Australian Government

Department of Health and Ageing

Therapeutic Goods Administration

Required Advisory Statements for Medicine Labels Explanatory Notes

Update 6

April 2011

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REQUIRED ADVISORY STATEMENTS FOR MEDICINE LABELS – UPDATE 6 EXPLANATORY NOTES

PURPOSE

This document is to provide stakeholders with an extended background explanation of the proposed changes to the *Required Advisory Statements for Medicine Labels* (RASML) *Update 6*. This document should be read in conjunction with *Required Advisory Statements for Medicine Labels* (RASML) Update 6 - dated February 2011.

Explanatory Notes

RASML Update 5

Update 5 was drafted in 2009 and was released for the public consultation process in July 2009. As a result of the public consultation period, the RASML Update 5 was amended and agreed upon by the Therapeutic Goods Committee in November 2009. However, it was never published due to upcoming amendments in the *Therapeutic Goods Act 1989* and the version of RASML in use is the RASML Update 4.

RASML statements included in Update 5 have been consulted and accepted, therefore are not open to current consultation. The following provides the background information only for inclusion of RASML statements in update 5.

1. Alpha casozepine enriched - Hydrolysed milk protein

In October 2008, the CMEC reviewed an application for the use of 'alpha-casozepine enriched hydrolysed milk protein' as an active ingredient in Listed medicines. The CMEC noted that this ingredient is derived from cow's milk so products containing this ingredient will be required to include a label statement to this effect, which is consistent with RASML statement 38. In addition, the CMEC noted that a similar bovine milk-derived ingredient, bovine colostrum powder, is required to include the RASML statement 139: '*This product is not suitable for use in children under the age of 12 months except on professional health advice'*.

The CMEC recommended approval of the substance as an active ingredient in Listed medicines for oral ingestion, subject to the inclusion of label statements consistent with the following:

- RASML statement 38: *"Derived from cow's milk"*, and
- RASML statement 139: *"This product is not suitable for use in children under the age of 12 months except on professional health advice*".

The RASML statement outlined above have been accepted in RASML update 5 and apply to the labelling of all non-prescription products containing alpha-casozepine enriched hydrolysed milk protein.

2. Anticholinergic products

The NDPSC, at its October 2007 meeting, raised concerns about the existing labelling requirements of anticholinergic products. The recommendation made by the NDPSC was that all scheduled OTC anticholinergic products, including products containing hyoscine butylbromide, should include a warning statement about the risk of using such products for an extended period of time as they have potential to mask serious condition. The suggested wording for the warning statement was: *"This product should not be used for more than two to three days without medical advice."*
The RASML update 4 consultation document (released in June 2008) subsequently included a proposal that the above statement be applied to products containing anticholinergic substances (when included in an OTC Schedule to the SUSDP and for oral use).

During the RASML consultation process, stakeholders raised concerns about the clarity of the proposed wording and also the appropriateness of the statement for products intended for the prevention of travel/motion sickness. In response to comments received during the RASML consultation process, the TGA sought advice from MEC regarding the issues raised during the consultation. In December 2008, the MEC considered these issues and made the following recommendations regarding appropriate requirements for scheduled OTC products containing anticholinergic agents indicated for antispasmodic/antidiarrhoeal use:

- RASL statement 180: *"If the condition persists after two days of treatment, seek medical advice as soon as possible"*

The RASML statement outlined above has been accepted in RASML Update 5.

3. Butoconazole (new Schedule 3 active)

The National Drugs and Poisons Schedule Committee (NDPSC), at its October 2006 meeting, rescheduled vaginal preparations containing butoconazole from Schedule 4 (Prescription Only Medicine) to Schedule 3 (Pharmacist Only Medicine) of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). *"Butoconazole in preparations for vaginal use"* was included in Schedule 3 of the SUSDP (effective date: 1 May 2007).

In October 2007, the Medicines Evaluation Committee (MEC) (considered the advisory statement requirements for S3 butoconazole vaginal preparations, with reference to the current RASML requirements for other OTC imidazole vaginal products (ie, clotrimazole, econazole and miconazole), which are as outlined below:

- RASML statement 16: *"See a doctor if you are pregnant or diabetic."*
- RASML statement 66: *"Seek medical advice before first course of treatment."*
- RASML statement 74: *"See a doctor if problem returns."*
- RASML statement 75: *"See a doctor (or) (dentist) if no better after (Insert number of days as per approved Product Information) days."*

The MEC recommended that OTC products containing butoconazole for vaginal use should include the RASML advisory statements 16, 66, 74 and 75, consistent with the requirements for other Schedule 3 OTC imidazole vaginal products.

The RASML statements listed above have been accepted in RASML Update 5.

4. Chitosan

In August 1998, the CMEC recommended that chitosan was suitable for use as an active ingredient in Listable medicines subject to inclusion of a label statement in relation to the effect of chitosan on the absorption of other drugs (subject to advice from a chemist) and a statement advising that the product is of seafood origin.

Since its inception in 2001, the Electronic Listing Facility (ELF) has required that chitosan products include the following label statements:

- RASML statement 181: *"Chitosan should be taken at least one hour after any other medication as it may reduce the effect of other medication (or words to that effect)"*, and
- RASML statement 182: For powdered dose forms – *"Do not take powder alone. Mix with food or fluid"*, and
- RASML statement 164: *"Derived from seafood"*.

The RASML statements listed above have been accepted in RASML update 5 and apply to the labelling of all non-prescription products containing chitosan.

5. Chlorhexidine

In April 2006, the MEC was requested to consider whether any label warnings should be required on the labelling of therapeutic products for human use containing chlorhexidine. The MEC was advised of the Adverse Drug Reactions Advisory Committee (ADRAC) review of reported adverse reactions to products containing chlorhexidine and the NDSPC's recommendation to include chlorhexidine (except in preparations containing 1 % or less of chlorhexidine or solid dosage formulations) in Schedules 5, 6 or 7 of the SUSDP. Both committees had concerns regarding the toxicity of products containing chlorhexidine. The ADRAC was concerned about the potential for rare, but severe, allergic reaction to chlorhexidine and the lack of information on this issue provided to consumers. The ADRAC review of chlorhexidine-containing products adverse reactions indicated that most frequently reported events related to topical reactions and allergic reactions. The NDPSC recommended the abovementioned scheduling of chlorhexidine due to concerns about inhalational toxicity and severe eye irritancy.

The MEC agreed with the ADRAC and NDPSC recommendations and recommended that OTC topical therapeutic products for human use containing chlorhexidine should include the following RASML statements:

- RASML statement 79: *"Avoid contact with eyes."*
- RASML statement 85: *"If in eyes, rinse well with water."*
- RASML statement 114: *"Mild irritation may occur; stop use if it becomes severe."*

The MEC did not recommend the inclusion of any cut-off percentage for these requirements.

The RASML statements listed above have been accepted in RASML update 5 and apply to all OTC topical products containing chlorhexidine, including preparations for topical use on mucosal surfaces.

6. Folic acid

Listed medicines that provide a daily dose of 400-500 micrograms of folic acid or folate are permitted to be indicated for reducing the risk of having a child with spina bifida/neural tube defects when taken daily for one month before conception and during pregnancy. However,

Listed medicines that make such claims are also required to include the following label advisory statement:

- RASML statement 183: *"Do not exceed the stated dose except on medical advice. If you have had a baby with a neural tube defect/spina bifida, seek specific medical advice (or words to that effect)".*

Since its inception in 2001, the ELF has required that these folic acid products include the above label statement.

The RASML statement outlined above has been accepted in RASML update 5 and applies to the labelling of all folic acid containing non-prescription products indicated for reducing the risk of having a child with spina bifida/neural tube defects when taken daily for one month before conception and during pregnancy.

7. Fluconazole

The RASML requirement for fluconazole supplied as Schedule 3 medicines (fluconazole in single-dose oral preparations containing 150 mg or less of fluconazole for the treatment of vaginal candidiasis) was considered by the MEC in December 2008. The current RASML only requires statement 75 on the labels of OTC products containing fluconazole whilst statements 16, 66, 74 and 75 (see above for advisory statements wording) are required for OTC (Schedule 3) vaginal preparations containing imidazole antifungal agents (clotrimazole, econazole or miconazole) for the treatment of vaginal candidiasis. The MEC considered that consistent label statements should be applied (where appropriate) for OTC preparations containing fluconazole and OTC preparations containing imidazole antifungal agents for the treatment of vaginal candidiasis. However, the current advisory statement, that pregnant patients should see a doctor before use (RASML statement 16), is not appropriate for fluconazole as it is in pregnancy category D in the "Prescribing medicines in pregnancy - An Australian categorisation of risk of drug use in pregnancy" handbook. Therefore, the advisory statement, *"Do not use if pregnant."* (RASML statement 13) was recommended instead of RASML statement 16.

The following RASML statements are required for fluconazole:

- RASML statement 13 : "Do not use if pregnant"
- RASML statement 66: *"Seek medical advice before first course of treatment."*
- RASML statement 74: *"See a doctor if problem returns."*
- RASML statement 75: *"See a doctor (or) (dentist) if no better after (Insert number of days as per approved Product Information) days."*
- RASML statement 177: *"See a doctor before use if you are diabetic."*

The RASML statements listed above have been accepted in RASML Update 5.

8. Hydroxyanthracene derivatives

In September 1998, the CMEC reviewed the safety of herbs containing hydroxyanthracene derivatives (anthranoids). These herbs, which generally have a laxative effect, include senna (*Cassia* spp.), rhubarb (*Rheum* spp.), aloe (*Aloe* spp.), buckthorn (*Rhamnus catharticus*), cascara (*Rhamnus purshianus*) and frangula (*Rhamnus frangula*). Although these herbs can be useful for treating short-term constipation, excessive and long-term use can cause potassium loss, reliance on laxative use, and serious bowel problems.

The CMEC recommended that products containing hydroxyanthracene derivatives should be required to include certain label advisory statements. Label warnings are required on all products containing a daily dose of 10 mg or more of hydroxyanthracene derivatives from all sources in the MRDD, whether or not the products are promoted as laxatives. Products containing less than 10 mg of hydroxyanthracene derivatives in the maximum recommended daily dose (MRDD) may require warning statements depending upon claims being made for these products and the nature of other ingredients in these products.

In August 2006, the CMEC reviewed the safety of hydroxyanthracene derivatives, and recommended that the existing regulatory arrangements were appropriate, including labelling requirements, as outlined below:

i) <u>Products making a laxative claim and with a daily dose of 10 mg or more derived from hydroxyanthracene derivatives:</u>

- RASML statement 184: *"Drink plenty of water (or words to that effect)"*
- RASML statement 185: *"Prolonged use may cause serious bowel problems (or words to that effect)"*
- RASML statement 186: *"Do not use when abdominal pain, nausea or vomiting are present, or if you develop diarrhoea. If you are pregnant or breast feeding, seek health practitioner advice before taking this product (or words to that effect)"*
- RASML statement 4: *"Use in children under 12 years is not recommended"*; and
- RASML statement 77: *"If symptoms persist consult your health care practitioner (or words to that effect)"*.

ii) <u>Products NOT making a laxative claim and with a daily dose of 10 mg or more derived from hydroxyanthracene derivatives:</u>

- RASML statement 185: *"Prolonged use may cause serious bowel problems (or words to that effect)"*
- RASML statement 186: *"Do not use when abdominal pain, nausea or vomiting are present, or if you develop diarrhoea. If you are pregnant or breast feeding, seek health practitioner advice before taking this product (or words to that effect)"*
- RASML statement 134: *"This product may have a laxative effect"*
- RASML statement 187: *"This product contains [name of herb(s) or chemical component(s)]"*
- RASML statement 4: *"Use in children under 12 years is not recommended"*; and

- RASML statement 77: *"If symptoms persist consult your health care practitioner (or words to that effect)"*.

iii) Products making a laxative claim and with a daily dose of less than 10 mg derived from hydroxyanthracene derivatives:

- RASML statement 184: *"Drink plenty of water (or words to that effect)"*
- RASML statement 185: *"Prolonged use may cause serious bowel problems (or words to that effect)"*
- RASML statement 4: *"Use in children under 12 years is not recommended"*; and
- RASML statement 77: *"If symptoms persist consult your health care practitioner (or words to that effect)"*.

iv) Products NOT making a laxative claim and with a daily dose of less than 10 mg derived from hydroxyanthracene derivatives:

Label warnings are only required if linked to other ingredients in the product.

The requirement for the above label statements has been included in the ELF since its inception, but has not been in previous versions of the RASML.

The RASML statements listed above have been accepted in RASML update 5 and the same warnings apply to the labelling of all non-prescription products containing hydroxyanthracene derivatives.

9. Iron-containing compounds

In May 2003, the CMEC recommended that Listed medicines containing iron compounds (**except** iron-containing multivitamin/mineral products indicated for general nutritional support, and which do not make specific iron-deficiency related claims) should include the following label advisory statement:

- RASML statement 188: *"Not for the treatment of iron deficiency"*.

The requirement for the label statement has been included in the ELF since July 2005.

The RASML statements outlined above have been accepted in RASML update 5 and apply to the labelling of all non-prescription products containing iron, unless they are specifically indicated for the treatment of iron-deficiency.

10. Pantoprazole (new Schedule 3 active)

The NDPSC, at its June 2005 meeting, rescheduled pantoprazole from Schedule 4 to Schedule 3 of the SUSDP. *"Pantoprazole in oral preparations containing 20 mg or less of pantoprazole for the relief of heartburn and other symptoms of gastro-oesophageal reflux disease, in packs containing not more than 14 days of supply"* was included in Schedule 3 (effective date 1 May 2008).

In June 2008, the MEC considered the warning statement requirements for OTC products containing pantoprazole and recommended that the RASML should require the same warning statements for pantoprazole as are currently required for the OTC histamine H_2-receptor antagonists.

The following RASML statements which are currently required for OTC histamine H_2-receptor antagonists, are to apply for OTC pantoprazole products:

- RASML statement 60: *"CAUTION – This preparation is for the relief of minor and temporary ailments and should be used strictly as directed."*
- RASML warning statement 72: *"If symptoms persist or recur within two weeks of completing the course, consult a doctor."*

The RASML statements listed above have been accepted in RASML Update 5.

11. Potassium chloride

In March 2009, the CMEC reviewed an application for the use of potassium chloride as an active ingredient in Listed medicines for oral rehydration therapy. The CMEC noted that excess administration of potassium may cause hyperkalaemia, which may in turn disrupt neural conduction resulting in cardiac arrhythmias and cardiac arrest. Individuals with renal impairment are at particular risk of developing hyperkalaemia.

The potassium content of some glucosamine products was also reviewed by the CMEC in February 2008. The Committee recommended that the labelling of products containing glucosamine sulfate-potassium chloride complex should include the following label advisory statement:

- *"Contains potassium. If you have kidney disease or are taking heart or blood pressure medicines, consult your doctor or pharmacist before use. Keep out of reach of children".*

The above statement is consistent with statements that are in the current RASML as follows:

- RASML statement 165: *"Contains [amount of potassium] potassium"*
- RASML statement 166: *"If you have kidney disease or are taking heart or blood pressure medicines, consult your doctor or pharmacist before use"*; and
- RASML statement 1: *"Keep out of reach of children*".

The CMEC recommended that potassium chloride in Listed medicines used for oral rehydration, should also include the above statements subject to appropriate label requirements.

The RASML statements listed above have been accepted in RASML update 5 and apply to the labelling of all non-prescription oral rehydration products containing potassium chloride.

12. Psoralea corylifolia

In April 2008, the CMEC reviewed the safety of *Psoralea corylifolia*, which is currently approved for use in Listed medicines with no restrictions. The CMEC noted that *P. corylifolia* contains psoralens and that high doses of *P. corylifolia* resulted in an increase in photosensitivity.

The CMEC recommended that the use of *P. corylifolia* as an ingredient in Listed medicines should be limited to preparations of the fruit/seed containing less than 1.1 per cent psoralen per recommended daily dose, and should be subject to the inclusion of a label advisory statement informing consumers of the photosensitizing potential of psoralen, such as:

- RASML statement 189 *"This product may cause photosensitization."*

The RASML statement outlined above has been accepted in RASML update 5 and the same warning apply to the labelling of all non-prescription products containing *P. corylifolia*.

13. Psyllium

Psyllium (or Ispaghula) is the common name used for several members of the plant genus *Plantago* whose seed husks are often used as a source of dietary fibre in over-the-counter laxatives and fibre supplements.

Since its inception in 2001, the ELF has required that products containing psyllium fibre that give a dose for children must include the following label statement:

- RASML statement 190: *"Should only be used for children on medical advice (or words to that effect)."*

The RASML statements listed above have been accepted in RASML update 5 and apply to labelling of all non-prescription products containing psyllium.

14. Pyridoxal, pyridoxamine, and pyridoxine

Neurotoxicity is a well known adverse reaction associated with vitamin B6 when taken at high doses and for long periods. Currently medicines containing 50 to 200 mg of vitamin B6 per recommended daily dose are required to have one of the following label statements:

- RASML statement 53: "WARNING – This medication may be dangerous when used in large amounts or for a long period"; or
- RASML statement 56: "WARNING – This product contains pyridoxal which may be dangerous when used in large amounts or for a long time"; or
- RASML statement 57: *"WARNING – this product contains pyridoxamine which may be dangerous when used in large amounts or for a long time."* ; or
- RASML statement 58: *"WARNING – this product contains pyridoxine which may be dangerous when used in large amounts or for a long time."*

In February 2008, the Complementary Medicines Evaluation Committee (CMEC) reviewed the appropriateness of these current label warning statements following a report of sensory neuropathy in an individual taking up to 600 mg/day vitamin B6 for 3-4 years. The primary concern of the Committee lay with the ambiguity of the warnings for vitamin B6, in that consumers are not clear as to what "large amounts" or "a long period" mean. CMEC considered that there should be specific information on the label to alert consumers to the early warning signs of vitamin B6 toxicity and the action to be taken if these should arise. The Committee therefore recommended the revision of the current warning statements for non-prescription medicines containing from 50 to 200 mg vitamin B6 (pyridoxine, pyridoxal, pyridoxamine) per recommended daily dose to:

For single ingredient products:

- RASML statement 178: "*WARNING – Stop taking this medication if you experience tingling, burning or numbness and see your healthcare practitioner as soon as possible*".

For multi-ingredient products:

- RASML statement 179: "*WARNING – Stop taking this medication if you experience tingling, burning or numbness and see your healthcare practitioner as soon as possible. Contains vitamin B6*".

The RASML statements listed above have been accepted in RASML Update 5

15. Vegetable oil phytosterol esters

In June 2008, the MEC reviewed an application for the use of 'vegetable oil phytosterol esters' as an active ingredient in Listed medicines. Although the MEC had no concerns regarding the safety of phytosterols or phytosterol esters as part of a normal diet, it noted that the Australian Heart Foundation has recommended that a daily intake of phytosterols in excess of 2-3 g/day does not offer an additional benefit in terms of reducing low-density lipoprotein cholesterol. In addition, the MEC noted that it was not advisable for pregnant or lactating women and children to lower cholesterol levels. The MEC recommended that the ingredient could be approved for use as an active ingredient in Listed medicines, subject to the inclusion of label advisory statements to the following effect:

- *"There is no benefit, in lowering cholesterol, of having more than 3 g/day of phytosterols from all sources. Consult a health professional if you usually eat margarine or other products which claim cholesterol-lowering benefits"; and*
- *"Use is not recommended in children under five years, or pregnant or breastfeeding women".*

The proposed label statements were reviewed by the CMEC in August 2008. The CMEC agreed that an advisory statement indicating that there is no benefit from taking more than 3 g of phytosterols per day was appropriate, but that the wording of the statement should be simplified. In addition, the CMEC considered that therapeutic goods containing phytosterols would generally not be recommended for children, so it was not necessary for the label advisory statement to include wording in relation to children. However, Members considered that a statement indicating that these products were not suitable for pregnant or lactating women would be

beneficial and recommended the following revised label advisory statements for products containing ‘vegetable oil phytosterol esters’:

- RASML statement 191: *“There is no benefit from taking more than 3 g/day of phytosterols from all sources”; and*
- RASML statement 15: *“Not recommended for use by pregnant or lactating women”*.

The RASML statements listed above have been accepted in RASML update 5 and apply to the labelling of all non-prescription products containing vegetable oil phytosterol esters.

RASML Update 6

The following provides the background information for inclusion of RASML statements in update 6.

1. Alpha hydroxy acids

Under the Australian Regulatory Guideline on Over-the-counter Medicines (ARGOM 2003), it is noted that there is evidence to suggest that the use of topical products containing alpha hydroxy acids (such as glycollic acid, lactic acid, citric acid and other fruit acids) may make users more sensitive to sunlight and especially to the ultraviolet (UV) radiation component of sunlight. UV exposure can damage the skin and at high doses, especially over a long period, can cause skin cancer.

ARGOM 2003 requires that the following statements should be included in the labelling of products containing alpha hydroxy acids:

- *This product may make your skin more sensitive to sunlight;*
- *Sun exposure should be limited by using a sunscreen and by wearing protective clothing;*
- *If you have sensitive skin, test this product on a small area of skin before applying it to a large area;*
- *Transient stinging or irritation may occur when using this product. If irritation persists, discontinue use;* and
- *Not recommended for use on children or infants.*

The inclusion of these advisory statements in the proposed update of the RASML will formalise this requirement.

2. Anaesthetics, dermal

ARGOM 2003 requires that labels of dermal preparations containing a local anaesthetic agent should include a label warning statement such as:

- *If irritation occurs, stop use immediately and seek medical advice*
- *Do not apply to large areas of the body except on the advice of a health care practitioner*

The inclusion of these advisory statements in the proposed update of the RASML will formalise this requirement.

3. Anaesthetics, lozenges

ARGOM 2003 requires that labels of lozenges containing a local anaesthetic agent should include a label warning statement such as:

- *Do not take hot food or drink soon after using this product because it may burn your mouth.*

Where indicated for use in children, the labels of lozenges containing a local anaesthetic agent should also include a label warning statement such as:

- *Do not give to children under six years of age, unless recommended by a doctor, pharmacist or dental professional*

The inclusion of these advisory statements in the proposed update of the RASML will formalise this requirement.

4. Camphor

ARGOM 2003 advises that the directions for use for dermal preparations containing camphor should indicate that the product is not to be applied to infants under 12 months of ages unless on the advice of a physician. Therefore, the following statement is recommended:

- *Do not apply to infants under 12 months of age except on the advice of a doctor*

The inclusion of the warning statement in the proposed update of the RASML will formalise this requirement.

5. Carthamus tinctorius flower

Following a review of the safety of this herb, the Advisory Committee on Complementary Medicines (ACCM) recommended that the TGA mandate this statement <http://www.tga.gov.au/committee/accm/accm-2010-02.htm>

- The RASML statement 14: "Do not use if pregnant or likely to become pregnant"

This label statement will apply to all Listed medicines from 1 July 2011. The TGA has contacted sponsors of existing products, as well as CM industry associations to advise them of this requirement.

The inclusion of the warning statement in the proposed update of the RASML will formalise this requirement.

6. Chlorhexidine

The MEC was advised of the Adverse Drug Reactions Advisory Committee (ADRAC) review of reported adverse reactions to products containing chlorhexidine and the NDSPC's recommendation to include chlorhexidine (except in preparations containing 1 % or less of chlorhexidine or solid dosage formulations) in Schedules 5, 6 or 7 of the SUSDP. Both committees had concerns regarding the toxicity of products containing chlorhexidine. The ADRAC was concerned about the potential for rare, but severe, allergic reaction to chlorhexidine and the lack of information on this issue provided to consumers. The ADRAC review of

chlorhexidine-containing products adverse reactions indicated that most frequently reported events related to topical reactions and allergic reactions.

The TGA proposes the following warning statement be included on labelling of all non-prescription products for mucosal surfaces containing chlorhexidine:

- *WARNING – This product contains chlorhexidine. Severe allergic reactions can occur. Stop use if this occurs' is proposed to be included on labelling of all non-prescription products for mucosal surfaces containing chlorhexidine*

7. Choline Salicylate

In July 2009, the MEC was requested to advice on whether products containing non-aspirin salicylates that are intended for topical application to the oral mucosa of children should be required to include the label warnings which are required for oral products containing aspirin. The committee recommended that the RASML warnings that are required for aspirin should not be required for choline salicylate. However, as use of excessive quantities may result in salicylate toxicity, the Committee therefore recommended the following warning statement for non-prescription medicines containing choline salicylate.

- *Do not exceed the recommended dose. Excessive or prolonged use can be harmful.*

8. Coal Tar

During an evaluation on the safety and efficacy of OTC preparations containing coal tar, it was noted that the safety of coal tar on children under 2 years of age had not been established. In addition, although no human data are available on the effects of using coal tar during pregnancy or lactation, the presence of mutagens in the urine has been reported following topical application of coal tar[1]. It was therefore recommended that the labels of all topical products containing coal tar should therefore include warnings such as:

- *Not recommended for use on children under 2 years of age except under the direction and supervision of a doctor.*
- *Not recommended for use during pregnancy or while breastfeeding.*

As coal tar may cause hypersensitivity reactions and irritation, labels of products containing coal tar should also include warnings such as the following:

- *If irritation occurs, discontinue use.*
- *Avoid contact with the eyes.*
- *Do not use for prolonged periods except on the advice of a doctor.*

[1] Wheeler LA, Saperstein MS & Lowe NJ. Mutagenicity of urine from psoriatic patients undergoing treatment with coal tar and ultraviolet light. J Invest Dermatol 77:181-185; 1981.

In addition, unless otherwise justified, products that are intended for use in psoriasis should include a warning such as:

- *Do not use this product with other forms of psoriasis therapy such as UV radiation or prescription drugs unless directed to do so by a doctor.*

9. Excipients

The approval of the following substances:

Butyl ester of pvm/ma copolymer
DEA-Oleth-3 phosphate
Diethylhexyl-2,6-naphthalate
Erythrulose
Ethyl butylacetyl-aminopropionate
Stearamidopropyl PG-dimonium chloride phosphate
Stearyl dimethicone
Sucrose polycottonseedate

for use as excipient(s) in a non prescription product for topical use requires the following statements.

- *Avoid contact with eyes*
- *May be irritant to the eyes (or words to that effect*

The inclusion of this advisory statement in the proposed update of the RASML will formalise this requirement.

10. Fluorides

In alignment with the information consulted at time of drafting the new version of the Australian Regulatory Guideline on Over-the-Counter Medicines (ARGOM)

The following statements are proposed to be included on labelling of all non-prescription products for fluoride containing products:

- *Do not use if pregnant;*
- *Use of this product is not necessary in areas supplied with fluoridated water; and*
- *Do not use except on the advice of a dentist*

11. Laxatives

ARGOM 2003 advises that products containing senna, aloe or cascara should contain a lable statement such as:

- *Do not use when abdominal pain, nausea or vomiting, is present. If you are pregnanat or breast feeding, seek medical advice before taking this product.*

The inclusion of the warning statement in the proposed update of the RASML will formalise this requirement.

12. Non Steroidal Anti-inflammatory Drugs (NSAIDs)

7.1 ARGOM 2003

ARGOM 2003 requires the following statements

<u>For orally administered products containing ibuprofen:</u>

- *Do not use in the presence of a stomach ulcer or other stomach disorders, impaired kidney function or heart failure*

<u>For orally and topically administered products containing ibuprofen:</u>

- Do not take/use if you are allergic to aspirin, ibuprofen, or other medicines for pain relief

The inclusion of these advisory statements in the proposed update of the RASML will formalise this requirement. The TGA also proposes that the same warnings should also be included on the labelling of all non-prescription products containing NSAIDs

7.2 Committee Recommendation

<u>For orally administered products containing NSAID:</u>

In February 2010, the Advisory Committee on Non Prescription Medicines (ACNM) (Formerly Medicines Committee [MEC]) was requested for advice on whether advisory statements relating to kidney damage in people who are fluid depleted, particularly children, should be required on the labels of all oral non-prescription NSAID products. MEC agreed that labels of non prescription products containing NSAIDs should be required to include a warning regarding the risks of kidney damage associated with dehydration (e.g. after prolonge periods of vomiting or diarrhoea). The Committee therefore recommended the following warning statement for non-prescription medicines containing NSAIDs:

- *Ask your doctor or pharmacist before use if you are dehydrated, or have diarrhoea or vomiting.*

<u>For topically administered products containing NSAID:</u>

In May 2010, ACNM reviewed an application to register dermal preparation of diclofenac recommended that the following warning statement to be included on all dermal preparations of NSAIDs

- *Unless a doctor has told you to, do not use [this product/product name] with other medicines that you are taking regularly.*

The TGA proposes that the above same warnings should also be included on the labelling of all dermal preparations containing NSAIDs

13. Oral Rehydration salts

In September 2009, the Therapeutic Good Listing Notice No.3 and No.4 requires the following advisory statements for preparations that contain potassium chloride and sodium bicarbonate as their therapeutically active ingredient in oral rehydration therapy:

- *Use only as directed*
- *If diarrhoea persists, seek medical advice*
- *when indicated for use in children, the directions for use on the product label includes the following additional directions:*

Age of child	**Additional Directions**
Under 6 months	Medical advice should be sought if diarrhoea persists for more than 6 hours.
Under 3 years	Medical advice should be sought if diarrhoea persists for more than 12 hours.
3-6 years	Medical advice should be sought if diarrhoea persists for more than 24 hours.
Over 6 years	Medical advice should be sought if diarrhoea persists for more than 48 hours.

The inclusion of these advisory statements in the proposed update of the RASML will formalise this requirement.

14. Proton Pump Inhibitors (PPI)

In February 2010, the Advisory Committee on Non Prescription Medicines (ACNM) (Formerly Medicines Committee [MEC]) reviewed an application to register an OTC product containing rabeprazole. In considering the potential interactions of other medicines with rabeprazole the Committee agreed the RASML should require the statement:

- *Ask your doctor or pharmacist before use if you are taking other medicines regularly*

The Committee proposes that the same warnings should also be included on the labelling of all non-prescription products containing proton pump inhibitors.

15. Pollen

Since its inception in 2001, the Electronic Listing Facility (ELF) has required that chitosan products include the following label statements:

- *When the ingredient is collected by bees and included in Listed medicines.*

The above statement has not been included in previous versions of the RASML. The inclusion of this advisory statement in the proposed update of the RASML will formalise this requirement.

16. Vasoconstrictor eye drops

ARGOM 2003 requires the following statements following the advice from the Royal Austrakian College of Ophthalmologists:

- *Prolonged use may be harmful;*
- *Consult a doctor or pharmacist if using other eye products;*
- *Do not use if you have glaucoma or other serious eye conditions; and*
- *If symptoms persist, consult a doctor,*

The inclusion of these advisory statements in the proposed update of the RASML will formalise this requirement.