapeutic goods may not have been fully considered. It is likely that there may also be an impact on products registered by APVMA and foods regulated by ANZFA, although these types of products are outside ASMI's representation. ASMI urges the Scheduling Secretariat to ensure that there has been adequate co-ordination between the relevant agencies (NICNAS, TGA, APVMA and ANZFA) prior to the publication of the agenda, and greater detail and transparency on the rationale behind the proposals on the agenda to enable industry to assess the proposals adequately and comment appropriately.

We have reviewed the entire agenda and to the extent possible, have commented on any specific items which are clearly of relevance to our members. Some agenda items are clearly not relevant,

however given the ambiguity and lack of detail in the agenda, ASMI cannot be certain that all relevant sections and matters in the agenda have been identified. For this reason, our general comments below that relate to the impact on therapeutic goods, should be considered as comments in relation to each agenda item for the purposes of providing a post-meeting response.

Identification of substances

Chemical nomenclature is complex and ASMI has experienced difficulty finding the uses of many of the substances listed in the agenda and assessing whether there is potential impact on the therapeutic goods industry. It would be helpful to industry if the agenda provided some additional, very brief information on the uses of substances (e.g. whether the substance is agricultural chemical, use in cosmetics, industrial chemical or precursor). If available, the CAS number could also be provided in the agenda so that interested parties can more quickly ascertain potential impact and cross reference to other databases such as the TGA e-BS ingredient list and the NICNAS search facility.

Salts and derivatives

According to the principles of scheduling, a Schedule entry includes preparations containing the poison in any concentration and all salts and derivatives of the poison unless stated otherwise (Part 1, Interpretation, subparagraph 1(2).

Some of the items on the agenda include broad substance names such as "sulfites" which a search of the TGA e-BS site shows are present in many different salts and derivatives and are also included in therapeutic goods.

ASMI expresses concern that some therapeutic goods, regulated by the TGA may inadvertently be affected by the proposed amendments and urges the ACCS to consider the following issues when determining any possible amendments:

- Amendments to schedules for any of the chemicals should be carefully drafted and worded in such a way that therapeutic goods are excluded.
- Care should be taken so that entries are as specific as possible so as not to affect all salts and derivatives (unless clearly intended), as some salts and derivatives of substances may be present in therapeutic goods.

ACCS Agenda – Scheduling proposals for substances

ASMI has assessed the entire agenda and some of the proposals do not appear to be relevant to the therapeutic goods industry. However given the limited information provided, the complexity of nomenclature and the large number of possible salts and derivatives, we cannot be certain that no impact exists and we would appreciate the opportunity to provide further comment on any of the agenda items should possible impact be identified following the release of the Delegate's interim decisions.

The following substances listed on the agenda have been identified as possibly being components in fragrances:

- ***1,3-Cyclohexadiene-1-carboxylic acid, 4,6,6-trimethyl-, ethyl ester***
- ***2,Furancarboxaldehyde (furfural)***
- ***3,7-Dimethyl-2,6-octadienal isomers (CITRAL, geranial and neral)***

- ***Tetrahydrofuran***

ASMI is unclear on what cut-off concentrations have been proposed, and requests the ACCS to consider that while not all of these ingredients appear on the TGA e-BS ingredient list, some of these substances may be included in proprietary ingredients that are used in therapeutic goods. For this reason, ASMI requests the ACCS consider existing usage within proprietary ingredients and to propose cut-off concentrations that will not impact existing use in proprietary ingredients and in therapeutic goods.

ASMI also has particular concerns with the following proposals, where the possibility for impact on therapeutic goods has been more clearly identified –

- ***2,Butanone, also known as methyl ethyl ketone oxime – new Schedule 6 entry with consideration of appropriate cut off to unscheduled***: ASMI notes that the proposed amendment for this entry is not limited to cosmetic products and notes that the TGA-eBS system contains an ingredient entry for methyl ethyl ketone. Given that scheduling entries apply to "salts and derivatives", and acknowledging that there is a lack of detail or rationale in the agenda, ASMI is concerned about the possibility that there may be some impact on therapeutic goods.
- ***Methanol***: While the wording of the proposed scheduling amendment clearly refers to cosmetic use, ASMI notes that methanol is used during the manufacture of some therapeutic goods and requests the ACCS to confine any changes to schedules so that therapeutic goods are not affected.
- ***Pyridine, 2-chloro-6-(trichloromethyl) – new Schedule 6 entry and inclusion in Appendix F, with warning statements to be determined***: ASMI notes that the proposed amendments have not been confined to cosmetics or domestic products. Although there does not appear to be an impact on therapeutic goods, ASMI requests careful drafting of the wording of any scheduling amendments so that there is no unintended impact on therapeutic goods.
- ***Sulfites - new Schedule 5 entry for sulfites, with appropriate amendments to the current Schedule 5 entry for sodium metabisulfite, to align with EU restrictions on the use of sulfites in cosmetics and to consider appropriate cut-offs to exemption from the proposed Schedule 5 entry***: ASMI notes that the TGA e-BS system has many entries for sulfites. These include calcium sulfite, potassium metabisulfite, sodium bisulfite, sodium sulfite anhydrous, and sodium sulfite heptahydrate. It can be assumed that there would be many more salts of sulfurous and disulfurous acids. These products are included as ingredients in many therapeutic goods as well as cosmetics. ASMI believes that the proposed amendments to scheduling for "sulfites" should be very specific and be drafted to ensure that therapeutic goods are not affected. This can be done by ensuring that any schedule entry is clearly limited to use in cosmetics.
- ***Tetrahydrofuran – new Schedule 5 entry***: A search of the TGA e-BS for tetrahydrofuran results in two ingredient entries – one of which has an Australian Approved Names (AAN) and the other an Approved Device Name (ADN). ASMI believes that the proposed amendment as written could possibly have an impact on therapeutic goods and should be more specific so that it excludes therapeutic goods.
- ***Triethanolamine – amend the Schedule 5 entry to consider altering the scheduling cut-off clause for cosmetic preparations to 2.5 per cent or less of triethanolamine and to consider other restrictions on the use of triethanolamine in tattoo removal cosmetics applied intradermally***: It should be noted that some therapeutic goods (used as topical analgesic preparations for the relief of joint and muscle aches and pains due to arthritis and

rheumatism) contain triethanolamine salicylate as an active ingredient. ASMI urges the ACCS to ensure that any scheduling amendment specifies that salts and derivatives of triethanolamine should be excluded from the schedule entry. The current Schedule 5 entry for triethanolamine currently excludes salts and derivatives and we believe that consistency should be maintained for any further amendments.

- ***Zinc lactate - new Schedule 6 entry for zinc lactate except in toothpastes containing 2.5 per cent or less of zinc lactate***: It is noted that there are some inconsistencies with ARTG entry restrictions for this ingredient when used in toothpastes. The ARTG entry for the ingredient also proposes a usage limit of 2.0 per cent or less for dermal use.

Conclusion

ASMI is concerned at the lack of transparency and rationale behind the scheduling proposals for the list of substances. Although it can be assumed that some of the proposals have arisen from the NICNAS review, this has not been made clear. A further issue of concern is that there may be a lack of co-ordination between the various agencies with the possibility that products such as therapeutic goods, foods and veterinary products may also be affected by the proposals for scheduling amendments.

ASMI requests the ACCS to carefully consider the possible impact of the scheduling proposals on therapeutic goods, and care should be taken to ensure that any amendments are clearly and carefully drafted to exclude any impact on these products. Care should also be taken, where necessary, to exclude salts and derivatives from some scheduling entries, such as the triethanolamine entry, so that active ingredients of certain therapeutic goods are not affected.

As an industry representative, ASMI is a key stakeholder in scheduling matters and we are keen to provide further input as required. We look forward to the Delegate's interim decisions and greater detail on the final scheduling proposals.

Yours sincerely,

[redacted]

[redacted]

14 November 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT 2601

Email: SMP@health.gov.au

Dear Sir/Madam

Re: Public Comment Submission to the November 2013 meeting of the Advisory Committee On Chemicals (ACCS) and the Joint meeting of the ACCS and the Advisory Committee on Medicine Scheduling (ACMS)

I refer to the notice published on 17 October 2013, inviting public submissions, with respect to certain substances, addressing a matter raised in s.52E of the *Therapeutic Goods Act 1989*.

[redacted] does not wish to comment at this time on the proposed amendments to the poisons standard referred by the delegate for scheduling advice.

[redacted] is an interested party and stakeholder with regard to the nominated substances and would appreciate being advised of the Committees' considerations and the Delegate's interim decision, with the opportunity for further submission, if appropriate.

Yours sincerely,

[redacted]

[redacted]

[redacted]

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT
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14.11.2013

Dear Sir/Madam,

RE: Comments on Proposed amendments referred by the Delegate for scheduling advice for consideration by the Advisory Committee on Chemicals Scheduling (ACCS)

[redacted] would like to provide comments on a number of the proposed amendments referred by the Delegate to the Committee of Chemicals Scheduling (ACCS).

ACCS Agenda – General comments

[redacted] notes that a number of proposals for various chemical substances have been referred to the Committee for consideration. Many of the chemical substances proposed are contained in cosmetic products and therapeutic goods, however it has been difficult to adequately assess the impact of the proposals due to the lack of detail provided.

Further information on the background and rationale behind the proposals, the concern with the chemical substance, and how the substance is used in industry would assist us in conducting our assessments.

Additionally the nomenclature used for the chemical substances has been very confusing as there may be a number of synonyms for the one chemical substance. Using CAS numbers or INCI names are preferable as they are internationally recognised and would make it much quicker and easier for us to ascertain potential impact.

[redacted] have provided the below comments for some of proposals.

3,7-Dimethy-2,6-octadienal isomers (CITRAL, geranial and neral) - Proposal for a new Schedule 5 entry with a yet to be determined low concentration cut-off.

Citral is contained in a number of [redacted] leave on and rinse off cosmetic products, and is usually a part of a proprietary fragrance or flavour rather than an individual ingredient in formulations. As such the concentration of Citral in the proprietary fragrances and flavours used in our products is very low, (0.0001%-0.002%). All fragrances used have been assessed for safety by IFRA.

IFRA are an internationally recognised association which assesses the safety and toxicity of fragrances globally. IFRA works closely with regulators and stakeholders to issue and update comprehensive safety standards. Its members account for 90% of the global production volume of fragrance compounds and the IFRA Code of Conduct prescribes the behaviour that is expected of them. Its comprehensive global compliance programme also

[redacted]

[redacted]

independently spot checks fragranced products to ensure their compliance with the IFRA Code of Practice[1]. The IFRA standard for Citral is attached for your information[2].

[redacted] cosmetic products undergo rigorous safety testing in humans during their development. Tests may include cumulative irritiation studies tested by independant dermatologitsts, RIPT (repeat insult patch testing), photoallergy and phototoxicity testing. Our formulations which contain Citral are supported by these safety studies.

OVERSEAS REGULATORY CLASSIFICATION FOR CITRAL

COUNTRY	RESTRICTIONS
European Union	The presence of the substance must be indicated on product labelling when its concentration exceeds: - 0.001% in leave-on products - 0.01% in rinse-off products
New Zealand	The presence of the substance must be indicated on product labelling when its concentration exceeds: - 0.001% in leave-on products - 0.01% in rinse-off products
USA	No specific limits required
Canada	No specific limits required

The above are key country classifications of Citral. There are no restrictions on use of Citral in any of the 4 key regions listed in the table. The only requirement is for product labelling to include the ingredient when above a certain concentration in the EU and New Zealand. Currently in Australia Citral is unscheduled and has no specific labelling requirements when used in cosmetics. Additionally there are no regulatory or safety issues in the key global markets above that we are aware of for the use of Citral in cosmetic products.

The impact of including cosmetic products containing Citral under schedule 5 of the Poisons Standard would be that products such as [redacted] bath washes, which are considered safe for their intended use by consumers, would be captured and would be required to include strict warning statements on consumer packaging, including the words CAUTION on the front label. This is not appropriate nor warranted for cosmetic baby products which have been used by consumers for many years without any serious safety issues.

In summary, [redacted] view is that Citral should remain unscheduled as the safety of the ingredient when used in fragrances has been established by IFRA. Citral has been used in fragrances contained in [redacted] cosmetic products for many years with no known safety issues. Additionally no other market restricts the use of Citral in cosmetic products. If a Schedule 5 entry is adopted we strongly urge the Committee and the Delegate to exempt the use of Citral in fragrances and flavours contained in cosmetic products. An example would be as per the below:

[redacted]

[redacted]

SCHEDULE 5

3,7-Dimethy-2,6-octadienal isomers (CITRAL, geranial and neral) ***except*** *in preparations for cosmetic use.*

Triethanolamine - Proposal to amend the triethanolamine Schedule 5 entry to consider altering the scheduling cut-off clause for cosmetic preparations to 2.5 per cent or less of triethanolamine and to consider other restrictions on the use of triethanolamine in tattoo removal cosmetics applied intradermally.

Triethanolamine (TEA) is contained in a number of [redacted] cosmetic and therapeutic products including TGA listable sunscreens and cosmetic facial cleansers and moisturisers. TEA is used in these products in varying concentrations as a pH adjuster.

The TGA recognise TEA as a safe excipient ingredient for use in Over the Counter (OTC), Prescription, Listable medicines, and devices. It is currently used in a number of products such as listable sunscreens for example Neutrogena Ultra Sheer Dry touch Sunscreen Lotion SPF 50+ (AUST L 202300), unscheduled OTC medicines such as Pinetarsol (AUST R 10624) and Metsal Analgesic Gel (AUST R 17510) as well as in cosmetics such as Clean & Clear Essentials Foaming Facial Wash.

[redacted] cosmetic products undergo rigorous safety testing in humans during their development. Tests may include cumulative irritiation studies tested by independant dermatologitsts, RIPT (repeat insult patch testing), photoallergy and phototoxicity testing. Our formulations which contain TEA in concentrations compliant with current scheduling are supported by these safety studies.

OVERSEAS REGULATORY CLASSIFICATION FOR TRIETHANOLAMINE (TEA)

COUNTRY	RESTRICTIONS
European Union	Non-rinse off products max authorised concentration in finished cosmetic product is 2.5%. For non-rinse off products and other products the following requirements must be met: -Do not use with nitrosating systems - Minimum purity: 99% - Maximum secondary amine content: 0.5% (applies to raw materials) - Maximum nitrosamine content: 50 microgram/kg - Keep in nitrite-free containers
New Zealand	No restriction on use
USA	No restriction on use. The general rule is to follow the safety conclusions that are identified in CIR reports, where available
Canada	No restriction on use

The above are key country classifications of TEA. There are no restrictions on use of TEA in New Zealand, USA or Canada. The European Union restricts the use of TEA in non

[redacted]

[redacted]

rinse off (ie leave on) cosmetics to 2.5%. There is no restriction on concentration for rinse off products in the EU. Currently in Australia TEA is in Schedule 5 of the Poisons Standard as follows:

SCHEDULE 5

TRIETHANOLAMINE (excluding its salts and derivatives) ***except*** *in preparations containing 5 per cent or less of triethanoamine.*

Changes to scheduling should not consider just one well known geography such as the EU. Other large western market requirements such as the USA should be taken into consideration so as to not disadvantage non-European based companies in the market.

Additionally there are no regulatory or safety issues in the key global markets above that we are aware of for use of TEA in cosmetic or therapeutic products.

The impact of reducing the allowable unscheduled concentration of TEA from 5% to 2.5% would be that products such as sunscreens, cleansers, moisturisers, and other unscheduled OTC medicines which contain TEA at concentrations between 2.5 percent and 5 percent, which are considered safe for their intended use by consumers, would be required to include strict warning statements on consumer packaging, including the words CAUTION on the front label. This is not appropriate nor warranted for these types of consumer products, considering they have been used for many years without any serious safety concerns.

SAFETY SUMMARY

Triethanolamine (TEA) is an amino alcohol used in cosmetic formulations as surfactant or pH adjuster. It is reported to have been used in 3756 cosmetics at concentrations of up to 6% in leave-on formulations, 19% in rinse-off formulations, and 0.7% in products that are diluted for use.

In 1983, the CIR Panel[3] concluded that TEA is safe for use in cosmetic formulations designed for discontinuous, brief use followed by thorough rinsing from the surface of the skin.

In 2013[4] the CIR Panel decided to reopen that safety assessment to include more related TEA-containing ingredients. This time, they concluded that TEA and the 31 related TEA-containing ingredients are safe in the present practices of use and concentration. TEA should not be used in products containing N-nitrosating agents. The nitrosation of the ethanolamines may result in the formation of N-nitrosodiethanolamine (NDELA), which is carcinogenic in laboratory animals.

TEA can be a dermal irritant in both animals and humans, but it has not been shown to be a sensitizer. TEA was negative for genotoxic effects. Clinical skin testing of TEA and cosmetic products containing TEA and DEA showed mild skin irritation in concentrations above 5%. There was very little skin sensitization. There was no phototoxicity or photosensitization reaction with products containing up to 20.04% TEA.

Based on the above information, it can be stated that the use of TEA in cosmetic products in concentrations below 5% can be regarded as safe.

[redacted]

[redacted]

In summary, [redacted] proposes that the scheduling of TEA remains as per the current schedule, and that the current allowable concentration in unscheduled products of up to 5% remains unchanged.

Yours faithfully,

[redacted]

REFERENCES

1. www.ifraorg.org/
2. IFRA standard for CITRAL
3. Journal of the American College of Toxicology, 2(7): 183-235, 1983) on request
4. International Journal of Toxicology, 32 (S1): 59S-83S, 2013) on request

[redacted]

The Secretary
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CANBERRA ACT 2601

Email: SMP@health.gov.au

Dear Sir/Madam

Public Comment Submission to the November 2013 meeting of the Advisory Committee on Chemicals Scheduling (ACCS)

We refer to the notice published on 17 October 2013 inviting public submissions, with respect to certain substances, addressing a matter raised in s.52E of the *Therapeutic Goods Act 1989.*

Accord Australasia Limited is the peak national industry association that represents the hygiene, cosmetic & specialty chemicals industry.

Accord wishes to provide information on:

- **1,3-cyclohexadiene-1-carboxylic acid, 4,6,6-trimethyl-, ethyl esters;**
- **2-amino-5-ethylphenol;**
- **2-furancarboxaldehyde (furfural);**
- **3,7-dimethyl-2,6-octadienal isomers (citral, geranial and neral);**
- **Benzidine-based dyes;**
- **C11-C15-secondary, ethoxylayed, oxirane and oxirane, ethyl (oxirane);**
- **Diethylene glycol monobutyl ether;**
- **Ethylene glycol monomethyl ether;**
- **Mercaptoacetic acid;**
- **Methanol;**
- **Pentanoic acid, 3-methyl-2-oxo-, ethyl ester;**
- **Sulfites – i.e. salts of sulfurous and disulfurous acids;**
- **Tetrahydrofuran;**
- **Triethanolamine;**
- **Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]-; and**
- **Zinc lactate;**

for consideration at the November 2013 meeting of the ACCS.

Please see attached submission for details.

Accord notes that a number of proposals related to fragrances and flavours. We believe that a separate process for considering fragrance and flavours is needed considering their unique use pattern.

We also note that there were a number of re-scheduling proposals that did not appear to

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demonstrate that the current scheduling controls are inadequate. Accord is concerned that such proposals are being put forward. Without justification for the need for re-scheduling, this can significantly add to the regulatory burden on industry as we are required to defend the current controls.

Accord is an interested party and stakeholder with regard to the nominated substances and would appreciate being advised of the Committees' considerations and the Delegate's interim decision, with the opportunity for further submission, if appropriate. Given the short time frame for comments and large number of substances on the agenda, Accord was unable to analyse the proposals in depth and would welcome an opportunity to provide further in-depth comments on a smaller subset of chemicals that are considered to pose a regulatory concern.

We look forward to further advice from the ACCS, ACMS and the Delegate. Should the Committees or the Delegate require any additional information from Accord at this stage please do not hesitate to contact me on [redacted].

Yours faithfully

[unsigned for electronic submission]

[redacted]

ACCS meeting: November 2013

1,3-cyclohexadiene-1-carboxylic acid, 4,6,6-trimethyl-, ethyl esters

While we understand from the scheduling proposal that 1,3-cyclohexadiene-1-carboxylic acid, 4,6,6-trimethyl-, ethyl esters can be used as a fragrance component, Accord has had no information from Members on the use of the substance. As the identity of many fragrance components are considered commercial in confidence by the suppliers, it is possible that the substance is being used in consumer products and cosmetics and disclosed on the label simply as “fragrance”.

Accord has also contacted the International Fragrance Association (IFRA) for information on several of the ACCS agenda items but has received no specific information on controls for this substance.

It is our view that control of fragrances and flavour components through the scheduling system is unwieldy and inefficient. This is particularly true when an international scientific assessment and risk management body like IFRA publishes Codes of Practice and Standards that are specifically relevant for fragrance and flavours. More information on IFRA is provided in our comments for the agenda item, furfural.

Accord would support a separate discussion on the controls of fragrance and flavours rather than through individual scheduling consideration of each fragrance and flavour.

ACCS meeting: November 2013

2-amino-5-ethylphenol

Accord is unaware of the reasons (e.g. adverse events, hazard/risk assessment) behind this scheduling proposal. Accord notes that the CAS number for 2-amino-5-ethylphenol is 182499-90-7.

We understand that there is a 2012 Scientific Committee on Consumer Safety (SCCS) opinion on 2-amino-5-ethylphenol hydrochloride (CAS Number 149861-22-3). As this is a hydrochloride salt of the substance proposed for scheduling, and the scheduling proposal appears to reflect the conclusion of this 2012 SCCS opinion we have assumed that the proposal is based on the SCCS opinion on the hydrochloride salt.

Accord understands that 2-amino-5-ethylphenol hydrochloride is used in hair dyes, including in Australia.

It is important to note that while the SCCS opinion concludes that 2-amino-5-ethylphenol hydrochloride is safe for use in oxidative hair dyes at up to 1% (except for sensitisation potential), we note that the terms of reference for the SCCS opinion only asked the SCCS to consider a maximum concentration of up to 1%. This is therefore not necessarily the maximum safe concentration. It is also important to note that the SCCS consideration related to 1% in the in-use preparation i.e. diluted for use, rather than in the purchased concentrated products.

We also note that the EU has not (as yet) placed any restrictions on the use of the substance in cosmetics.

Accord in principle we does not support restrictions on substances that are out of line with our major trading partners. Any consideration on scheduling of 2-amino-5-ethylphenol should ensure that the limitation applies to the diluted hair dye for use rather than to the product packaged for sale.

ACCS meeting: November 2013

2-furancarboxaldehyde (furfural)

Accord has no information on the use of furfural as an industrial chemical i.e. as a solvent, dye, ion exchange agent, adhesive, etc. We also have no information on the use of furfural in Australia in cosmetics and in consumer products.

Accord understands that furfural is a naturally occurring flavour/fragrance that is also added to manufactured food and cosmetics. According to the Scientific Committee on Consumer Safety (SCCS) report on furfural in 2012, "*furfural has been identified in foods, including fruits, vegetables, beverages, bread and bread products. The highest reported concentrations were found in wheat bread (0.8–14 ppm) [mg/kg], cognac (0.6–33 ppm), rum (22 ppm), malt whisky (10–37 ppm), port wine (2–34 ppm) and coffee (55–255 ppm). The concentrations of furfural in juices were 0.01–4.93 ppm*".

While the NICNAS IMAP report implies that it is the SCCS opinion that a concentration limit of 10 ppm in finished cosmetic products is considered safe i.e. unsafe above that level, we believe that this SCCS opinion has been taken out of context by NICNAS. In the 2012 SCCS opinion, the SCCS was only asked to assess whether furfural can be considered safe for the consumer when used up to the proposed pragmatic concentration limit of 10 ppm in finished cosmetic products and not beyond. The response was that the use of furfural with a maximum concentration limit of 10 ppm in the finished cosmetic product, including oral products, does not pose a risk to the health of the consumer i.e. the SCCS did not consider concentrations above 10 ppm.

While we note that furfural is likely to be used in very small amounts as a fragrance in cosmetics and consumer products, unfortunately we are unable to quantify this. Accord however also notes that there appear to be no restrictions placed on the use of furfural in cosmetics or consumer products in either the EU or the USA.

One of the reasons for this may be that in most countries, the International Fragrance Association (IFRA)[1] Code of Practice[2] is accepted for fragrance and flavour. The IFRA Standard[3] sets the limit on furfural at 10 ppm for skin contact products and 500 ppm for non-skin contact products.

While we understand that it may not be the role of the ACCS or the Delegate to decide whether to adopt the IFRA Code into the Australian cosmetics and consumer products regulatory framework, we believe that this is an issue that must be considered. It is not practical or efficient to reconsider all fragrance and flavours through the scheduling process. When there is an international body like IFRA that investigates issues surrounding flavours and fragrance in depth, it makes little sense to duplicate this work. This is particularly the case when most companies comply with the IFRA Code voluntarily.

We note that the New Zealand Cosmetic Products Group Standard has already adopted the IFRA Code.

Accord suggests a separate discussion, if possible, on the adoption of internationally accepted standards like the IFRA Code.

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[1] http://admin-ifra.alligence.com/Files/Documents/1/en-us/GD/22156_GD_2006_12_15_IFRA_Code_of_Practice_-_Body_&_8_Appendices_-_Dec_2006.pdf

[2] http://www.ifraorg.org/view_document.aspx?docId=22182

[3] http://www.ifraorg.org/view_document.aspx?docId=22594

If the ACCS believes that it is necessary to schedule furfural for industrial applications, given the likely use of furfural in small quantities in cosmetics and consumer products, the prevalence of furfural in foods, the lack of limitations in cosmetics in the EU and the USA and the fact that most companies are complying with the IFRA Code, Accord suggests excluding furfural from scheduling when used as a fragrance or flavour in cosmetics.

Furthermore, any scheduling consideration of furfural should ensure that other furan based fragrances and indeed other furan based chemicals for use other than as fragrances are not inadvertently caught in the scheduling of furfural.

ACCS meeting: November 2013

3,7-dimethyl-2,6-octadienal isomers (citral, geranial and neral)

Accord understands that citral is a commonly used fragrance and flavour in cosmetics and consumer products. Citral is a turpenoid present in oils of some plants (e.g. lemon, lime, orange, lemon myrtle, lemon grass, etc.) that gives the plant the lemony fragrance and flavour. Unsurprisingly, citral is added to cosmetics and consumer products as a fragrance (for citrus scent). Geranial and neral are the two isomers which constitute citral.

Several of Accord's Members have confirmed that citral is used in cosmetics and consumer products in Australia, with fairly high concentrations in air care products (over 10%).

While we note that there are other fragrance compounds that are closely related to citral that may also be used widely (e.g. citrol), Accord had to focus on citral due to the short timeframe for comments and the large number of agenda items. Accord requests that any scheduling decisions made should reflect the fact that industry may not have had sufficient time to consider the impact of scheduling decisions on all derivatives of citral and other substances on the agenda.

Accord notes that in the EU and the USA citral must be disclosed on the label of cosmetic products when used in rinse-off products at concentrations greater than 0.01% and in leave on products at concentration greater than 0.001%. This recognises that citral can cause allergic reactions in some individuals. We also note that there appear to be no restrictions on neral or geranial, or citral when used in consumer products.

The IFRA Standard restricts the use of citral in some consumer products and cosmetics.

We note once again that the use of the scheduling process for fragrances and flavours is inefficient. We therefore support a separate discussion on the controls of fragrance and flavours rather than commenting on each individual fragrance and flavour.

ACCS meeting: November 2013

Benzidine-based dyes

Accord notes that benzidine and its salts are already controlled by workplace regulators in all States and Territories that have adopted the Model Work Health and Safety legislation. Benzidine and its salts are listed in the Prohibited carcinogen table (Table 10.1) of Schedule 10 (Prohibited carcinogens, restricted carcinogens and restricted hazardous chemicals) of the Model Work Health and Safety Regulations. As such, we do not believe that it is necessary to include benzidine and its salts in Schedule 7.

We do not believe that benzidine or its salts are being used in any formulated chemical products in Australia. On this basis, and based on the hazard posed by the substance, Accord supports including benzidine and its salts (excluding derivatives) in Appendix C with a scheduling cut-off of 0.1% to align with the Model Work Health and Safety Regulations.

Accord however does not support including all benzidine derived dyes in Appendix C. We note that the NICNAS IMAP tier II report includes several benzidine derived dyes that are considered to pose similar risks to benzidine and its salts. We also note that there are a number of other dyes that are derivatives of benzidine that have not been considered by NICNAS including 3,3'-dichlorobenzidine (CAS# 91-94-1), *o*-tolidine (2,2'-dimethyl-4,4'-benzidine, CAS# 119-93-7), *o*-dianisidine (2,2'-dimethoxy-4,4'-benzidine, CAS# 119-90-4) and 3,3',4,4'-tetraaminodiphenyl (CAS# 91-95-2). Unlike benzidine and its salts, these substances are not included in Schedule 10 of the Model Work Health and Safety Regulations. Accord also notes from our quick search of available information, that while they are structurally related, not all of the derivatives appear to pose the same carcinogenicity concerns.

Accord also notes that certain benzidine dyes are allowed to be used in cosmetics.

We are concerned that an Appendix C Scheduling entry for all benzidine derived dyes will have unintended consequences of banning currently useful substance, without properly considering the risks and benefits of their uses. For example, Accord is aware that Pigment Yellow 12, a benzidine based dye is currently used in Australia in temporary hair dyes and is permitted in cosmetics in other countries. Benzidine orange (or pigment orange, C.I. 21110) is also used in cosmetics in other countries such as Japan.

In 2010 the US EPA ran a screening level hazard characterisation of another benzidine based dye (Pigment Yellow 14) as part of the High Production Volume (HPV) Challenge Program[4]. We would therefore assume that there is at least one benzidine based dye that is used in high volume in USA and presumably elsewhere, possibly including Australia.

Accord suggests the following wording:

Apppendix C

Benzidine *excluding derivatives except in preparations containing 0.1 per cent or less benzidine.*

[4] http://www.epa.gov/hpvis/hazchar/5468757_CI%20Pigment%20Yellow%2014_March2010.pdf

ACCS meeting: November 2013

C11-C15-secondary, ethoxylayed, oxirane and oxirane, ethyl (oxirane)

Accord is unsure of the substance being proposed for scheduling or the scheduling proposal.

Accord notes that the substance name does not appear to make sense i.e. does not represent a sensible chemical structure.

The substance name “C11-C15- secondary, ethoxylated, oxirane and oxirane, ethyl (oxirane)” does not make sense for a number of reasons. Firstly, “ethoxylated” means reacted with oxirane (synonym for oxirane is ethylene oxide). We initially thought oxirane may have been accidentally repeated but noticed that “oxirane, ethyl” which we assume refers to butylene oxide, is not referenced in the substance name (e.g. butoxylated). Further the word “secondary” should refer to an alkyl chemical structure like alcohols e.g. secondary ethoxylated alcohol – this does not appear to be the case.

Accord has already raised this issue with the Scheduling Secretariat prior to making this submission, and has been informed that our comments have been passed on to the Delegate and NICNAS. We assume from this that the scheduling proposal originated from NICNAS, possibly from the IMAP process. Accord notes that there are a number of IMAP tier II reports related to ethoxylated, and ethoxylated and propoxylated alcohols. However we note that none of these appear to be identified as secondary alcohols, and none of them are butoxylated.

More intriguingly, the Scheduling proposal linked to this substance appears to relate only to oxirane and not ethoxylated alcohols. This is particularly strange as oxirane is already scheduled as an S7 chemical by its synonym ethylene oxide. The proposal is suggesting S6 inclusion without any reference to the existing S7 entry which does not have a cut-off for scheduling.

We are unsure whether this is a badly worded down-scheduling proposal for ethylene oxide, or simply an error.

Accord is interested in any scheduling proposals for ethoxylated alcohols or scheduling amendment proposals for ethylene oxide. However, we strongly urge the Scheduling Committee to seek comments again with a substance name that makes sense and a scheduling proposal that links with the substance name, rather than relying on the input from stakeholders on the notice for scheduling published in October.

ACCS meeting: November 2013

Diethylene glycol monobutyl ether

Accord notes that the scheduling proposal for diethylene glycol monobutyl ether (INCI name butoxydiglycol) relates to the addition of first aid instructions, warning statements and general safety directions.

While the scheduling proposal is unclear on the appropriateness or otherwise of the current scheduling cut-off for butoxydiglycol, based on the NICNAS IMAP report on the substance Accord has assumed that there were no concerns raised with the current scheduling exemption for products containing 10% or less butoxydiglycol.

Information we have received so far indicates that butoxydiglycol is used in concentrations less than 10% in most consumer and cosmetic products.

Accord is unsure of the new first aid, warning and safety directions being proposed and the reasons for these. It is our understanding that companies that are using this substance at above 10% in their formulation are providing appropriate statements on the label to enable safe use of their products. This is only to be expected for products carrying the “CAUTION” signal heading.

If specific first aid, warning and safety directions are considered necessary, we believe there needs to be further consultation with industry including the proposed specific statements to ensure that the impact on companies using this substance is minimised (need for new artwork/template, relabelling, etc.).

ACCS meeting: November 2013

Ethylene glycol monomethyl ether

Accord seeks clarification from the Scheduling Committee and the Delegate whether the schedule entry for ethylene glycol monoalky ether also applies to diethylene glycol monoalkyl ethers. We note that the derivative rule may mean that the diethylenes are captured by the ethylene schedule entry.

This would also explain the scheduling proposal. We believe that the proposal was put forward by NICNAS from the IMAP process. However, Accord was unable to find an IMAP report for ethylene glycol monomethyl ether. There was however an IMAP report for diethylene glycol monomethyl ether, and we believe this scheduling proposal reflects the recommendations from that IMAP report.

Feedback from Members and our international sister organisations is that ethylene glycol monomethyl ether is not used in cosmetics. Accord supports addition of ethylene glycol monomethyl ether for cosmetic use in Appendix C.

While we suspect that diethylene glycol monomethyl ether is also not used in cosmetics (as it is also on the prohibited list in the EU Cosmetics Directive), Accord respectfully suggests that if diethylene glycol monomethyl ether is captured by the ethylene glycol monomethyl ether entry, that this be made clear in the Delegate's Interim Decisions as a minimum to allow comments from companies that are potentially impacted.

ACCS meeting: November 2013

Mercaptoacetic acid

It is Accord's understanding that mercaptoacetic acid is used in hair straightening, perming and colouring products as well as depilatory products. We also understand that the substance has industrial use as a corrosion inhibitor.

Accord notes that mercaptoacetic acid (or thioglycolic acid) is not currently scheduled. However, it is in Annex III (restricted use) of the EU Cosmetics Directive. The safety of mercaptoacetic acid has also been reviewed by the Cosmetic Ingredients Review (CIR) panel. The CIR conclusion was that thioglycolic acid is "*safe for use in hair straighteners permanent waves, tonics, dressings, and so forth, wave sets, other noncoloring hair products, and hair dyes and colors, at concentrations up to 15.2%; hairdressers should avoid skin contact and minimize consumer skin exposure; safe for use in depilitories when formulated to be non-irritating under conditions of recommended use*".

Accord tentatively supports scheduling of mercaptoacetic acid (with cross reference to thioglycolic acid in the index) as S6 with exemptions for cosmetic products containing 15.2% or less mercaptoacetic acid.

Accord proposes the following wording:

Schedule 6

Mercaptoacetic acid *except in cosmetics containing 15.2 per cent or less mercaptoacetic acid.*

ACCS meeting: November 2013

Methanol

Accord understands that the scheduling proposal for methanol arises from the NICNAS IMAP process. As far as we are aware, there has been no significant new information put forward in the IMAP process to suggest that the current scheduling of methanol is inappropriate. We understand that IMAP simply looked at the EU Cosmetics Directive and suggested aligning with it.

Accord does not agree with this approach to adopting the EU Cosmetics Directive. In the EU, cosmetic ingredients do not go through a pre-market approval process. The Cosmetics Directive is there to provide "boundaries" to limit or prohibit the use of substances that have sufficient evidence to suggest that they may be harmful when used in cosmetics. In this, its role is not dissimilar to the Schedule system except for much narrower scope.

In Australia, NICNAS assesses all new cosmetics ingredients unless they meet the exemption criteria. NICNAS is also currently tasked with assessing all chemical substances on AICS including those used in cosmetics. NICNAS can then refer the substance (either through the new or existing chemicals process) to the Scheduling process for risk management controls.

Where we currently have controls in place in Australia through scheduling and there is no evidence to suggest that it is inadequate, there is no case for a re-scheduling proposal. It is simply not good enough to state that the EU Directive has different controls.

Accord is not opposed to adopting an EU style Cosmetics Directive. However we should not have to comment on each and every cosmetic substance on the EU Directive through the IMAP and Scheduling processes. This is highly inefficient.

If it is the policy decision that an EU style Cosmetics Directive should be implemented in Australia then this should follow a proper reform process, including cost/benefit considerations. It must also be remembered that ingredients are not assessed pre-market in the EU.

Accord notes that methanol is used in Australia in both cosmetics and consumer products, but in most cases (particularly in cosmetics) is present as a denaturant in ethanol. As far as we are aware, there have been no concerns raised with the current scheduling controls.

Accord does not support the proposed amendment to methanol scheduling.

ACCS meeting: November 2013

Pentanoic acid, 3-methyl-2-oxo-, ethyl ester

While Accord understands that this substance was assessed by NICNAS and added to the Australian Inventory of Chemical Substances (AICS) in April 2013, we have no further information on this substance.

Accord notes that it can be difficult for industry to identify chemicals used in their products, particularly for cosmetics, when the common name for the substance is not made available. While we understand that this substance may be an industrial chemical, if consideration of the substance includes its use in cosmetics and consumer products, we request that the INCI name and common name of the substance be made available for further comments.

ACCS meeting: November 2013

Sulfites - i.e. salts of sulfurous and disulfurous acids

Accord does not believe that sulfites require scheduling controls when used in cosmetics.

Sulfites are naturally occurring in food and are also commonly added to food as preservatives. We understand that sulphites are also used in medicines. We do not believe sulphites in cosmetics can be considered in isolation without considering the prevalent nature of sulphites in foods we eat, beverages we drink and medicines we take.

While we understand that there are a significant number of individuals with sulfite allergies, we also note that serious reactions to sulfites are rare and ingredient labelling disclosure (required by the Australian Competition and Consumer Commission) should inform those individuals suffering from sulfite allergies.

Accord does not support scheduling of sulfites.

ACCS meeting: November 2013

Tetrahydrofuran

Tetrahydrofuran is a commonly used industrial solvent. While we understand that tetrahydrofuran may be used in consumer products, Accord has not received any feedback from Members that it is currently being used in Australia.

While Accord notes that tetrahydrofuran is an irritant, we are unsure whether it is more irritating than other organic solvents. All organic solvents are irritating because they de-fat the skin.

Accord does not believe that tetrahydrofuran or other organic solvents require scheduling controls. However, if any scheduling is considered necessary for tetrahydrofuran, we believe that the ACCS and the Delegate should cast the net wider and capture all organic solvents for their irritation potential. This would also require further consultation and consideration of the impact on industry.

Any scheduling consideration should also be limited to tetrahydrofuran (and any other solvents) rather than to salts and derivatives to ensure that other substances are not inadvertently captured e.g. a number of fragrances are derivatives of tetrahydrofuran.

ACCS meeting: November 2013

Triethanolamine

Triethanolamine (TEA) is widely used in cosmetics, consumer products and in industrial applications. In cosmetics and consumer products, TEA is used as a neutralising agent/pH adjustor.

Accord notes that the Scheduling proposal includes consideration of tattoo removal "cosmetics" applied intradermally. As cosmetics cannot be applied intradermally (by definition cosmetics can only be applied to intact skin) we believe that this consideration should go to the ACMS. We have no comments on intradermal application of TEA.

TEA is currently included in Schedule 5. The entry reads:

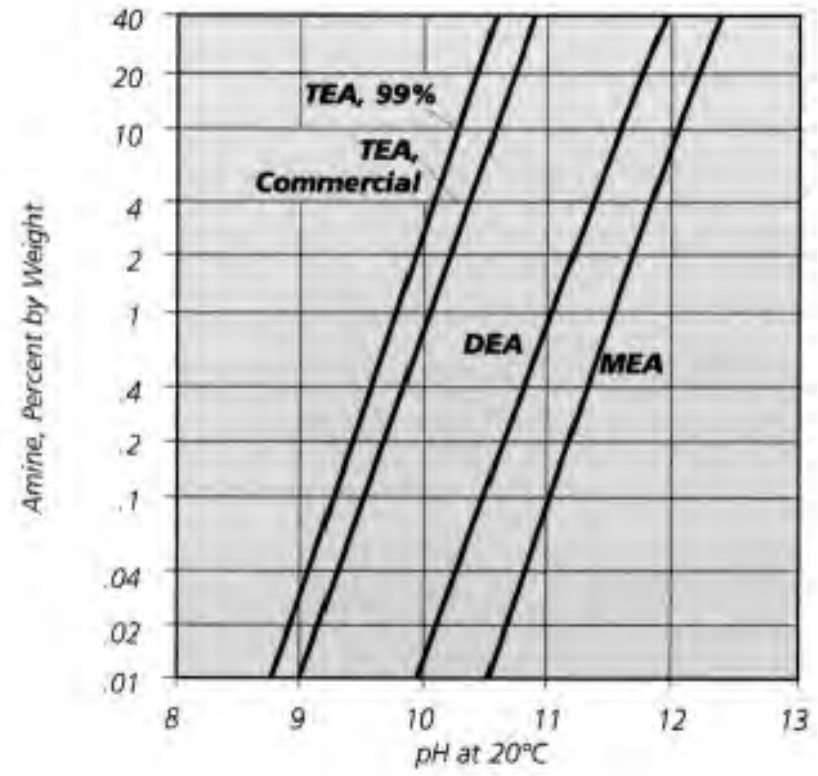
> ***Triethanolamine*** *(excluding its salts and derivatives) except in preparations containing 5 per cent or less triethanolamine.*

Accord understands that the main concern for TEA is the irritation potential. Based on the information in the NICNAS IMAP report on TEA, Accord deduces that irritation is likely to be induced by chemical reaction between TEA and the skin and eyes rather than through other mechanisms e.g. TRPV1 receptor agonist. The irritation potential should therefore relate to the un-neutralised TEA and not the salts of the TEA, which we believe was also the rationale for the current schedule entry.

It is Accord's view that re-scheduling of TEA is unwarranted. We are unaware of any concerns raised with consumer or cosmetic products containing TEA with the current scheduling controls. This may be partly due to TEA being used at levels lower than allowed by current scheduling.

As TEA is used as a pH adjustor, we do not expect that TEA would be present in finished cosmetic products at high levels. In fact, when we consider the pH scale against TEA concentration (please see graph next page – from DOW Chemicals information sheet on ethanolamines[5]), we believe most cosmetic products are likely to contain well below 1% TEA.

5 http://msdssearch.dow.com/PublishedLiteratureDOWCOM/dh_017d/0901b8038017d302.pdf?filepath=amines/pdfs/noreg/111-01375.pdf&fromPage=GetDoc



Feedback from some industry members is that determination of the concentration of TEA itself in a product i.e. not its salts, can be quite difficult. TEA is a weak alkali and its interaction with weak acids within a formulation can sometimes be hard to determine.

Anecdotally, one of our Members believed that they may have had high levels of TEA in their products (up to 10%) but the product pH was at around 7 i.e. neutral pH. It was therefore highly unlikely that TEA was present in the product in its alkaline form. It was only after close scrutiny of all potential reactions within the formulation that they were able to confirm that TEA was not present in the product at high levels.

While Accord does not support re-scheduling of TEA, if any re-scheduling was to be considered, it may be more meaningful to equate pH of the product containing TEA with TEA concentration. We would however strongly recommend further consultation on such consideration, with a focus on potential cost to industry, and also seeking appropriate pH cut-off for exemption from scheduling.

ACCS meeting: November 2013

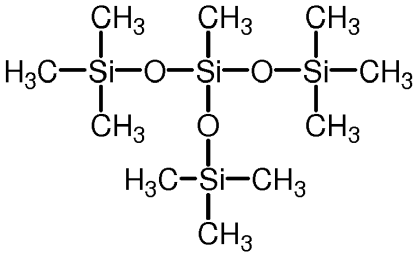
Trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[(trimethylsilyl)oxy]-

Accord understands that the scheduling proposal for trisiloxane, 1,1,1,3,5,5,5-heptamethyl-3-[trimethylsilyl)oxy]- (better known as methyl trimethicone) arises from the NICNAS New Chemicals Assessment of the chemical.

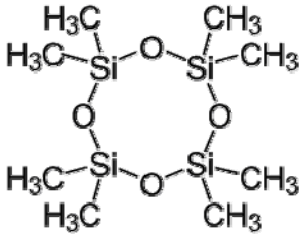
Accord has serious concerns with a number of aspects of the NICNAS assessment of methyl trimethicone and the scheduling proposal from scientific assessment and risk management view-points.

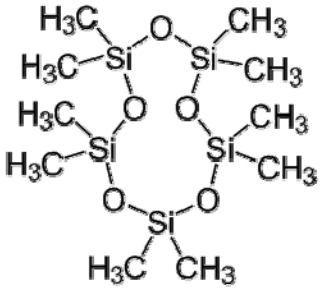
Accord notes that the human health assessment, particularly the setting of the Margin of Exposure was based on the No Observed Adverse Effects Level (NOAEL) of "analogues" D4 (octamethylcyclotetrasiloxane) and/or D5 (Decamethylcyclopentasiloxane). We understand that it was NICNAS' decision to assign D4 and D5 as "analogues" of methyl trimethicone.

Below is the chemical structure of methyl trimethicone:



And below are the chemical structure of D4 and D5 respectively:





Accord fails to see the structural similarity between methyl trimethicone and D4/D5. All of these substances are silicone based and are similar in molecular weight, however this is where the similarities appear to end.

Without providing scientific justification for assigning D4/D5 as analogues of methyl trimethicone (e.g. mode of action for D4/D5 is known and it is likely, based on scientific logic that can be explained, that methyl trimethicone will also trigger the same toxicological response as D4/D5), the use of D4/D5 data for risk assessment of methyl trimethicone is inappropriate. Accord was unable to find such scientific justification in the public reports of NICNAS assessments. The only justification NICNAS put forward for the use of D4/D5 as analogues is that the three substances have similar molecular weight, water solubility, partition co-efficient and vapour pressure.

If we were to consider all chemicals with similar physicochemical properties mentioned above as analogues, then *n*-hexane, benzene and cyclohexane should all be considered carcinogens

(since benzene is a known carcinogen). Similarly, ethylene glycol and propylene glycol, butanol and isopropanol would be considered as analogues and therefore to pose similar risks. There are endless such examples. Clearly this would be a mistake.

The test data for methyl trimethicone is available in NICNAS assessment reports, although not for all endpoints, and shows that the substance is not irritating to the skin or eyes, not mutagenic or genotoxic, shows no evidence of being a sensitiser and has low toxicity (the LD50 value for acute oral toxicity test on rats was >2000 mg/kg).

Based on the information on methyl trimethicone, we do not believe that the substance should be scheduled.

Accord is also baffled that NICNAS appears to have requested scheduling for methyl trimethicone but not for D4 or D5. Considering that the data NICNAS put forward to support scheduling of methyl trimethicone is actually for D4 and D5 it is surprising that there is no mention of D4 or D5 in the scheduling proposal.

Furthermore, while NICNAS used information from the 2010 EU SCCS opinion on D4 and D5[6], it did not consider the conclusions from the same report nor the regulatory controls currently in place in the EU. The conclusion in the 2010 EU SCCS opinion on D4/D5 was that they do not pose a risk to human health when used in cosmetic products. It is therefore not surprising that neither D4 nor D5 are restricted for use in cosmetics in the EU. We are also unaware of any restrictions in the USA.

Accord does not support scheduling of methyl trimethicone, D4 or D5 based on all available information on these substances.

[6] http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_029.pdf

ACCS meeting: November 2013

Zinc lactate

Accord notes that the proposal to schedule cosmetic products containing 2.5% or more zinc lactate has been put forward by NICNAS based on their New Chemicals assessment on zinc lactate for use in cosmetic toothpaste.

Accord does not believe that lactic acid is of any concern as it is a common, naturally occurring substance that is often found naturally in food and also added to food. We understand that any concerns with zinc lactate relate to the potential for over-consumption of zinc. The percentage of zinc in zinc lactate is approximately 30% (conservatively estimating).

While the International Cosmetic Ingredient (INCI) Dictionary and Handbook lists deodorant agent, cosmetic astringent and cosmetic biocide as the uses of zinc lactate, we understand that it is rare for zinc lactate to be used in cosmetics, based on information provided to us by our sister organisation in the USA (they have one reported use of zinc lactate in a product).

Zinc is used in food as an acceptable mineral additive (See Food Standards Australia and New Zealand (FSANZ) Standard 1.3.1[7]). Zinc lactate is also specifically mentioned in the FSANZ Standard 2.9.5[8]. Zinc lactate is also used in complementary medicines.

Based on the *Notes of Guidance for Testing of Cosmetic Ingredients and Their Safety Evaluation 8th revision* published by the Scientific Committee of Consumer Safety (SCCS) in 2012[9], the estimated daily exposure to toothpaste for adults is 2.75g. The SCCS report also estimates that approximately 5% of the toothpaste will be "retained" once dilution and rinsing is factored in i.e. the "daily dose" of toothpaste for adults is 137.5mg.

Currently medicines containing zinc compounds for human internal use in preparations with a recommended daily dose of 25mg or less zinc are excluded from scheduling requirements. Between 25mg and 50mg, the preparations are exempted when compliant with the requirements of the *Required Advisory Statements for Medicine Labels*.

If we are to consider limiting zinc to 25mg or less per day, the toothpaste can contain up to 60% zinc lactate. We do not believe that a substance used as a deodorant/biocide is likely to be used in the product at such high levels.

The product notified to NICNAS contained 2.5% zinc lactate, or approximately 0.75% zinc. At this level, even if dilution factors are not taken into account i.e. the full average daily amount of toothpaste used (2.75g) is ingested, the zinc taken from toothpaste would be below 25mg (approximately 20mg).

Given that medicines containing zinc compounds that are intended to be ingested are unscheduled when the daily dose of zinc is 25mg less, based on the information above, it is Accord's view that zinc lactate as an ingredient in cosmetics does not require scheduling.

[7] http://www.comlaw.gov.au/Series/F2008B00614
[8] http://www.comlaw.gov.au/Details/F2013C00147
[9] http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_006.pdf

accord
hygiene, cosmetic & specialty products industry

The Secretary
Scheduling Secretariat
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Email: SMP@health.gov.au

Dear Sir/Madam

Public Comment Submission to the November 2013 joint meeting of the Advisory Committee on Chemicals Scheduling (ACCS) and the Advisory Committee on Medicines Scheduling (ACMS)

We refer to the notice published on 17 October 2013 inviting public submissions, with respect to certain substances, addressing a matter raised in s.52E of the *Therapeutic Goods Act 1989*.

Accord Australasia Limited is the peak national industry association that represents the hygiene, cosmetic & specialty chemicals industry.

Accord wishes to provide information on **the cosmetic use and personal care use definition**, **ethanol, 2-(dimethylamino)-** and **salicylic acid** for consideration at the November 2013 joint-meeting of the ACCS and ACMS.

Please see the attached submission for details.

Accord is an interested party and stakeholder with regard to the nominated substances and would appreciate being advised of the Committees' considerations and the Delegate's interim decision, with the opportunity for further submission, if appropriate.

We look forward to further advice from the ACCS, ACMS and the Delegate. Should the Committees or the Delegate require any additional information from Accord at this stage please do not hesitate to contact me on [redacted]

Yours faithfully

[redacted]

[redacted]

14 November 2013

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ACCS/ACMS joint-meeting: November 2013

Cosmetic use and personal care use

Accord provided comments to the Delegate's Interim Decisions for iodocarb and cocoyl glycinate from the July 2013 ACCS meeting agenda. In our comments, we sought clarification on the differentiation between "cosmetic" and "personal use" products, noting that the term "personal use" was being used for the first time in the Poisons Standard.

While there are no definitions for "cosmetic" or "personal use" in the Poisons Standard, the term "cosmetic" is currently used in the Poisons Standard. Also, the definition for "cosmetic" exists in other legislation and is well understood by industry.

The definition of "cosmetic" is provided in the *Industrial Chemical (Notification and Assessment) Act 1989* (Cth):

> ***cosmetic*** means:
> (a) a substance or preparation intended for placement in contact with any external part of the human body, including:
> (i) the mucous membranes of the oral cavity; and
> (ii) the teeth;
> with a view to:
> (iii) altering the odours of the body; or
> (iv) changing its appearance; or
> (v) cleansing it; or
> (vi) maintaining it in good condition; or
> (vii) perfuming it; or
> (viii) protecting it; or
> (b) a substance or preparation prescribed by regulations made for the purposes of this paragraph;
> but does not include:
> (c) a therapeutic good within the meaning of the *Therapeutic Goods Act 1989*; or
> (d) a substance or preparation prescribed by regulations made for the purposes of this paragraph.

The *Trade Practices (Consumer Product Information Standards) (Cosmetics) Regulations 1991* (Cth) made under the *Trade Practices Act 1974* (Cth) also defines "cosmetic product":

> ***cosmetic product*** means a substance or preparation intended for placement in contact with any external part of the human body, including:
> (a) the mucous membranes of the oral cavity; and
> (b) the teeth;
> with a view to:
> (c) altering the odours of the body; or
> (d) changing its appearance; or
> (e) cleansing it; or
> (f) maintaining it in good condition; or
> (g) perfuming it; or
> (h) protecting it.

The *Trade Practices (Consumer Product Information Standards) (Cosmetics) Regulations 1991* (Cth) exempts the following from the requirements of the regulations:

(a) therapeutic goods within the meaning of the *Therapeutic Goods Act 1989*; or
(b) free samples of a cosmetic product; or
(c) testers of a cosmetic product.

Accord notes that while the wording may be slightly different, two definitions, "cosmetic" in the *Industrial Chemical (Notification and Assessment) Act 1989* (Cth) and "cosmetic product" in the *Trade Practices (Consumer Product Information Standards) (Cosmetics) Regulations 1991* (Cth) are consistent.

Accord suggests adopting the simpler definition of "cosmetic" into the Poisons Standard. i.e.

cosmetic means a substance or preparation intended for placement in contact with any external part of the human body, including:
(a) the mucous membranes of the oral cavity; and
(b) the teeth;
with a view to:
(c) altering the odours of the body; or
(d) changing its appearance; or
(e) cleansing it; or
(f) maintaining it in good condition; or
(g) perfuming it; or
(h) protecting it.

If the Scheduling Committees believe that there is a need to distinguish the difference between cosmetic products and therapeutic goods that may also have cosmetic function e.g. therapeutic toothpastes, Accord suggests adding the following statement:

but does not include a therapeutic good within the meaning of the *Therapeutic Goods Act 1989*.

If the above definition of "cosmetic" is adopted, then we do not believe there is a need to adopt a definition for "personal care", as we are unaware of "personal care" products that would not meet the above definition of "cosmetic" that are relevant for scheduling purposes.

Further we could not support the introduction of a new definition for "personal care" to be set in the Poisons Standard, a legislative instrument, without first assessing the potential for wider impact. As the use of the term "cosmetic" has demonstrated, where the definition of a term does not exist in the relevant legislation, the definition can be "borrowed" from another source, particularly if that definition is well known.

We therefore strongly urge the Committees to consider setting the definition for "cosmetic" and not for "personal care".

ACCS/ACMS joint-meeting: November 2013

Ethanol, 2-(dimethylamino)-

Accord notes that ethanol, 2-(dimethylamino)- (otherwise known as dimethylaminoethanol (DMAE) or deanol) has both therapeutic and non-therapeutic uses.

We understand that the Schedule 4 entry for deanol was initially concerned with orally ingested medicine for treating attention deficit-hyperactivity disorder, Alzheimers's disease, autism. We understand that there is some research showing that deanol may be transformed in the liver into choline and acetylcholine.

While we have had no reports of Australian industrial uses of deanol, we understand that internationally dimethylaminoethanol is used:

- in water-reducible coating formulations,
- as a raw material to make dimethylaminoethyl methacrylate, and
- as a corrosion inhibitor in boiler water condensate return lines.

It is also our understanding that salts and derivatives of deanol e.g. dimethyl aminoethanol tartrate and dimethylaminoethyl ceterate are used in cosmetics (skin and hair conditioning agents).

Accord therefore supports amendments to the Schedule 4 entry of deanol to exempt industrial, cosmetic and topical therapeutic (e.g. sunscreens) uses of deanol and its derivatives from scheduling.

Accord suggests the following wordings:

Deanol for therapeutic use excluding topical therapeutic use.

ACCS/ACMS Joint-meeting: November 2013

Salicylic acid

Accord notes that the scheduling proposal for salicylic acid includes amendments to the current Schedule 3 and 4 entries for salicylic acid. We were only able to locate a Schedule 3 entry for salicylic acid – Accord requests confirmation that there are no other entries for salicylic acid, and the proposal relates only to the amendment of the Schedule 3 entry and creation of a potential new Schedule 5 entry.

We note that a Schedule 4 entry exists for aspirin, a derivative of salicylic acid (acetylsalicylic acid). We believe this may have been the basis for the confusion caused, although we also note that there are Schedule 2, 4, 5 and 6 entries for aspirin. To remove any confusion, Accord suggests amending the current salicylic acid schedule entry to exclude aspirin (noting that salts and esters of salicylic acids have similar properties to salicylic acid).

The purpose of the proposed scheduling amendment appears to be alignment the Australian cosmetic use of salicylic acid with that of the EU. This proposal appears to be based on the NICNAS IMAP tier II report on salicylic acid and its salts, which in turn is based on the information in the 2001 Opinion of the Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP).

Accord notes that the SCCNFP was requested to respond to two specific questions. These were:

1. *Concerns the evaluation of the safety of salicylic acid for other specific nonpreservative purposes: leave-on formulations (face and general creams) and rinse-off products (make-up removers, shower gels, shampoos and hair conditioners) at a level of 2 %, leave-on hair care products at 1 % salicylic acid level and the use of salicylic acid as a preservative in other cosmetic products at the 0.5 % concentration.*
2. *Can salicylic acid and its salts safely be used for non-preservative purposes in cosmetic rinse-off hair products at a maximum concentration of 3 %?"*

The SCCNFP responded to these questions, and stated its opinion:

> *"On the bases [sic] of the information provided for consideration, the SCCNFP considers that salicylic acid is safe for "other uses" than as a preservative, at a concentration up to 2.0 % for the leave on and rinse-off cosmetic products and at a concentration up to 3.0 % for the cosmetic rinse-off hair products."*

The opinion reached by the SCCNFP is therefore predicated on the question it was requested to answer.

We note that the margin of safety was calculated based on the following scenario:

- NOAEL value of 75mg/kg bw/day (rat oral teratogenicity study),
- Body weight of 60 kg,
- Maximum skin absorption rate of 20% (regardless of whether the product is leave on or rinse-off), and
- Daily use of a range of products all containing the maximum amount of salicylic acid being considered i.e. hand cream (2%), face cream (2%), leave on hair product (1%), shampoo (3%), other rinse-off products (2%) and all other cosmetics (0.5% as preservative).

This is a very conservative scenario. Firstly, it is unlikely that the maximum absorption rate of 20% will be reached for all products, particularly rinse-off products. Secondly, it is unlikely that all

the products will contain the maximum allowed levels of salicylic acid. Thirdly, the quantity of “all other cosmetics” containing salicylic acid as a preservative used daily is given as 12g. This is a fairly large quantity – equivalent to approximately three to four whole lipsticks. Further, it is highly unlikely that any individual will use the full range of cosmetics detailed in the SCCNFP opinion, all containing salicylic acid, daily.

Even so, the margin of safety for the scenario was calculated to be 133.

Accord does not believe that the SCCNFP opinion provides an appropriate basis for the proposed Scheduling amendment because it is too conservative, and it was responding to a specific question of using salicylic acid at a maximum concentration of 3% in any cosmetic product.

It is Accord’s view that we should be looking at the Australian history of use for salicylic acid, and whether current scheduling conditions have caused any cause for concern. As far as we are aware, there have been no concerns raised with the current scheduling of salicylic acid. Even in the IMAP report, we note that NICNAS is merely suggesting that we align with the EU rather than being critical of the current scheduling and its outcomes.

If we were to consider international harmonisation, we must also consider our other close trading partner, the USA. It is our understanding that there are no limitations placed on the use of salicylic acid in cosmetics in the USA. It is our understanding that at the February 2000 meeting of the Cosmetic Ingredient Review (CIR) Expert Panel, the Panel reached the tentative conclusion that the use of salicylic acid related substances in cosmetics is "*safe as used when formulated to avoid irritation and when formulated to avoid increased sun sensitivity*".

We note that this is a different focus to the SCCNFP opinion which focussed on the NOAEL value for teratogenicity.

Given these considerations, Accord respectfully suggests maintaining status quo for salicylic acid scheduling.

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12th November 2012

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601

Dear Sir or Madam,

Re: Invitation for public comment – ACCS and joint ACCS/ACMS Meetings, November 2013
ASMI comment – ACMS meeting

We refer to the notice inviting public comment under Regulation 42ZCZK of the Therapeutic Goods Regulations and would like to provide comment on the scheduling proposals that are to be considered by the joint ACCS/ACMS meetings in November 2013. The comments submitted below address matters raised in s.52E of the *Therapeutic Goods Act 1989*. Thank you for providing the opportunity to comment.

ASMI (Australian Self Medication Industry) is the peak body representing companies involved in the manufacture and distribution of consumer health care products (non-prescription medicines) in Australia. ASMI also represents related businesses providing support services to manufacturers, including advertising, public relations, legal, statistical and regulatory consultants.

ASMI provides the following comments in relation to each of the matters on the agenda of the joint ACCS/ACMS meeting.

Cosmetic use / Personal care use – Proposal to include definitions, such as cosmetic use and / or personal care use, in Part 1 of the SUSMP to better define these terms and their intent and purpose.

ASMI supports the inclusion of a definition for "cosmetic use" in the Poisons Standard. "Cosmetic use" is a term that is currently used within the Poisons Standard and ought to be defined; inclusion of a definition in Part 1 appears to be a suitable approach.

It would be appropriate for the definition of "cosmetic use" to reflect the definition of a "cosmetic" in other relevant legislative instruments. ASMI notes that the term "cosmetic" is defined slightly differently in two legislative instruments.

The Trade Practices (Consumer Product Information Standards) (Cosmetics) Regulations 1991 (section 3) provides the following definition of a cosmetic product:

> ***cosmetic product*** means a substance or preparation intended for placement in contact with any external part of the human body, including:

(a) the mucous membranes of the oral cavity; and
(b) the teeth;
with a view to:
(c) altering the odours of the body; or
(d) changing its appearance; or
(e) cleansing it; or
(f) maintaining it in good condition; or
(g) perfuming it; or
(h) protecting it.

The definition in the Trade Practices (Consumer Product Information Standards) (Cosmetics) Regulations 1991 provides for the following exemptions from the requirements:

(a) therapeutic goods within the meaning of the *Therapeutic Goods Act 1989*; or
(b) free samples of a cosmetic product; or
(c) testers of a cosmetic product.

The Industrial Chemical (Notification and Assessment) Act 1989 (section 5) defines "cosmetic" as follows:

cosmetic product means
(a) a substance or preparation intended for placement in contact with any external part of the human body, including:
(i)the mucous membranes of the oral cavity; and
(ii) the teeth;
With a view to:
(iii) altering the odours of the body; or
(iv) changing its appearance; or
(v) cleansing it; or
(vi) maintaining it in good condition; or
(vii) perfuming it; or
(viii) protecting it; or
(b) a substance or preparation prescribed by regulations made for the purposes of this paragraph;
But does not include:
(c) a therapeutic good within the meaning of the Therapeutic Goods Act 1989; or
(d) a substance or preparation prescribed by regulations made for the purposes of this paragraph.

The Therapeutic Goods Act 1991 defines *therapeutic use*:

therapeutic use means use in or in connection with:
(a) preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury in persons; or
(b) influencing, inhibiting or modifying a physiological process in persons; or
(c) testing the susceptibility of persons to a disease or ailment; or
(d) influencing, controlling or preventing conception in persons; or
(e) testing for pregnancy in persons; or
(f) the replacement or modification of parts of the anatomy in persons.

Although the definition of "cosmetic" in the Trade Practices (Consumer Product Information Standards) (Cosmetics) Regulations 1991 is substantially similar to that provided in the Industrial

Chemical (Notification and Assessment) Act 1989 in that both definitions exclude therapeutic goods, there is a key difference in that the definition in the Trade Practices (Consumer Product Information Standards) Regulations 1991 pertain mainly to labelling standards, accounting for the exclusion of samples and testers from the definition.

The definition of "cosmetic" in the Industrial Chemical (Notification and Assessment) Act 1989 is more relevant in defining the nature of a cosmetic and does not exclude samples and testers, therefore ASMI's preference is for this definition to be used in the Poisons Standard Part 1.

ASMI notes that unlike "cosmetic", the term "personal care" and "personal care use" is not currently used in the existing legal framework. For this reason, ASMI sees no need to introduce this new term as the existing entries of the Poisons Standard will not relate to it.

If a strong rationale exists for the introduction of a definition for "personal care use", then this should be provided to stakeholders together with the proposed definition and the opportunity for further consultation should be provided.

Ethanol,2-(dimethylamino)- Proposal to include ethanol,2(dimethylamino)- in Schedules 5 or 6 and to make relevant amendments to the current Schedule 4 entry for deanol

Deanol for therapeutic use

ASMI notes that there is one export only listing for a product containing deanol and that there are no registered products containing deanol on the ARTG. Deanol is mentioned in the medical literature as a precursor to acetylcholine[1], thought to have uses for the treatment of childhood hyperactivity, autism and behavioural disorders. There are no recent citations for the use of the substance for these conditions and most publications date from the 1960s and 1970s.

ASMI believes that the current scheduling for deanol (Schedule 4) is appropriate.

Ethanol, 2-(dimethylamino)- for non-therapeutic use

A brief review of the literature shows that some substances related to ethanol, 2-(dimethylamino) have uses in the cosmetics industry as well as industrial uses.

In order to accommodate other non-therapeutic uses for deanol and its salts and derivatives, ASMI would have no objection to the current Schedule 4 entry to be amended to read "Deanol for therapeutic use" or similar.

Salicylic acid – Proposal to amend the current Schedules 3 and 4 entries for salicylic acid and possibly create a new Schedule 5 entry to align with EU restrictions on the use of salicylic acid in cosmetics to a maximum concentration of 3%

ASMI notes that the Poisons Standard has one Schedule 3 entry for salicylic acid, for salicylic acid for dermal use except in preparations containing 40% or less of salicylic acid. There is no Schedule 4 entry for salicylic acid.

The ARTG includes salicylic acid in many therapeutic goods for a range of uses that include:

- Preparations for treatment of warts – contain salicylic acid up to 17%
- Preparation for treatment of cradle cap – contains salicylic acid 6%

[1] Lewis JA, Young R. Deanol and methylphenidate in minimal brain dysfunction. Clin Pharmacol Ther 1975;17(5): 534-540

- Keratolytic ointments and creams – contain salicylic acid 2% to 5% (approximately)
- Shampoos for scalp conditions such as seborrhoeic dermatitis – contain salicylic acid 2%
- Antifungal preparations – contain salicylic acid 4%
- Mouth ulcer paints and gels – contain salicylic acid 2% approximately

The ARTG also has entries for registered products containing triethanolamine salicylate at concentrations of 100 mg/g to 150 mg/g, used for the relief of muscle aches and pains due to arthritic and rheumatic conditions.

Most of the therapeutic goods mentioned above are currently unscheduled.

There is no evidence of safety concerns with these types of products. They are regulated appropriately by the TGA.

ASMI believes that there should be no change to the regulation of these products and the current Schedule 3 entry for therapeutic goods containing salicylic acid is appropriate.

ASMI has concerns about the proposal for a Schedule 5 entry with an exemption for cosmetic use in concentrations up to 3%. In an attempt to apply a maximum cosmetic use for the substance, there may be an unnecessary and inappropriate impact on therapeutic products.

ASMI feels strongly that:

- The current scheduling of therapeutic goods that contain salicylic acid is appropriate and the status quo should be retained;
- If any changes are required to set an upper limit for salicylic acid content of cosmetics, the wording of the schedule entry should be carefully drafted to apply only to cosmetics and to ensure that there is no impact on therapeutic goods;

Conclusion

As an industry representative, ASMI is a key stakeholder in scheduling matters and appreciates the opportunity to comment on the scheduling proposals to be considered by the joint ACCS/ACMS November 2013 meeting.

ASMI supports the inclusion of a definition for a cosmetic in Part 1 of the Poisons Standard, and feels that the current definition provided by the Industrial Chemical (Notification and Assessment) Act 1989 is the most appropriate. Any definition of a cosmetic should exclude therapeutic goods, as defined in the Therapeutic Goods Act 1989. In principle, ASMI is supportive of a definition that is aligned with relevant existing legislation.

There is no currently applicable definition of personal care use in any related legislation. ASMI therefore believes that any proposed definition of "personal care use" should be provided to stakeholders and separately consulted.

ASMI believes that the scheduling of deanol and salicylic acid is appropriate and the status quo should be retained. However, use of these substances for cosmetic and industrial purposes is outside the scope of ASMI representation. Any proposals for scheduling amendments that may be required to accommodate these products should be carefully considered and drafted in such a way that the wording is clear and that there is no consequential impact on scheduling of therapeutic goods.

ASMI is keen to provide further input as required. We look forward to the Delegate's interim decisions.

Yours sincerely,

[redacted]

The Secretary
Scheduling Secretariat
GPO Box 9848
CANBERRA ACT
2601

14.11.2013

Dear Sir/Madam,

RE: Comments on Proposed amendments referred by the Delegate for scheduling advice for consideration by the Advisory Committee on Medicines Scheduling (ACMS)

[redacted] would like to provide comments on a number of the proposed amendments referred by the Delegate to the Committee of Medicines Scheduling (ACMS).

Cosmetic use; Personal Care use - Proposal to include definitions, such as cosmetic use and/or personal care use, in Part 1 of the SUSMP to better define these terms and their intent and purpose.

[redacted] agree that a clear definition for 'cosmetic' should be included in the Poisons Standard, since this is a term currently used within the standard. [redacted] align with ACCORD and ASMIs view that the definition of 'cosmetic' should be based on that used in either the Trade Practices Cosmetics Regulations 1991 or the Industrial Chemical (Notification and Assessment) Act 1989.

The following definition is proposed:

cosmetic means a substance or preparation intended for placement in contact with any external part of the human body, including:
(a) the mucous membranes of the oral cavity; and
(b) the teeth;

with a view to:
(c) altering the odours of the body; or
(d) changing its appearance; or
(e) cleansing it; or
(f) maintaining it in good condition; or
(g) perfuming it; or
(h) protecting it.

If the above definition of cosmetic is adopted, then we do not see the need to include a separate definition for 'personal care use' within the standard. Personal care products that have a cosmetic purpose would be captured by the definition proposed above and any other personal care products not fitting the definition of a cosmetic, such as articles, are not relevant for scheduling purposes. Additionally the term 'personal care use' is not currently used in the existing legal framework.

[redacted]

[redacted]

We therefore propose that the Committee and the Delegate only consider inclusion of a definition for 'cosmetic' within the Poisons Standard.

Salicylic acid - Proposal to amend the current Schedules 3 and 4 entries for salicylic acid and possibly create a new Schedule 5 entry to align with EU restrictions on the use of salicylic acid in cosmetics to a maximum concentration of 3 per cent.

[redacted] align with ACCORD's view that the Committee and the Delegate should consider the history of use of salicylic acid within Australia and whether there are any issues with current scheduling, rather than only using the SCCNFP opinion.

As far as we are aware, there have been no concerns raised with the current scheduling of salicylic acid. Additionally the Cosmetic Ingredient Review (CIR) Expert Panel has previously recommended that the use of salicylic acid related substances in cosmetics is "safe as used when formulated to avoid irritation and when formulated to avoid increased sun sensitivity."

[redacted] therefore propose that the Committee and the Delegate retain the current scheduling of salicylic acid.

Yours faithfully,

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Closing date for submission – 26 September 2013

[redacted]

[redacted]

[redacted]

[redacted]

Comments on Proposed Amendments

[redacted] has considered the proposed amendments to the SUSMP of relevance to community pharmacy, with particular reference to Section 52E(1) of the Therapeutic Goods Act 1989. We provide comments for the following proposed amendments in line with the rationale for our position provided above:

- Proposal for a new Schedule 3 entry for esomeprazole in oral preparations containing 20mg or less per dosage unit for the relief of symptoms for gastro-oesophageal reflux (heartburn) and symptoms of gastro-oesophageal reflux disease in packs containing not more than 14 days' supply.
- Proposal to either amend the current Schedule 3 entry or create a new Schedule 2 entry for macrogols when in liquid concentrate preparations for oral use in adults and children over 12 years of age for laxative use, with a potential inclusion of a concentration cut off and/or limited pack size.

1. Esomeprazole – Proposal for a new Schedule 3 (S3) entry for oral preparations containing 20mg or less in packs containing not more than 14 days supply

Esomeprazole is a proton pump inhibitor (PPIs) that has been available for many years on the Australian market as a Prescription Only Medicine for the treatment of acid-related gastrointestinal (GI) disorders. Four other PPIs, pantoprazole, omeprazole, lansoprazole and rabeprazole have also been available and are now listed as a Schedule 3 medicine in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), for low dose products for the relief of heartburn and other symptoms of gastro-oesphageal reflux disease (GORD), in packs containing no more than 14 days' supply.

Although GORD has not been declared a National Health Priority Area, it causes a high disease burden on the Australian community. Knox et al. (2008) estimate the prevalence of GORD in Australia to be over 9 per cent of the general population which equates to 2 million being affected by this condition.[9] The estimated prevalence of GORD in the Australian community is similar to that of osteoarthritis, asthma or depression.[10] Studies have shown the use of PPIs in the management of GORD and other gastric related disorders has dramatically improved the options and welfare of patients.[11] As such, greater access to such products is important.

Comparison to other PPIs

Esomeprazole has been shown to demonstrate a superior pharmacokinetic/pharmacodynamic profile than the racemic product omeprazole.[12] Esomeprazole is rapidly absorbed in both healthy adult populations and GORD patients, has a good tolerability profile and low potential for drug interaction. [13]

Supply Pack Size

Consistent with our previous positions on PPIs, [redacted] supports pack sizes containing no more than 14 days' supply. [redacted] believes availability for a maximum of a fortnight is consistent with the intent of the down-scheduling proposal to increase consumer access to PPIs for short-term relief of acute heartburn and GORD symptoms.

This supply pack size is also consistent with evidence that recommends that OTC PPIs should not be used for more than 4 weeks without consulting a doctor and if symptoms are not relieved within 2 weeks of continuous treatment, a doctor should also be consulted. [14]

While consumers can purchase two packs of 14 in a single transaction, such requests would prompt questions from a pharmacist to ensure safe and responsible use.

Recommended dosage rates and long term exposure

The tolerability and safety of esomeprazole has also been shown to be comparable to other PPIs.[15] Short-term tolerability has been documented in GORD at doses of 20-40mg/day.[16] Considering the scheduling proposal is for oral preparations containing 20mg or less per dosage unit, this is well within the limits of average tolerability.

Side effects

The most common adverse events reported in treatment for esomeprazole are headaches, diarrhoea and nausea.[17] However, the overall safety of esomeprazole indicates a safe tolerability profile in both paediatric and adult patients over short- and long-term periods of evaluation.[18]

Recommendation

Studies have shown esomeprazole to have a similar safety proposal compared to other PPIs such as omeprazole, while offering superior efficacy outcomes. As noted, most of the other PPIs are already available as Pharmacist Only (S3) medicines. Consequently, [redacted] supports the proposal for a new Schedule 3 entry for esomeprazole in oral preparations containing 20mg or less per dosage unit for the relief of symptoms for gastro-oesophageal reflux (heartburn) and symptoms of gastro-oesophageal reflux disease in packs containing not more than 14 days' supply.

2. Proposal to either amend the current Schedule 3 entry or create a new Schedule 2 entry for macrogols when in liquid concentrate preparations for oral use in adults and children over 12 years of age for laxative use, with a potential inclusion of a concentration cut off and/or limited pack size.

[redacted] notes that the proposal is vague and does not offer clear direction to respondents on specific dosages being proposed. It is also not clear what is meant by 'amending' the current Schedule 3 entry. This makes a targeted response difficult in relation to issues such as tolerability, abuse and overall safety in relation to dosages. [redacted] recommends a specific dosage amount and scheduling distinction be nominated in order to give respondents clearer direction in relation to researching specific evidence in which to form the basis for support or rejection of a scheduling proposal.

Products on ARTG

Macrogol is the International Non-proprietary Name for polyethylene glycol and is used as a laxative to treat constipation. [19] It is currently listed as a Schedule 3 medicine for preparations for oral use for bowel cleansing prior to diagnostic, medical or surgical procedures. [20]

There are currently 33 products that contain macrogols that are either listed/registered on the Australian Register of Therapeutic Goods (ARTG), most of which are exempt from scheduling.[21] The fact the current Schedule 3 classification is purely based on a specific indication has resulted in some illogical and potentially confusing registrations on the ARTG. For example, the product Glycoprep-C Flavoured Gastrointestinal lavage is registered on the ARTG both as a Schedule 3 (Pharmacist Only) and as an unscheduled substance.[22] [23] This is spite of the fact the pack size and the dosages of active ingredients are identical. In several other cases, many products containing macrogol have a scheduling exemption, irrespective of the pack size. Furthermore, products with low amounts of macrogol such as Laxitol are listed on the ARTG but come with a multitude of warning statements.[24] In contrast there are several registered products that have much higher doses of marcogol, such as molaxole[25], but contain no warning statements at all.

[redacted] understands the logic behind limiting scheduling changes to liquid preperations as the potential for accidental misuse is more likely to occur with these preparations compared to the powder preparations which are contained in sachets with recommended dosages. However, [redacted] believes in order to promote the quality use of medicines, macrogols should be scheduled based on dosage and pack size, not just on dosage form and specific indications.

[redacted]

Constipation

Chronic constipation is a common functional disorder of the gastrointestinal tract, affecting up to 35 per cent of the general population, and especially the elderly.[26] However its definition as perceived by the patient can vary, making it difficult to understand the problem and self-selecting appropriate therapeutic measures. Therefore the most effective treatment approach to treating chronic constipation needs a thorough understanding of a patient's compliant to enable health professionals to choose treatment options that are most efficacious for the individual patient.[27] In patients with no known secondary causes of constipation, conservative non-pharmacologic treatment measures (such as regular exercise, increased fluid intake, and bowel habit training) are generally recommended as initial treatment options. [28]

In elderly populations, constipation is more common with 50 per cent of community-dwelling and 74 per cent of nursing home residents regularly affected. [29] In older populations, constipation may have underlying causes such as loss of mobility, side effects from medications, underlying diseases or impaired anorectal sensation. [30] Similarly to the general population, a detailed medical history in relation to medications and co-morbid problems may help identify underlying causes of constipation.

Recommended Dosage

Several of the aforementioned products on the ARTG that are currently unscheduled, contain significantly more than the recommended daily dosage in each packet sachet. The effective dose of macrogol ranges from 0.7 to 1.5g/kg/day in constipated patients of any age. In addition, the recommended maximum daily dosage of macrogol is between 10-20 g/day for adults and children aged 8 years and over. [31] As such, patients that only require a mild laxative effect to alleviate general constipation should only need a small concentration to ameliorate symptoms. It is therefore questionable whether products that contain significantly higher dosages of macrogol than the recommended daily dosages should be unscheduled.

With macrogols being freely available from general stores such as supermarkets, it reduces the likelihood of clinical assessments being undertaken by healthcare professionals such as pharmacists that would likely identify underlying causes of constipation, advising patients regarding the potential development of other associated chronic conditions and determining the most effective treatment plan. In these instances, this could result in underlying causes of constipation going untreated, particularly with high dose products being available to purchase in stores that do not offer access to trained health professionals.

[redacted]

Recommendation

Scheduling amendment(s) based on a recommended daily dosage with pack sizes consistent with short term use is the recommended outcome in order to foster the quality use of medicines. If a patient's symptoms are not ameliorated sufficiently through an initial conservative treatment plan, or a product is being taken for bowel cleansing in preparation for a colonoscopy or surgery, advice from a health professional is warranted. Interaction with a health professional may also foster the promotion of non-pharmacological treatments in mild cases of constipation and the quality use of medicines in more chronic cases. This is likely to result in more effective treatment outcomes over the long term.

[redacted]

[redacted]

Reference Sources:

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[redacted]

[redacted]

26 September 2013

The Secretary, Medicines & Poisons Scheduling
Office of Chemical Safety and Environmental Health (MDP 88)
GPO Box 9848
Canberra
ACT 2601

Dear Sir/Madam

Re: Macrogol - Proposal to either amend the current Schedule 3 entry or create a new Schedule 2 entry for macrogols when in liquid concentrate preparations for oral use in adults and children over 12 years of age for laxative use, with a potential inclusion of a concentration cut off and/or limited pack size.

[redacted] wishes to provide comment on the proposal to amend the scheduling of concentrated macrogol solutions. There is currently only one liquid concentrate macrogol product on the ARTG, which is MOVICOL Liquid Concentrate.

Background

[redacted] is the sponsor of the Movicol range of products, which contain macrogol 3350 and electrolytes. All are unscheduled.

MOVICOL powder for solution sachet	AUST R 60786
Macrogol 3350 with Electrolytes powder for solution sachet	AUST R 136195
MOVICOL - HALF powder for solution sachet	AUST R 109758
MOVICOL JUNIOR powder for solution sachet	AUST R 160225
MOVICOL Flavour Free powder for oral solution	AUST R 181834
MOVICOL Chocolate powder for oral solution	AUST R 181835
MOVICOL JUNIOR CHOCOLATE powder for solution sachet	AUST R 207698
MOVICOL LIQUID ORANGE FLAVOUR oral liquid concentrate	**AUST R 212114**

The Movicol range of products contain macrogol 3350 plus sodium chloride, potassium chloride and sodium bicarbonate as the active ingredients. All of the Movicol products are unscheduled, and are indicated *"For effective relief from constipation, treatment of chronic constipation. Movicol is also effective in resolving faecal impaction, defined as refractory constipation with*

faecal loading of the rectum and/or colon confirmed by physical examination of the abdomen and rectum."

In addition, Movicol-Half, Movicol Junior and Movicol Junior Chocolate are also indicated for use in children aged 2 years and above, as follows.

"For effective relief of constipation in adults. For treatment of chronic constipation in adults and children aged 2 years and older. For resolving faecal impaction, defined as refractory constipation with faecal loading of the rectum, or the rectum and colon, confirmed by physical examination of abdomen and rectum, in adults and children aged 2 years and older. For prevention of recurrence of faecal impaction in children aged 2 years and older. Use in children 2 years and older should be limited to 12 weeks except under medical supervision."

Movicol Liquid is not indicated for use in children under 12 years of age.

The first Movicol product (Movicol powder for solution sachet) was launched in Australia in 1998, and additional strengths and flavours have followed. Movicol is currently only sold through pharmacy. It is promoted to both health care professionals and the general public. The 13.125 g (adult) strengths of Movicol are also available as a Pharmaceutical Benefit.

Movicol is both widely prescribed and also recommended OTC by pharmacy staff. In the calendar year 2012, there were 993,787 PBS prescriptions dispensed for Movicol adult strength 30s, and 490,017 units of Movicol were sold OTC in pharmacies.

Macrogol products are used extensively for the treatment of constipation, and this is supported by a considerable amount of clinical trial data for both adults and children. They are well tolerated and have a good safety profile consistent with their unscheduled status in Australia.

Macrogol 3350 with electrolytes is recommended as the first line treatment for constipation in children and young people[1] and a Cochrane review[2] has found macrogol should be used in preference to lactulose in both adults and children.

Regulatory History

Movicol Liquid was developed as a convenient dosage option with a new flavour. Movicol Liquid is a concentrate that must first be diluted with water.

Movicol Liquid was approved by the TGA in July 2013. Movicol Liquid has not yet been launched in Australia, but has been launched in a number of other countries (Attachment 1).
In all these jurisdictions, within each country, there is no difference in scheduling between Movicol Liquid and Movicol powder.

As with the rest of the current Movicol range, Movicol Liquid will be sold only through pharmacy.

[1]CG 99 Constipation in children and young people. Diagnosis and management of idiopathic childhood constipation in primary and secondary care Issued: May 2010. http://guidance nice.org.uk/CG99/Guidance
[2] Lee-Robichaud H, Thomas K, Morgan J, Nelson RL. Lactulose versus Polyethylene Glycol for Chronic Constipation Cochrane Database Syst Rev. 2010 Jul 7;(7):CD007570. doi: 10.1002/14651858.CD007570.pub2.

The currently marketed Movicol products require reconstitution of powder in water, which can take up to 3 minutes. Offering patients a liquid formulation which is quicker to prepare would result in improved patient convenience and compliance.

To prepare a dose of Movicol (powder for oral solution);

- The contents of one Movicol sachet is mixed with 125 mL of water.

To prepare a dose of Movicol Liquid;

- 25 mL of Movicol Liquid is mixed with 100 mL water to provide a final volume of 125 mL.

When prepared as directed, both contain the same amount and concentrations of macrogol 3350 and electrolytes.

Macrogol Used in Bowel Preps

The proposal before the committee refers to amending the current Schedule 3 entry for macrogol.

The current schedule 3 entry for macrogol products is;

- *MACROGOLS in preparations for oral use for bowel cleansing prior to diagnostic, medical or surgical procedures.*

It should be noted that the doses of macrogol used in bowel preparation products are considerably higher than those in macrogol laxative products.

One Movicol sachet contains 13.125 g of macrogol, while the amount of macrogol 3350 in a bowel preparation product such as Moviprep is 200 g.

In 2002 the then NDPSC reviewed a proposal for macrogol 3350 for laxative use to be placed in schedule 4. Following review, the committee agreed that the unscheduled status of macrogol 3350 laxatives was appropriate on the basis that;

- There were no adverse event reports in Australia associated with laxative use of macrogol 3350 and sodium picosulfate: and
- There was no evidence associating laxative use of these substances with electrolyte disturbance, severe gastrointestinal disturbance or misuse.

In the intervening years, Movicol products have been extensively used in the community as laxatives, and no safety concerns warranting their rescheduling have been raised. We believe that the introduction of a new dosage form (macrogol liquid concentrate) does not alter the risk benefit balance. In assessing the appropriate scheduling, the following factors should be taken into account;

- the risks and benefits of the use of a substance

The risks and benefits for Movicol Liquid are no different from those for Movicol powder for oral solution.

- the purposes for which a substance is to be used and the extent of use of a substance

  The risks and benefits for Movicol Liquid are no different from those for Movicol powder for oral solution. [redacted] expects that some users will switch from Movicol sachets to the liquid based on convenience to patients and carers, and that this will particularly occur in nursing homes.

- the toxicity of a substance

  The risks and benefits for Movicol Liquid are no different from those for Movicol powder for oral solution. Macrogol 3350 is an inert polymer, and is virtually unabsorbed from the body. The small amount that may be absorbed is excreted renally. The amounts of active ingredients are the same, however, there are different excipients in Movicol Liquid; sucralose, benzyl alcohol, hydroxybenzoates, and orange flavour. All these excipients are considered suitable for use in unscheduled medicines, and do not justify a change in scheduling.

- the dosage, formulation, labelling, packaging and presentation of a substance

  The risks and benefits for Movicol Liquid are no different from those for Movicol powder for oral solution. [redacted] understand there are concerns that patients may think that Movicol Liquid may be consumed undiluted, but the presentation of the product makes it very clear that the product must be diluted with water before taking. This is clearly indicated on the outer carton, bottle label and pack insert (Attachment 2).

  Advice to dilute the product before use is prominent on the carton, bottle label and in the pack insert. The pack inset also contains an illustration that makes it clear how the measuring cup can be used to add 100 mL of water to 25 mL of Movicol Liquid. The pack insert also states *"It is essential to dilute MOVICOL Liquid as directed. This will help to reduce any potential risk of dehydration."*

  Movicol Liquid concentrate has a very concentrated and salty taste, and this would discourage a person from drinking it undiluted. If it were to be taken undiluted, there is no evidence that harm would result.

  A review of the [redacted] global safety database (as at September 2013) has identified only one report where the product was taken undiluted. There was no adverse event reported as a result of this undiluted use.

  While there are no other macrogol solutions on the market in Australia, [redacted] notes that in Germany, an undiluted macrogol solution is approved for the treatment of constipation (Dulcolax Balance M liquid), which contains 5 gram of macrogol 4000 in 10 mL of water. Dulcolax M Balance liquid has a neutral taste and the manufacturer advises that it may be taken **without** being diluted, but it is recommended to keep hydrated by drinking a glass of water or other fluids (e.g fruit juices). A copy of the package insert for this product and an English translation are provided (Attachment 3)

In relation to the pack size, the 500 mL bottle contains 20 doses, which for a patient suffering chronic constipation, would last between 7 and 20 days (the recommended dose range for chronic constipation for adults is 1 – 3 doses daily). Recent data obtained from an external agency indicated that the average dose of Movicol used by patients with chronic constipation is 1.5 sachets daily. A 500 mL bottle is an appropriate size; a smaller bottle will limit the number of doses, and require the user to return to the pharmacy more frequently, or to buy multiple bottles at a single visit.

[redacted] believes that the current unscheduled status of Movicol Liquid is appropriate, and that the presentation of the product makes it clear (without the need for intervention by pharmacy staff) that the product requires dilution prior to use. The risk/benefit for macrogol liquids has not been shown to be different from macrogol powder for solution, and on that basis there are no grounds to amend the current schedule 3 entry for macrogol, or create a new Schedule 2 entry for concentrated macrogol liquids.

Yours faithfully

unsigned for electronic submission

[redacted]

ATTACHMENT 1

Overseas Regulatory Status – Movicol Liquid

Country	Launched	Status	Liquid the same as powder
United Kingdom	1 June 2011	Pharmacy	Yes
Ireland	2012	Prescription	Yes
Netherlands	1 January 2012	Prescription	Yes
Spain	31 January 2012	Prescription	Yes
Italy	28 May 2012	Prescription	Yes
Portugal	1 February 2012	Pharmacy	Yes
Switzerland	10 September 2012	Prescription	Yes
Sweden	2012	Pharmacy	Yes
Austria	9 March 2012	Pharmacy	Yes
Belgium	3 October 2011	Pharmacy	Yes
Luxembourg	1 December 2011	Pharmacy	Yes
Germany	2011	Pharmacy	Yes

ATTACHMENT 2

OM-2012-00372-3 s31 3rd July 2013

MOVICOL® LIQUID
Orange flavour
Must Be Diluted Before Use

EFFECTIVE CONSTIPATION TREATMENT THAT WORKS BY REHYDRATING THE STOOL TO RESTORE COMFORTABLE BOWEL MOVEMENTS

- ✓ MOVICOL® is not a stimulant laxative
- ✓ MOVICOL® acts locally in the bowel and is not absorbed by the body
- ✓ Easy to use, simply mix with water and take at any time of the day (refer to leaflet)
- ✓ Part of the MOVICOL® range, trusted for more than 15 years.

For effective relief of constipation and the treatment of chronic constipation. Also for the treatment of medically diagnosed faecal impaction.

ADULTS AND CHILDREN OVER 12 YEARS OF AGE.

DOSAGE:

THIS PRODUCT MUST BE DILUTED BEFORE USE. USE THE MEASURING CUP PROVIDED.

Constipation:
One dose per day. A dose consists of 25 mL of MOVICOL® Liquid mixed with an extra 100 mL of water. If necessary, increase to 2–3 doses per day.

Faecal Impaction:
8 doses per day.

Read the package leaflet before use.
Do not exceed the maximum daily dose.
www.movicol.com.au

Effective relief of constipation and treatment of chronic constipation

Concentrate for oral solution
500 mL AUST R XXXXX
NORGINE

Each 25 mL of MOVICOL® Liquid Orange Flavour contains:

Macrogol 3350	13.125 g
Sodium chloride	350.7 mg
Sodium bicarbonate	178.5 mg
Potassium chloride	46.6 mg

Also contains benzyl alcohol, ethanol (alcohol) and hydroxybenzoates.

See leaflet for full ingredient list.

Store below 30°C.
Do not refrigerate or freeze.
Discard product 30 days after first opening.

After mixing with water, the prepared solution should be kept covered. Throw away any prepared solution not used within a 24 hour period.

MOVICOL® and the Norgine logo are trademarks of the Norgine Group of Companies.

Drink plenty of water. Increase fibre in diet except in cases of medicine induced constipation. Prolonged use of laxatives is undesirable and may lead to dependence. If symptoms persist, seek medical advice.

The total amount of sodium contained in the maximum daily dose for faecal impaction is 1.5 g. If diluted as recommended, the sodium content will not affect the net balance of sodium in the body.

NORGINE
Norgine Pty Ltd,
3/14 Rodborough Road
Frenchs Forest, NSW 2086
AUSTRALIA
Made in France

5 012748 004221

Batch and expiry date will be added here at manufacture.

print free area

Each 25 mL of MOVICOL® Liquid Orange flavour contains:

Macrogol 3350	13.125 g
Sodium chloride	350.7 mg
Sodium bicarbonate	178.5 mg
Potassium chloride	46.6 mg

Also contains benzyl alcohol, ethanol (alcohol) and hydroxybenzoates.
See leaflet for full ingredient list.

ADULTS AND CHILDREN OVER 12 YEARS OF AGE.

DOSAGE:

This product must be diluted before use.

Constipation: One dose per day. A dose consists of 25 mL of MOVICOL® Liquid mixed with an extra 100 mL of water. If necessary, increase to 2–3 doses per day.
Faecal Impaction (as diagnosed by a doctor): 8 doses per day.

Do not exceed the maximum daily dose.
Not recommended for children below 12 years of age. Read the package leaflet before use. Keep out of reach of children. Store below 30°C. Do not refrigerate or freeze. Discard product 30 days after first opening.

Norgine Pty Limited, 3/14 Rodborough Road, Frenchs Forest NSW 2086

Date opened .... /.... /.....

MOVICOL® LIQUID

Orange flavour

Must Be Diluted Before Use

Effective relief of constipation and treatment of chronic constipation

Concentrate for oral solution

500 mL

AUST R XXXX

NORGINE

Batch and expiry date will be added here at manufacture.

Patient Information Leaflet

MOVICOL LIQUID Orange flavour

Concentrate for oral solution

THIS PRODUCT MUST BE DILUTED WITH WATER BEFORE USE

Please read this leaflet carefully before taking your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

What is this medicine?

This medicine is called MOVICOL Liquid. Each 25 mL dose contains:

Macrogol 3350	13.125 g
Sodium chloride	350.7 mg
Sodium bicarbonate	178.5 mg
Potassium chloride	46.6 mg

When 25 mL is made into a drink by adding 100 mL of water, it contains:

Sodium	65 mmol/L
Chloride	53 mmol/L
Bicarbonate	17 mmol/L
Potassium	5.4 mmol/L

It also contains orange flavour, the preservatives benzyl alcohol, methyl hydroxybenzoate (E218), ethyl hydroxybenzoate (E214) and the sweeteners sucralose (E955) and potassium acesulfame (E950).

A 500 mL bottle contains 20 doses of MOVICOL Liquid. It comes with a 25 mL measuring cup.

What is MOVICOL Liquid used for?

This medicine helps you to have a comfortable bowel movement even if you have been constipated for a long time. It also works in faecal impaction (as diagnosed by your doctor). MOVICOL Liquid is for use in adults and children 12 years of age or over.

Before you take MOVICOL Liquid

Do not take this medicine if your doctor has told you that you have:

- an obstruction in your intestine (gut)
- a perforated gut wall
- severe inflammatory bowel disease, like ulcerative colitis, Crohn's disease, or toxic megacolon
- paralysis of the bowel
- an allergy to macrogol or any of the ingredients.

If you have a heart condition you should not take more than two doses of MOVICOL Liquid in any one hour.

MOVICOL Liquid is for use in adults and children 12 years of age or over. Safety in children 12 years of age and under has not been established. Other MOVICOL products are available for use in children under 12 years.

If you are pregnant or breast feeding, talk to your doctor before you take MOVICOL Liquid.

Laxative products such as MOVICOL Liquid have the potential to interact with other medications, by altering their absorption. There have been isolated reports of medicines for epilepsy being less effective. Close monitoring of the effects of your medications may be necessary when you commence or cease to take MOVICOL Liquid regularly. It is important that you should discuss this with your doctor.

How to take MOVICOL Liquid

Adults and Children over 12 years of age.

This product must be diluted before use.

One dose is 25 mL of MOVICOL Liquid diluted with 100 mL of water, to make a total volume of 125 mL.

Constipation:

The recommended dose is one dose daily.

This can be increased to 2 or 3 doses daily if necessary. If extended treatment is required for constipation, do not exceed the maximum recommended dose of 3 doses daily.

Faecal impaction:

The dose is 8 doses a day taken within 6 hours. You may need to take this dose for up to 3 days. If you have a heart condition, do not take more than 2 doses in any one hour.

How to mix:

Open the bottle and measure 25 mL using the measuring cup. Pour the Liquid into a glass and then add 100 mL of water (see diagram below).

1. Use the measuring cup provided to measure 25 mL of MOVICOL Liquid and pour it into a glass.
2. Use the same measuring cup to measure 4 lots of 25 mL of WATER (100 mL total) and add this to the same glass to make a total volume of 125 mL.

When the MOVICOL Liquid Orange flavour solution is clear, drink it.

If you are taking MOVICOL Liquid for faecal impaction, it may be more convenient to add eight 25 mL measures to 800 mL of water. It is essential to dilute MOVICOL Liquid as directed. This will help to reduce any potential risk of dehydration.

Please rinse the measuring cup after use and replace it on the bottle. Any diluted MOVICOL solution not used within 24 hours should be disposed of.

Drink plenty of water. Increase fibre in diet except in cases of medicine induced constipation. Prolonged use of laxatives is undesirable and may lead to dependence. If symptoms persist seek medical advice.

If you take too much MOVICOL Liquid and get bad diarrhoea, stop taking it until it stops. If constipation recurs, you should check with your doctor or pharmacist before taking a new course of MOVICOL Liquid. If you are worried, contact your doctor or pharmacist.

What about side effects?

Sometimes people have stomach ache or rumbles, or an allergic reaction, or feel bloated or sick. You may have diarrhoea especially when starting to take MOVICOL Liquid. If you feel weak, breathless, very thirsty with a headache, or get puffy ankles stop taking MOVICOL Liquid and tell your doctor. Tell your doctor or pharmacist if you think MOVICOL Liquid is causing you any problem.

How to store MOVICOL Liquid

Store your medicine at room temperature (below 30°C). Do not use it after the expiry date on the label. Discard any remaining MOVICOL Liquid 30 days after first opening the bottle. You can mark the discard date on the bottle label.

After you have diluted MOVICOL Liquid Orange flavour in water, if you cannot drink it straight away, keep it covered. Throw away any diluted solution not used within a 24 hour period.

Keep all medicines out of the reach of children.

AUST R xxxxxx

Date:

Norgine Pty Limited,
3/14 Rodborough Road,
Frenchs Forest
NSW 2086

NORGINE

ATTACHMENT 3

Dulcolax® M Balance flüssig

5 g Macrogol 4000 in 10 ml Wasser
Lösung zum Einnehmen
Geschmacksneutral

Liebe Patientin, lieber Patient,
bitte lesen Sie die folgende Gebrauchsanleitung sorgfältig durch, denn sie enthält wichtige Informationen darüber, was Sie bei der Anwendung von Dulcolax® M Balance flüssig beachten sollen. Wenden Sie sich bei Fragen bitte an Ihren Arzt oder Apotheker.

Was ist DULCOLAX® M Balance flüssig und wofür wird es angewendet?

DULCOLAX® M Balance flüssig ist ein osmotisch wirksames Abführmittel.
DULCOLAX® M Balance flüssig ist ein in Wasser gelöstes Macrogol zur Anwendung bei akuter und chronischer Verstopfung bei Erwachsenen und Kindern ab 2 Jahren. Die Anwendung bei Kindern bis 8 Jahre sollte nur auf ärztliche Anweisung erfolgen. Bei Behandlung einer chronischen Verstopfung mit DULCOLAX® M Balance flüssig sollte die Verstopfungsursache ärztlich abgeklärt sein. DULCOLAX® M Balance flüssig ist für die tägliche Anwendung geeignet.

Zusammensetzung:
10 ml Lösung zum Einnehmen enthalten:
5 g Macrogol 4000 in gelöster Form.

Sonstige Bestandteile: Macrogol 400, Citronensäure, Kaliumsorbat (Konservierungsmittel) und gereinigtes Wasser.

Die geschmacksneutrale Lösung ist frei von Aromastoffen, Zucker, Alkohol, Kochsalz sowie anderen Salzen*.
* frei von Kaliumchlorid, Natriumhydrogencarbonat

DULCOLAX® M Balance flüssig ist eine transparente, geruchs- und geschmacksneutrale Lösung.

Durch das hohe Wasserbindungsvermögen von Macrogol 4000 – vergleichbar mit einem flüssigen Schwamm – kann viel Flüssigkeit in den Darm transportiert und so der verhärtete Stuhl aufgeweicht werden. DULCOLAX® M Balance flüssig erhöht den Flüssigkeitsgehalt des Stuhls und regt durch das vergrößerte Stuhlvolumen die natürliche Darmbewegung an. Der Wirkstoff Macrogol 4000 wird weder im Blutkreislauf aufgenommen, noch erfolgt eine Verstoffwechselung im Magen-Darm-Trakt. Der Wirkstoff wird unverändert ausgeschieden.

DULCOLAX® M Balance flüssig enthält keine Zucker und ist daher für Diabetiker oder für Patienten, die eine Galaktose-freie Diät einhalten müssen, geeignet.

DULCOLAX® M Balance flüssig enthält kein Kochsalz sowie keine anderen Salze* und ist daher auch für Patienten, die auf eine salzarme Diät achten müssen, geeignet (z. B. Herz-Kreislauf-Patienten).
** frei von Kaliumchlorid, Natriumhydrogencarbonat*

Wie ist DULCOLAX® M Balance flüssig einzunehmen?

Nehmen Sie DULCOLAX® M Balance flüssig immer genau nach der Anweisung in dieser Gebrauchsanleitung ein. Wenn Sie sich nicht ganz sicher sind, fragen Sie Ihren Arzt oder Apotheker.

Erwachsene und Kinder ab 8 Jahren:
Falls vom Arzt nicht anders verordnet, ist die übliche Dosis:

20 bis 40 ml Lösung (entspricht 10 bis 20 g Macrogol 4000) täglich, vorzugsweise als eine Dosis morgens.

Kinder von 4 bis 7 Jahren:
Die Anwendung bei Kindern bis 8 Jahre sollte nur auf ärztliche Anweisung erfolgen.
Falls vom Arzt nicht anders verordnet, ist die übliche Dosis: 16 bis 32 ml Lösung (entspricht 8 bis 16 g Macrogol 4000) täglich, vorzugsweise als eine Dosis morgens.

Kinder von 2 bis 3 Jahren:
Die Anwendung bei Kindern bis 8 Jahre sollte nur auf ärztliche Anweisung erfolgen.

Falls vom Arzt nicht anders verordnet, ist die übliche Dosis:

8 bis 16 ml Lösung (entspricht 4 bis 8 g Macrogol 4000) täglich, vorzugsweise als eine Dosis morgens.

Die Dosis von DULCOLAX® M Balance flüssig wird mit dem beigefügten Dosierbecher abgemessen und kann je nach erzielter Wirkung angepasst werden. Die empfohlenen Dosierungen können nach dem persönlichen Bedarf täglich oder alle 2 Tage eingenommen werden.

DULCOLAX® M Balance flüssig ist geschmacksneutral und kann unverdünnt eingenommen werden. Nach der Einnahme sollten Sie ein Glas Wasser oder sonstige Flüssigkeit (Fruchtsäfte, Tee etc.) trinken (ca. 150 ml). Alternativ können Sie DULCOLAX® M Balance flüssig auch dem Getränk Ihrer Wahl beimischen und so Ihre persönliche Geschmacksrichtung schaffen.

Bitte beachten Sie:
Der verdauungsregulierende Effekt von DULCOLAX® M Balance flüssig tritt gewöhnlich 24 bis 48 Stunden nach der Einnahme ein.
Kinder sollten DULCOLAX® M Balance flüssig nicht länger als 3 Monate einnehmen.

DULCOLAX® M Balance flüssig darf nicht eingenommen werden,

wenn Sie überempfindlich (allergisch) gegen Macrogol (Polyethylenglykol) oder einen der sonstigen Bestandteile von DULCOLAX® M Balance flüssig sind
wenn Sie eine bestehende Erkrankung haben, wie z. B.:
- eine schwere Darmerkrankung
- eine entzündliche Darmerkrankung (wie Colitis Ulcerosa, Morbus Crohn)
- einen Darmdurchbruch oder wenn die Gefahr eines Darmdurchbruchs besteht
- einen Darmverschluss oder wenn der Verdacht auf Darmverengungen besteht
- wenn Sie Schmerzen im Bauchraum unbestimmten Ursprungs haben.

Nehmen Sie dieses Produkt nicht ein, wenn eine der oben aufgeführten Krankheiten bei Ihnen vorliegt. Wenn Sie sich nicht ganz sicher sind, fragen Sie zuerst Ihren Arzt oder Apotheker bevor Sie DULCOLAX® M Balance flüssig einnehmen.

Besondere Vorsicht bei der Einnahme von DULCOLAX® M Balance flüssig ist erforderlich

Nach der Einnahme von Macrogol- (Polyethylenglykol-) haltigen Präparaten wurden sehr seltene Fälle von Überempfindlichkeitsreaktionen mit Hautausschlag und Gesichtsschwellung (Ödem) bei Erwachsenen beschrieben. Vereinzelt wurde von allergischen Reaktionen berichtet, die zu Ohnmacht oder Kreislaufkollaps und allgemeinem Unwohlsein führten.

Wenn Sie eines dieser Anzeichen bei sich bemerken, sollten Sie DULCOLAX® M Balance flüssig nicht mehr einnehmen und unverzüglich einen Arzt aufsuchen.
Da unter der Therapie mit DULCOLAX® M Balance flüssig Durchfälle auftreten können, sollten Sie vor der Einnahme Ihren Arzt oder Apotheker fragen, wenn Ihre Leber- oder Nierenfunktion beeinträchtigt ist, Sie Diuretika (Wasser-Tabletten) einnehmen, Sie älter sind und ein erhöhtes Risiko für niedrige Natrium- oder Kalium-Spiegel im Blut haben.

Schwangerschaft und Stillzeit
Da Macrogol 4000 kaum resorbiert wird, sind keine Auswirkungen auf eine Schwangerschaft oder auf den Säugling während der Stillzeit zu erwarten. DULCOLAX® M Balance flüssig kann während der Schwangerschaft und Stillzeit angewendet werden, die Einnahme sollte jedoch unter ärztlicher Aufsicht erfolgen.

Wechselwirkungen mit anderen Arzneimitteln
Die Wirkung einiger Arzneimittel wie z. B. Antiepileptika kann durch gleichzeitige Einnahme mit Dulcolax M Balance flüssig herabgesetzt werden. Bitte informieren Sie Ihren Arzt oder Apotheker, wenn Sie andere Arzneimittel einnehmen/anwenden bzw. vor kurzem eingenommen/angewendet haben, oder wenn andere Arzneimittel bei Ihrem Kind angewendet wurden/werden, auch wenn es sich um nicht verschreibungspflichtige Arzneimittel handelt.

Wenn Sie eine größere Menge DULCOLAX® M Balance flüssig eingenommen haben, als Sie sollten
Sie müssen mit Durchfällen rechnen, die nach Unterbrechen der Behandlung oder Verringerung der Dosis zum Stillstand kommen.
Hoher Flüssigkeitsverlust durch Durchfälle oder Erbrechen kann eine Korrektur des Elektrolythaushalts erfordern, weswegen Sie einen Arzt kontaktieren sollten.

Wenn Sie die Einnahme von DULCOLAX® M Balance flüssig vergessen haben
Nehmen Sie nicht die doppelte Dosis ein, wenn Sie die vorherige Einnahme vergessen haben.

Welche Nebenwirkungen sind möglich?

DULCOLAX® M Balance flüssig kann Nebenwirkungen haben, die aber nicht bei jedem auftreten müssen.
Die Nebenwirkungen waren im Allgemeinen schwach und vorübergehend:

Erwachsene:
Auch bei bestimmungsgemäßem Gebrauch kann es häufig zu Bauchschmerzen, Durchfall, Übelkeit, Erbrechen, Blähungen, Drang zur Stuhlentleerung und Stuhlinkontinenz kommen.

Sehr selten kann es zu Symptomen einer allergischen Reaktion wie Hautausschlag, Nesselsucht, Wasseransammlung im Gewebe, Gesichtsschwellung (im Rahmen eines Quincke Ödems) mit Schwellung der Lippen und/oder der Wangen, anaphylaktischer Schock kommen.

Mit unbekannter Häufigkeit (Daten wurden erst nach dem Inverkehrbringen erhoben) kann es zu erniedrigtem Natrium- und Kaliumgehalt im Blut sowie möglichem Flüssigkeitsmangel verursacht durch starken Durchfall, insbesondere bei älteren Patienten, kommen.

Kinder:
Auch bei bestimmungsgemäßem Gebrauch können häufig Bauchschmerzen, Durchfall, der Wundsein um den After verursachen kann, Übelkeit, Erbrechen und Blähungen auftreten.

Mit unbekannter Häufigkeit kann es zu allergischen (Überempfindlichkeits-) Reaktionen kommen.

Informieren Sie bitte Ihren Arzt oder Apotheker, wenn eine der aufgeführten Nebenwirkungen Sie erheblich beeinträchtigt oder Sie Nebenwirkungen bemerken, die nicht in dieser Gebrauchsanleitung angegeben sind.

Wie ist DULCOLAX® M Balance flüssig aufzubewahren?

Für Kinder unzugänglich aufbewahren!

Nach dem Öffnen der Flasche ist DULCOLAX® M Balance flüssig noch 6 Wochen haltbar.

Wie DULCOLAX® M Balance flüssig aussieht und Inhalt der Packung

DULCOLAX® M Balance flüssig ist eine transparente, geruchs- und geschmacksneutrale Lösung.

Die Lösung zum Einnehmen ist in Packungen mit 100 ml, 250 ml, 1000 ml und 1000 ml als Teil einer 10 x 1000 ml Bündelpackung erhältlich.

Hersteller:
Grünwalder Gesundheitsprodukte GmbH
Ruhlandstr. 5, 83646 Bad Tölz

CE 0044

Hersteller des Dosierbechers:
Bormioli Rocco e Figlio S.p.A., Str. Nazionale Emilie, 58, 43010 Castelguelfo, Italien (CE0373)

Vertrieb:
Boehringer Ingelheim Pharma GmbH & Co. KG
Vertriebslinie Thomae
Binger Str. 173, 55216 Ingelheim am Rhein
Telefon: 0 800/77 90 900, Telefax: 0 61 32/72 99 99
www.dulcolax.de

Apothekenexklusives Medizinprodukt

Stand der Information: November 2011.

Liebe Patientin, lieber Patient,
Dulcolax® M Balance flüssig ist ein Abführmittel zur Anwendung bei akuter und chronischer Verstopfung. Durch sein hohes Wasserbindungsvermögen transportiert der Wirkstoff Macrogol 4000 viel Flüssigkeit in den Darm und weicht so den verhärteten Stuhl auf. Der Wirkstoff erhöht den Flüssigkeitsgehalt des Stuhls, regt durch das vergrößerte Stuhlvolumen die natürliche Darmbewegung an und löst die Stuhlentleerung aus. Dulcolax® M Balance flüssig **enthält kein Kochsalz sowie keine anderen Salze*** und ist daher auch für Patienten geeignet, die auf eine salzarme Diät achten müssen (z. B. Bluthochdruckpatienten und Patienten mit Herzinsuffizienz).
* frei von Kaliumchlorid, Natriumhydrogencarbonat

Durch die flüssige Darreichungsform kann Dulcolax® M Balance flüssig mit dem beiliegenden Dosierbecher einfach **nach Ihrem persönlichen Bedarf dosiert werden.**

Dosierungsempfehlungen:
Erwachsene und
Kinder ab 8 Jahren: 20 bis 40 ml Lösung täglich
Kinder von 4 bis 7 Jahren: 16 bis 32 ml Lösung täglich
Kinder von 2 bis 3 Jahren: 8 bis 16 ml Lösung täglich

Ein weiterer Vorteil ist, dass die Lösung **geschmacksneutral** ist und unverdünnt eingenommen werden kann. Nach der Einnahme sollten Sie ein Glas Wasser oder sonstige Flüssigkeit (Fruchsäfte, Tee etc.) trinken (etwa 150 ml). Alternativ können Sie Dulcolax® M Balance flüssig auch einem Getränk Ihrer Wahl beimischen und so Ihre ganz persönliche Geschmacksrichtung schaffen.

Wenn Sie an weiteren Informationen zum Thema Verstopfung und Dulcolax® M Balance flüssig interessiert sind, senden wir Ihnen gerne unseren aktuellen Verdauungsratgeber zu. Bitte senden Sie den ausgefüllten Antwort-Coupon zurück und nennen Sie uns Ihre Adresse. Sie können den Ratgeber auch unter www.dulcolax.de im Internet downloaden.

Wir wünschen Ihnen gute Besserung
Ihr Dulcolax®-Team

Boehringer Ingelheim Pharma GmbH & Co. KG,
Abteilung Marketing CHC Deutschland, Marketing Dulcolax,
Binger Str. 173, 55216 Ingelheim am Rhein

Bitte senden Sie mir den aktuellen Dulcolax®-

DULCOLAX® M Balance liquid

5 g macrogol 4000 in 10 ml water
Solution for oral use
Neutral in taste

Dear Patient,
Please read all of this entire leaflet carefully because it contains important information about what you need to know about taking Dulcolax® M Balance liquid. If you have any questions, please ask your doctor or pharmacist.

What is DULCOLAX® M Balance liquid and what is it used for?

DULCOLAX® M Balance liquid is an osmotic laxative.
DULCOLAX® M Balance liquid is macrogol dissolved in water for use in acute and chronic constipation in adults and children 2 years of age and over. Do not use in children under the age of 8 years unless under a doctor's supervision. If using DULCOLAX® M Balance liquid to treat chronic constipation, a doctor must determine the cause of the constipation. DULCOLAX® M Balance liquid is suitable for daily use.

Composition:
10 ml of solution for oral use contains:
5 g macrogol 4000 in dissolved form.

Other ingredients: macrogol 400, citric acid, potassium sorbate (stabilizer), and purified water.

The solution is neutral in taste, free of aromatics, sugars, alcohol, sodium chloride and other salts*.
*free of potassium chloride, sodium bicarbonate

DULCOLAX® M Balance liquid is a clear and odourless solution which is neutral in taste.

Due to macrogol 4000's great capacity to bind to water – comparable to a liquid sponge – a large volume of fluid can be transported to the bowel, which softens the hardened stool. DULCOLAX® M Balance liquid increases the fluid volume in the stool and stimulates natural peristalsis through the increased stool volume. The active substance macrogol 4000 is not absorbed into the circulatory system or metabolized in the gastrointestinal tract. The active substance is excreted unchanged.

DULCOLAX® M Balance liquid does not contain any sugars and is therefore suitable for patients with diabetes or patients who have to follow a galactose-free diet.

DULCOLAX® M Balance liquid does not contain sodium chloride or any other salts* and is therefore also suitable for patients who have to follow a low-sodium diet (e.g., cardiovascular patients).
**free of potassium chloride, sodium bicarbonate*

How should DULCOLAX® M Balance liquid be taken?

Always take DULCOLAX® M Balance liquid exactly as indicated in this leaflet. You should check with your doctor or pharmacist if you are not sure.
Adults and children aged 8 years over:
If not otherwise prescribed by a doctor, the usual dose is:

20 to 40 ml solution (equivalent to 10 to 20 g macrogol 4000) daily, preferably taken as a single dose in the morning.

Children aged 4-7 years:
Do not use in children under the age of 8 years unless under a doctor's supervision.

If not otherwise prescr bed by a doctor, the usual dose is:
16 to 32 ml solution (equivalent to 8 to 16 g macrogol 4000) daily, preferably taken as a single dose in the morning.

Children aged 2-3 years:
Do not use in children under the age of 8 years unless under a doctor's supervision.

If not otherwise prescr bed by a doctor, the usual dose is:

8 to 16 ml solution (equivalent to 4 to 8 g macrogol 4000) daily, preferably taken as a single dose in the morning.

The dose of DULCOLAX® M Balance liquid can be measured using the included measuring cap. It can be adjusted depending on the desired effect. The recommended doses can be taken daily or every other day, depending on individual need.

DULCOLAX® M Balance liquid is neutral in taste and can be taken without being diluted. After taking this medicine you should drink a glass (approximately 150 ml) of water or other liquid (fruit juices, tea, etc.). Alternatively, you can also mix DULCOLAX® M Balance liquid into the beverage of your choice, thus flavouring it as you like.

Please note:
DULCOLAX® M Balance liquid's digestion-regulating effect usually takes 24 to 48 hours to work after ingestion.
Children should not take DULCOLAX® M Balance liquid for longer than 3 months.

Do not take DULCOLAX® M Balance liquid

if you are allergic (hypersensitive) to macrogol (polyethylene glycol) or any of the other ingredients of DULCOLAX® M Balance liquid
if you have a pre-existing disease such as:
– a severe intestinal disease
– inflammatory bowel disease (such as ulcerative colitis, Crohn's disease)
– an intestinal perforation or the risk of intestinal perforation
– intestinal obstruction or suspicion of an intestinal stenosis
– if you have abdominal pain of an unknown origin.

Do not take this product if you have any of the diseases listed above. If you are not sure, talk to your doctor or pharmacist before taking DULCOLAX® M Balance liquid.

Take special care when taking DULCOLAX® M Balance liquid

After taking products containing macrogol (polyethylene glycol), very rare cases of hypersensitivity reactions with a rash and facial swelling (oedema) have been descr bed in adults. Isolated cases of allergic reactions that lead to fainting or syncope and general malaise have been reported.

If you notice any of these side effects you should stop taking DULCOLAX® M Balance liquid and consult a doctor immediately.
Because treatment with DULCOLAX® M Balance liquid can cause runny diarrhoea, you should ask your doctor or pharmacist if your liver or kidney function is impaired, if you take diuretics, you are elderly or at high risk for having low sodium or potassium levels in the blood.

Pregnancy and breastfeeding
Because macrogol 4000 is barely absorbed, it is not anticipated to have any effect on pregnancy or on a baby who is being breastfed.
DULCOLAX® M Balance liquid can be used during pregnancy and breastfeeding, but should be taken under a doctor's supervision.

Interactions with other medications
The effect of some medicines, such as anti-seizure medications, can be decreased when taking Dulcolax M Balance liquid at the same time.
Please tell your doctor or pharmacist if you are taking/using or have recently taken/used any other medicines or if your child is being/has been given any other medicines, including medicines obtained without a prescription.

If you take more DULCOLAX® M Balance liquid than you should
You should expect to have diarrhoea, which will come to a stop after stopping treatment or reducing the dose.
The loss of a large volume of fluids due to diarrhoea or vomiting may require correction of the electrolyte balance, a reason for which you should contact your doctor.

If you forget to take DULCOLAX® M Balance liquid
Do not take a double dose to make up for a forgotten dose.

What side effects might occur?

DULCOLAX® M Balance liquid can cause side effects, although not everybody gets them.
The side effects have generally been minor and temporary:

Adults:
Even if used properly, abdominal pain, diarrhoea, vomiting, flatulence, the urge to evacuate the bowels and stool incontinence may commonly occur.

Very rarely, symptoms of allergic reaction may occur, such as rash, hives, accumulation of fluid in the tissues, facial swelling (in the form of angiooedema) with swelling of the lips and/or cheeks, anaphylactic shock.

The frequency of the side effects of low sodium and potassium levels in the blood and possible dehydration caused by severe diarrhoea is unknown (data were not collected before this medicine went on the market), but may be observed especially in elderly patients.

Children:
Even if used properly, abdominal pain, diarrhoea, which can cause soreness around the anus, nausea, vomiting and flatulence may frequently occur.

Allergic (hypersensitivity) reactions may occur, although the frequency is unknown.

If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

How should you store DULCOLAX® M Balance liquid?

Keep out of the sight and reach of children!

Do not use DULCOLAX® M Balance liquid after the expiration date which is stated on the carton and on the label on the bottle. The expiration date refers to the last day of that month. Please store DULCOLAX® M Balance liquid below 25°C. Store this medicine in the refrigerator.

After opening the bottle, DULCOLAX® M Balance liquid has a shelf life of 6 weeks.

What DULCOLAX® M Balance liquid looks like and contents of the package

DULCOLAX® M Balance liquid is a clear, odourless, and neutral to taste solution.

The solution for oral use is available in packages with 100 ml, 250 ml, 1000 ml, and 1000 ml as part of a 10 x 1000 ml bundled package.

Manufacturer:
Gruenwalder Gesundheitsprodukte GmbH
Ruhlandstr. 5, 83646 Bad Toelz **CE 0044**

Manufacturer of the measuring cup:
Bormioli Rocco e Figlio S.p.A., Str. Nazionale Emilie, 58,
43010 Castelguelfo, Italy (CE0373)

Distributed by:
Boehringer Ingelheim Pharma GmbH & Co. KG
Thomae Distribution Line
Binger Str. 173, 55216 Ingelheim am Rhein
Phone: 0 800/77 90 900, Fax: 0 61 32/72 99 99
www.dulcolax.de

Pharmacy-only medical product

[temperature symbol – below 25°C]

Date of revision of the text: November 2011.

Dear Patient,

DULCOLAX® M Balance liquid is a laxative that is used for acute and chronic constipation. Due to its high capacity to bind to water, the active substance, macrogol 4000, transports high volumes of fluids to the bowel, which softens the hardened stool. The active substance increases the volume of fluid in the stool, and the increased stool volume stimulates natural peristalsis, triggering stool evacuation. Dulcolax® M Balance liquid **does not contain any sodium chloride nor any other salts*** and is therefore also suitable for patients who have to follow a low-sodium diet (e.g. patients with high blood pressure and patients with heart failure).
*free of potassium chloride, sodium bicarbonate

Because it comes in a liquid pharmaceutical form, DULCOLAX® M Balance liquid **can be dosed simply and as needed on an individual basis** using the enclosed measuring cap.

Recommended dosages:
For adults and children age 8 and older. 20 to 40 ml solution daily
Children aged 4 to 7 years: 16 to 32 ml solution daily
Children aged 2 to 3 years: 8 to 16 ml solution daily

Another advantage is that the solution is **neutral in taste** and can be taken undiluted. After taking this medicine you should drink a glass (approximately 150 ml) of water or other liquid (fruit juices, tea, etc.). Alternatively, you can also mix Dulcolax® M Balance liquid into the beverage of your choice, thus flavouring it as you l ke.

If you are interested in more information on the topic of constipation and DULCOLAX® M Balance liquid, we would be happy to send you our current guide to digestion. Please send us the filled out reply form and give us your address. You can also download the guide from www.dulcolax.de.

We wish you a speedy recovery!
Your Dulcolax® Team

Boehringer Ingelheim Pharma GmbH & Co. KG,
Marketing Department CHC Germany, Marketing Dulcolax,
Binger Str. 173, 55216 Ingelheim am Rhein

Please send me the current DULCOLAX® digestion guide on the topic of constipation to:

Last name, first name _____
Street address _____
City, ZIP Code _____

[redacted]

Submission

November 2013 meeting of the Advisory Committee on Medicines Scheduling

SEP
2013

Purpose

[redacted] makes this submission in relation to one item (the proposal on esomeprazole) referred by the Delegate for scheduling advice to the November 2013 meeting of the Advisory Committee on Medicines Scheduling.

Recommendations

[redacted] *supports the proposal for a new Schedule 3 entry for esomeprazole for oral preparations containing 20 mg or less per dosage unit for the relief of symptoms for gastro-oesophageal reflux (heartburn) and symptoms of gastro-oesophageal reflux disease in packs containing not more than 14 days supply.*

Specific comments

Use of proton pump inhibitors

Non-prescription medicines for the treatment of heartburn and symptoms of gastro-oesophageal reflux disease (GORD) are widely available to Australian consumers. Proton pump inhibitors (PPIs) are regarded as first line therapy and considered to be more effective than histamine-2 receptor antagonists.[1]

Currently PPIs (except esomeprazole) for short term use are included in Schedule 3 (S3). Previous rescheduling decisions for rabeprazole, pantoprazole, omeprazole and lansoprazole were reportedly based on the good safety profile of each PPI, data supporting efficacy at the relevant doses, and that no significant new safety issues were reported since the change in classification in international markets. Several side effects of PPIs have been raised as concerns

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[1] Sigterman KE, van Pinxteren B, Bonis PA, Lau J, Numans ME. Short-term treatment with proton pump inhibitors, H2-receptor antagonists and prokinetics for gastro-oesophageal reflux disease-like symptoms and endoscopy negative reflux disease. Cochrane Database of Systematic Reviews, 2013, Issue 5. Art. No.: CD002095. DOI: 10.1002/14651858.CD002095.pub5.

[redacted]

previously, however, these relate to long term therapy[2,3,4] and there are also reports which moderate these concerns.[5,6]

As the Committee would be aware, [redacted] provides professional practice guidance to pharmacists on a number of S3 products. For short term use of PPIs, general principles include the following[7,8]:

- Immediate referral is recommended if: atypical or alarm symptoms are reported; symptoms are severe enough to impair quality of life; or there has been long term use or the need for a higher dose.

- For initial therapy, after consideration of the nature and frequency of symptoms, a two week course of PPI at the recommended dose is appropriate.

- Identify risk factors and consider any lifestyle modifications which may enhance the outcomes of PPI use.

- Referral for further investigation is recommended if: two weeks of continuous therapy has failed to adequately control symptoms; or symptoms recur following an initial course of therapy.

Professional practice guidance for pharmacists

In the event that esomeprazole is rescheduled to S3, [redacted] will review and update the current guidance document on the provision of PPIs as a Pharmacist Only Medicine. We would strongly advocate for the applicant of the rescheduling proposal to work in partnership with [redacted] to enable consolidation of available new evidence into the guidance document and to ensure other information relevant to esomeprazole is integrated. [redacted] will work to ensure accurate clinical content and consistent messages about all S3 PPIs can be developed and communicated to pharmacists who will then be able to inform consumers about therapy options, tailor advice according to their needs and circumstances, and assist consumers to maximise the benefits of their medicine.

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2 Vakil N. Prescribing proton pump inhibitors. Is it time to pause and rethink? Drugs, 72(4): 437–45 (2012).

3 Stuart RL, Marshall C. *Clostridium difficile* infection: a new threat on our doorstep. MJA, 194: 331–2 (2011).

4 National Prescribing Service. Pharmacy practice review: a counselling and action resource. Quality use of prescription PPIs. April 2009.

5 Brunner G, Athmann C, Schneider A. Long-term, open-label trial: safety and efficacy of continuous maintenance treatment with pantoprazole for up to 15 years in severe acid-peptic disease. Aliment Pharmacol Ther 24 April 2012. DOI: 10.1111/j.1365-2036.2012.05106.x

6 Chen J, Yuan YC, Leontiadis GI, Howden CW. Recent safety concerns with proton pump inhibitors. J Clin Gastroenterol, 46(2): 93–114 (2012).

7 Pharmaceutical Society of Australia. Guidance for provision of a *Pharmacist Only* medicine: proton pump inhibitors. November 2011.

8 Holtmann G, Bigard MA, Malfertheiner P, Pounder R. Guidance on the use of over-the-counter proton pump inhibitors for the treatment of GERD. Int J Clin Pharm, 33: 493–500 (2011). DOI: 10.1007/s11096-011-9489-y

[redacted]

Summary

In summary [redacted] believes the proposed new S3 entry for esomeprazole is clinically appropriate based on its inherent safety, efficacy and risk profile. It is also appropriate to have consistency in scheduling across all of the similar substances in the same class of medicine.

[redacted] would welcome the opportunity to work with the applicant to consolidate and disseminate any new evidence and up-to-date information on esomeprazole in the context of other S3 PPIs to assist pharmacists in their professional practice and to maximise the outcomes of therapy for consumers.

[redacted]

24 September 2013

[redacted]

Australian Self-Medication Industry Inc
Suite 2202, Level 22, 141 Walker Street,
North Sydney NSW 2060
PO Box 764, North Sydney NSW 2059
Ph +61 2 9922 5111 Fax +61 2 9959 3693
Email: info@asmi.com.au www.asmi.com.au
ABN 55 082 798 952

26 September 2013

The Secretary
Scheduling Secretariat
GPO Box 9848
Canberra ACT 2601

Dear Sir or Madam,

Re: Consultation – Invitation for public comment, ACMS Meeting November 2013
Esomeprazole – Proposal for a new Schedule 3 entry

We refer to the notice inviting public comment under Regulation 42ZCZK of the Therapeutic Goods Regulations and would like to provide comment on the proposal for a new Schedule 3 entry for esomeprazole.

ASMI (Australian Self Medication Industry) is the peak body representing companies involved in the manufacture and distribution of consumer health care products (non-prescription medicines) in Australia. ASMI also represents related businesses providing support services to manufacturers, including advertising, public relations, legal, statistical and regulatory consultants.

ASMI appreciates the opportunity to provide comment in relation to the above proposal.

Proton pump inhibitors (PPIs) are an established class of Schedule 3 medicines. Pantoprazole, lansoprazole, rabeprazole and omeprazole are currently entered in Schedule 3 when used at specific dosages for up to 14 days for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease (GORD).

Esomeprazole is the s-isomer of omeprazole, which is a racemic mixture of the R- and S- isomer. It has a similar benefit/risk profile to the PPIs that are currently Schedule 3[1] and therefore represents a logical addition to the PPIs already included in that schedule. All PPIs are recommended as standard initial therapy as a therapeutic trial in GORD[2], despite small differences in pharmacokinetic and other properties, such as degree of acid suppression.[3]

We believe that the safety profile, history of safe use, indication for short-term use and the ability of pharmacists to provide professional advice to ensure the quality use of medicines provides sound justification for esomeprazole being available as a Schedule 3 medicine.

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[1] Rossi S (ed). Australian Medicines Handbook. Adelaide: AMH Pty Ltd, 2011
[2] Gastrointestinal Expert Group (eds). Therapeutic Guidelines – Gastrointestinal. Therapeutic Guidelines Ltd, Melbourne. Version 4 2006.
[3] Edwards SJ, Lind T, Lundell L. Systematic review – Proton pump inhibitors (PPIs) for the healing of reflux oesophagitis – a comparison of esomeprazole with other PPIs. Aliment Pharmacol Ther 2006: 24: 743-750

ASMI therefore supports the proposal for inclusion of esomeprazole in Schedule 3, in oral dosage forms containing 20mg or less per dosage unit for the relief of symptoms of heartburn and other symptoms of gastro-oesophageal reflux disease, consistent with the Schedule 3 entry criteria for the other Schedule 3 PPIs.

We trust that the Committee will consider the merit of this proposal in terms of efficacy and safety of esomeprazole compared to currently available PPIs.

Yours sincerely,