SCHEDULING OF COSMETIC AND FRAGRANCE MATERIALS IN AUSTRALIA

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Review of Cosmetic Ingredient Scheduling

SCHEDULING OF COSMETIC AND FRAGRANCE MATERIALS IN AUSTRALIA
INTERIM REPORT

1 EXECUTIVE SUMMARY

[Pending]

2 GENERAL ISSUES

2.1 Notes on the Draft Phase I Report

This report is a progress draft of the Phase I review of scheduling arrangements for cosmetic ingredients. Many issues raised in this Draft require considerable further consideration and analysis in order to support specific options and/or recommendations. This draft has however canvassed a broad range of issues relevant to the overall review in order to provide context, and an indication of the general direction for the completed review. Equally in order to identify sub optimal procedures or processes that might lead to difficulties for key stakeholders, a preliminary survey of the overall regulatory environment is necessary.

2.2 Introduction

In 2016-2017, the Department of Health (Health) reviewed the Scheduling Policy Framework (SPF) and scheduling process for medicines and chemicals. That review identified that improvements were required to streamline the process by which chemicals are scheduled.

As part of a project seeking to consider opportunities to further amend and implement these changes, Health have requested an Expert Review of current process and scheduling decisions in relation to cosmetic and fragrance ingredients to identify how closely Australia's decisions align with other regulators (in particular the EU, UK and US). Of particular interest was an exploration of whether there are opportunities to harmonise chemical scheduling with comparable overseas regulators (CORs).

In conducting this review consideration has been given to a proposal from ACCORD Australasia Pty Ltd to create a new Appendix entry in the Poisons Standard for substances used in cosmetic products, including incorporating Annexes II-VI of the European Union (EU) Cosmetics Regulation (European Commission 2009), which details prohibited and restricted ingredients. Accord has also proposed mandating compliance with the International Fragrance Association (IFRA) Standards for fragrance materials (IFRA 2015).

The increased number of referrals of cosmetic ingredients to the ACCS noted by ACCORD has resulted from a NICNAS program to assess existing chemicals on the Australian Inventory of Chemical Substances that had been "grandfathered" onto the AICS at the commencement of the NICNAS scheme. This program of review is conducted under the Inventory Multi-tiered Assessment and Prioritisation process (IMAP). As a result of that process a number of cosmetic and fragrance ingredients on the AICS were identified for assessment and some of these have been referred piecemeal by NICNAS to the Advisory Committee on Chemicals Scheduling for consideration for inclusion in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSMP). The scheduling reconsiderations have given rise to concern amongst cosmetic and fragrance manufacturers in Australia regarding potential unintended consequences, perceived discordance with international regulations in major export markets and an expressed perception that the overall regulatory burden is disproportionate to the risk being managed. These concerns are outlined in more detail below, section 2.2.1.

In reviewing the scheduling process for cosmetic ingredients, a distinction is made between fragrances and flavours which are generally present in very low concentrations, and other ingredients such as surfactants which may be present at considerably higher levels. This first phase of the review has focused on the former in recognition of the low levels of use in cosmetic products, the low level of risk generally presented by these substances, and the consequent potential for disproportionate impacts of regulatory burdens placed on the cosmetics industry by scheduling decisions discordant with international practice in major markets.

Before examining the nature of the NICNAS Advice to the ACCS, and that committees' scheduling recommendations on cosmetic products, a consideration of the nature and scope of cosmetic ingredients, the regulatory environment

for such ingredients in Australia and the legislative objectives of scheduling is appropriate. Firstly however, the ACCORD concerns are presented in more detail.

2.2.1 ACCORD CONCERNS

ACCORD have raised a number of concerns which broadly fall under the following categories;

- **No provision to exempt trace levels of schedule 7, 8, 9, or 10** substances in cosmetic or fragrance materials
    - The sophistication of modern analytical techniques are such that a chemical can be detected and identified at levels considerably below that which could cause public health concerns under any plausible scenario.
    - Ethylene oxide (S7 substance) is a reagent in the production of poly ethoxylated alcohol or alkylphenol surfactants.
    - With modern analytical techniques low levels of residues are detectable would make products using these surfactants S7 products.
    - Whether these ethoxylated surfactants are derivatives of ethylene oxide is also unclear.

- **Inconsistencies in regulatory recommendations** between scheduling applications for related substances or substances with similar hazard profiles
    - recently encountered with the proposed scheduling and consideration by ACCS of benzyl salicylate, anise alcohol and cinnamaldehyde in 2017. The interim decisions (issued in May 2017) were not consistent with other recent scheduling decisions for substances that are also fragrance/flavour ingredients with similar toxicity profiles such as amyl cinnamaldehyde and hexyl cinnamaldehyde; geraniol (3,7-dimethyl-2,6-octadien-1-ol); and isoeugenol.
    - The interim decisions were also not consistent between the 3 substances, despite them all being fragrance/flavour ingredients with similar toxicity profiles and use patterns.
- **Inconsistencies with international regulations**
    - proposed scheduling for benzyl salicylate, anise alcohol and cinnamaldehyde were discordant with regulation under the EC Cosmetics regulation
- **Inconsistency within the SUSMP**, inconsistency with international controls and interpretation of derivatives, for example Geraniol (Rajeswarra Rao 2002)
    - Geraniol occurs in a range of essential oils in common use including, but not limited to, Palmerosa oil (~65%), Citronella oil (10-20%) and geranium oil (~10-30%).
    - Each of the essential oils is in Appendix B
    - By virtue of the level of geraniol in these oils, each is also in Schedule 6
    - palmarosa oil also contains geranyl acetate (approx. 20%), a condensation product of geraniol and acetic acid, readily converts to geraniol by hydrolysis, and therefore a derivative (?), captured by the geraniol schedule entry (ie. palmarosa oil is approx. 85% geraniol and derivative).
    - eg scheduling of hair dye colorants
        - Although the consistency alignment of cut offs for colorants with those internationally have improved significant inconsistency in the requirements for warning statements and signal headings remain
        - The EU Cosmetics Regulation does not routinely require statements such as "Keep out of reach of children" or "avoid exposure to skin" for hair dye products. If the finished product is otherwise unscheduled but requires additional labelling to meet an exemption from scheduling, all of the extra labelling will need to be added.
        - Ingredient warnings should not spill over into generic product labelling.

- The requirement for signal headers and their position on the first line of the label for scheduled substances is also unique to Australia for hair dye products and requires costly re-work of imported product labels.
- Example: resorcinol (final decision 31 October 2017)
  - The exemption form scheduling for hair lotions/shampoo products requires a warning statement about skin sensitisation potential.
  - From the data presented the risk of skin sensitisation is questionable at best at such low concentrations of resorcinol i.e. <0.5%.
  - This is out of step with the EU requirements for these same products containing resorcinol at 0.5% or less, where the label statement required is "Contains resorcinol" to allow consumers to make informed choices.
  - The disclosure of the presence of resorcinol in cosmetic products in Australia is already mandated under the ACCC Mandatory Standard for ingredient labelling.

2.3 The Regulatory Environment

The regulatory environment for chemicals in Australia is complex, duplicative, fragmented and prone to compartmentalization. The poisons scheduling process is only one small component of this regulatory environment and at the Commonwealth level intersects with the regulatory regimes for consumer products (ACCC), pesticides and veterinary chemicals (APVMA), human pharmaceuticals, complimentary medicines and medical devices (TGA), and industrial chemicals (NICNAS). Any individual chemical is likely to fall under the responsibilities of more than one of these agencies.

2.3.1 PRINCIPLES OF REGULATORY BEST PRACTICE

Regulation is not a morally neutral or costless process. All regulation imposes constraints, obligations or liabilities on individuals and/or corporations and therefore a cost. In an ideal regulatory environment, such imposts are strictly proportional to the risks or potential adverse outcomes associated with the activity being restricted, and the costs of implementation and compliance are proportionate to, and commensurate with, those associated with the risks being mitigated or obviated. Consistent with these considerations, the legislative foundation for Poisons scheduling incorporates a requirement to consider both risks and benefits of **products as supplied into the market,** without limitation to health risks and health benefits.

The principles of proportionality is widely recognised as a foundation of National and International Law and subsidiary regulation (Cottier 2012; Ferran 2015; OECD 1995; OECD 2012). The Office of Best Practice Review (OBPR) within the Department of Prime Minister and Cabinet (PMC) has noted that the Governments' commitment to the OECD 2012 Recommendation on Regulatory Policy and Governance (OECD 2012).

Traditionally the TGA has not conducted Regulatory Impact Statements for scheduling proposals. Arguably where such proposals are for medicines or agricultural and veterinary chemicals, the scheduling process is incidental to the broader regulatory process generally associated with a specific application for approval of a medicinal or agricultural product, and a RIS would not be indicated. Where a substantial number of proposals are for substances used in cosmetics however (or any other otherwise unregulated industry supplying domestic goods) and introduce new restrictions and imposts on that industry unrelated to the normal machinery of product or substance approval, these are not incidental or minor in their potential impact and the principles of the RIS process might at the least be addressed within the scheduling deliberations. More specifically where a substantial regulatory impost is likely, a consultation with the relevant industry would seem to be a minimal obligation to ensure that;

- the most appropriate risk proportionate regulatory response is identified,

- the most cost-efficient mechanism for addressing that response is adopted,
- a review of potential alternative approaches is undertaken.

For efficiency these considerations could be encompassed within class reviews such as for surfactants, perfume and flavor ingredients, colourants, preservatives etc. This approach would;

- reduce the cost to both industry and regulators by grouping related substances in the one risk analysis
    - provide opportunities for read across of data sets for related substances to compensate for missing or deficient data,
    - facilitate call in of data from potentially affected industry groups,
    - ensure unintended consequences or inconsistencies are minimized,
    - reduce the number of times that industry need to be engaged,
    - broaden the scope of industries involved and therefore distribute the burden of engagement more broadly
        - also increasing the likely availability of data
    - facilitate engagement of regulators across the broad range of chemicals to ensure a higher quality of risk assessment and consideration of unintended cross regulatory consequences.

The OBPR has produced a guide for determining where a RIS might be required. The types of regulatory impacts and compliance costs on industry that should be considered include;

- **Regulatory impacts including:**
    - changes to the number or type of products that businesses can offer, such as:
        - banning products or industry practices
        - changing the way products can be offered
    - impacts on consumer demand for certain products, such as:
        - increasing prices through the regulation's requirements
        - changing the information available to consumers
    - impacts on the ability of businesses to compete in the market or on their incentives to compete, such as:
        - creating a self-regulatory or co-regulatory regime
        - changing the requirements for a licence, permit or other authorisation
        - influencing the price or quantity of goods that are sold
        - setting standards for product or service quality
        - changing the prices or types of inputs available to businesses.
- **compliance costs:**
    - administrative costs
        - costs incurred by regulated entities mainly to demonstrate compliance with the regulation (usually record keeping and reporting costs)
        - costs incurred through complying with government taxes, fees, charges and levies, beyond the amount paid (for example, the time taken to pay a licence fee).
    - substantive compliance costs
        - costs that lead directly to the regulated outcomes being sought (usually purchase and maintenance costs for plant and equipment to meet regulatory requirements, fees paid to training providers, costs of providing information to third parties, and costs of operation—for example, energy costs).
- **delay costs:**
    - expenses and loss of income incurred by a regulated entity through one or both of:
    - an application delay—the time taken to complete an administrative application requirement that prevents the party from beginning its intended operations

- an approval delay—the time taken by the regulator to communicate a decision on the administrative application that prevents the party from beginning its intended operations (this includes the time taken to asses and consider an application).

- **Costs associated with the need to engage and respond to the process** –
  - of submission preparation
  - rescheduling application to fix errors
  - monitoring of outcomes
  - provision of expertise

Many of the considerations raised by the OBPR are clearly applicable where a wide range of substances within a number of chemical and use classes are being considered for scheduling action in an area that has not previously been routinely included in the process other than for overtly high-risk chemicals. This requirement has precedence for Cosmetics in the ACCC RIS on consumer product information standards (ACCC 2008)

2.3.2 WHAT IS A COSMETIC OR FRAGRANCE CHEMICAL

In Australia and Internationally the regulation of chemicals tends to be stratified according to artificial divisions between drugs, food constituents/additives, pesticides and industrial chemicals. These distinctions may, and often do, have validity in terms of exposure and use patterns, and therefore risk profiles, but have no basis in reality in terms of dividing the universe of chemicals into neat regulatory boxes, and have no impact or bearing on the hazard profile of chemicals. Surfactants used in cosmetics or pharmaceuticals are equally likely to be found in drilling muds, fracking fluids, pesticide formulations or a myriad of other industrial and domestic uses. Even a prescription medicine (S4) such as Deanol (also known as 2-dimethylaminoethanol) has local and international uses in cosmetics, paints, laquers and varnishes. Most fragrance chemicals are also found naturally in foods such as herbs and spices, complimentary medicines, and OTC products, often at higher levels than may be used in a fragrance. Geraniol for example occurs in a range of essential oils that have been formally considered for inclusion as an approved ingredient for listed medicines by ACCM or its predecessor CMEC and the Complementary and Over-the-counter Medicines Branch.

There is therefore significant potential for expedient, compartmentalized regulatory action by individual agencies through the scheduling mechanism to result in unintended consequences unless a broad consideration of the use patterns of individual and related classes of substance proposed for scheduling is undertaken.

Equally the toxicology data for an individual substance is likely to be distributed across a range of regulatory agencies with a substantial proportion of that data not visible to any individual agency. Isoeugenol for example was originally proposed for scheduling as a result of an application to the APVMA for use as a farmed fish anaesthetic. Subsequent review by NICNAS resulted in proposed amendments. Isoeugenol is additionally a component of clove oil, used as a food, and is also used medicinally as a local anaesthetic.

In addition to the broad overlap of individual substances across regulatory jurisdictions, individual chemicals do not exist in isolation of the remainder of the universe of chemical substances. Every individual chemical will exist as a member of broad classes or groups with related functions/properties or related structures. Chemical classes might for example include fatty acid esters of glycerol, or polyethoxylated surfactants or quaternary ammonium or phenolic disinfectants for example. Restrictions on one isolated member of a class may simply shift usage to closely related members with closely similar functional properties, or inadvertently and inappropriately capture "derivatives" with less hazardous profiles. Consequently, scheduling decisions not attached to a specific application for approval should not be limited to individual substances, but rather should consider related members of each relevant class. Considerations of cosmetic ingredients within classes may also;

- Facilitate consistency
- Improve the overall quality of data (through read across)

- Reduce regulatory impact

2.3.3 POTENTIAL SOURCES OF DISCORDANCE

Discordance between the risk assessments and risk management measures implemented by different agencies within a Nation and between international jurisdictions can occur for a range of reasons. These differences are not necessarily unintended or inappropriate as they may represent differences in patterns of use, risk tolerance, or pragmatic recognition of need specific to a location or jurisdiction.

Discordance may however also occur through;

- Frank errors of scientific interpretation
- A disconnect between the GHS hazard-based classification scheme and risk based regulatory schemes
- Too narrow a focus on individual chemical substances rather than classes
- Inadequate consideration of;
    - Use patterns
    - Presentation of products
    - Familiarity of consumers with common hazards
    - The intersection with individual compounds with derivatives/extracts of natural products
    - Intersection of regulatory regimes and cross regulatory impacts
    - Exposure patterns
    - Appropriate dose metrics
    - Dose response curves
    - Consistency across chemical classes
- Lack of appropriate expertise within the agency making a submission to the ACCS
- Organisational culture

The NICNAS regulatory environment was developed to manage the introduction of industrial chemicals into Australia. Under the tiered chemicals regulatory environment in Australia any chemical or pattern of use that is not captured by a chemicals regulator at a higher tier is captured by the NICNAS legislation. Thus, if a chemical or its use pattern is not a drug (Therapeutic Goods Act), food additive or food ingredient (Food Standards Australia New Zealand Act), Agricultural or Veterinary Chemical (Agricultural and Veterinary Chemicals Act), then the chemical comes under the NICNAS scheme. Cosmetics and fragrances come under the responsibilities of NICNAS through this interaction of the various chemicals regulations and not through an active or considered decision that cosmetics and fragrances are most appropriately managed under an industrial chemicals paradigm. Indeed the pattern of use and nature of the ingredients is more closely aligned with OTC and Complimentary medicines than with Industrial Chemicals.

The NICNAS processes and approach to chemical regulation closely, and intentionally, aligned with the Globally Harmonised System of Classification and Labelling of Chemicals (GHS). The GHS was developed primarily to ensure that chemicals in the workplace are clearly labelled to identify potential workplace hazards. Industrial chemicals and industrial chemical products in the workplace may be used in a multitude of processes, each with their unique potential risks of exposure, and therefore risks of harm. Risk therefore cannot be pre-assessed out of context of the environment of use. The GHS consequently is not a risk-based scheme and the labelling and classification is dominantly hazard based. Equally, industrial users of chemicals are required to consider potential occupational risks to their employees within the context of their facilities and processes and implement appropriate engineering or Personal Protection Equipment (PPE) procedures to minimize exposure and therefore risk.

The NICNAS approach to toxicology is largely procedural and is designed to align GHS categories and hazard Statements with toxicological endpoints. The assessments therefore lack nuance and are generally unsophisticated.

The approach to toxicology and risk assessment in the remaining chemicals agencies is interpretive and involves careful consideration of the nature, pattern and significance of findings in toxicology studies to ensure risk is defined.

Isoeugenol for example is non-genotoxic but produces tumors in rats and mice at high life time doses but without affecting survival of the animals. Although the chemical is correctly ***Hazard*** classified under the GHS as Cat 3 – limited evidence of carcinogenic effect, ***a risk categorization*** would state that the chemical is unlikely to present a carcinogenic risk to humans at the concentrations used, and the resultant exposures, in food and consumer products.

Risk communication is a critical aspect of consumer advice. Over stating risk through hazard-based categorization creates the risk of warning fatigue, where consumers cease to take warnings and health advice seriously due to the frequency with which otherwise innocuous products carry excessive hazard statements.

2.3.4 BASIC PRINCIPLES OF RISK ASSESSMENT

Human Health Risk Assessment (HHRA) although founded in the scientific interpretation of toxicology and exposure data, involves elements of organizational culture, accepted paradigm and process, and both legislated and organizational policy. Very real differences in risk management can arise from these inherent differences in approach even where there is full concordance in the hazard identification for a chemical. These differences may be entirely reasonable and reflect the differences in exposure between a worker handling bulk drums of a pure chemical versus a consumer using a cosmetic containing a few micrograms of the same chemical as a fragrance, or a pharmaceutical preparation used under the supervision and advice of a medical professional. An agency which routinely assesses chemicals used in a given range of use patterns may not have the experience or familiarity necessary to adequately assess the risk management requirements appropriate for a different pattern of use.

Risk is a function of hazard and exposure. Exposure in turn is a function of the type and use pattern of the product containing the substance of interest, including its concentration in the product, how the product is used, how frequently it is used and where it is used. Risk assessment is a multi-step process that includes;

- Hazard identification
    - What toxicological effects can a substance cause in experimental animals and humans across the achievable exposure range
- Hazard characterization
    - What specific toxicological effects are observed at what doses (the dose response curve)
    - What studies and what species are the most relevant for humans
    - Are the studies available likely to over or under-estimate the risk to humans
    - What does previous exposure of humans tell us about the hazard in humans
- Exposure Assessment
    - By what route will people be exposed
        - Oral, dermal, inhalational, parenteral
    - To what type of products will they be exposed
        - Cosmetic, home garden, pharmaceutical
    - In what concentration will the chemical be present
    - How much of the product is used
    - Where and how is it used
    - What other sources of exposure are there for this substance
- Risk Characterisation
    - What are the risks of the chemical when used as intended, at the concentrations in actual use in products as sold to the public.
    - Are there misuse scenarios that need to be considered?

2.3.5 THE NATURE OF POISONS SCHEDULING

The regulation of the control and use of medicines and chemicals in Australia to prevent public injury dates back more than 100 years. Originally each State and Territory created their own legislation. The early poisons legislation was focused on potent toxicants such as strychnine and arsenic or drugs of abuse such as opium or heroin, but as more substances were brought under control the concept of defined schedules was introduced. The development of poisons schedules in every State and Territory was duplicative of effort, and lead to inconsistencies in restrictions and controls. Consequently, a National Drugs and Poisons Scheduling Committee was formed to develop and maintain a uniform scheduling standard that could be adopted directly by the Jurisdictions. More recently this committee has been divided into a Chemicals Scheduling advisory Committee (ACCS) and a medicines Scheduling Advisory Committee (ACMS) both composed of members from each of the Australian Jurisdictions, the Commonwealth Department of Health and scientific experts.

Chemicals Scheduling has from the outset been intended to be a means to prevent or mitigate predictable harm to the public from substances and products that are, or are likely to become, in actual use in the community. There are many thousands of potentially toxic chemicals in use industrially or naturally occurring in ornamental or food plants in Australia. The Poisons Schedules have never been intended, and are not suitable, as a vehicle for cataloguing all

> *Although toxicity is one of the factors considered, and is itself a complex of factors, the decision to include a substance in a particular Schedule also takes into account many other criteria such as the purpose of use, potential for abuse, safety in use and the need for the substance.*

chemical substances with some future potential to be used in domestic products. The SUSMP reflects this philosophy and states in the introduction that:

5.1Legislative Requirements for Scheduling

An understanding of the legislative basis for the Poisons Standards, and in particular the matters that must be considered in determining the need to include a substance in the SUSMP, is essential in order to identify sources of potential discordance with international regulations and to identify any opportunities for improvement in the current process. The legislative basis for poisons scheduling is established in Chapter 6, part 6-3 of the Therapeutic Goods Act. Section 52 E of the Act specifies the matters that the Secretary must have regard to when considering the inclusion of a substance in a schedule of the SUSMP. In addition to AHMAC guidelines and the advice of the ASCC and ACMS these matters consist of (where relevant);

(a) the risks and benefits of the use of a substance;

(b) the purposes for which a substance is to be used and the extent of use of a substance;

(c) the toxicity of a substance;

(d) the dosage, formulation, labelling, packaging and presentation of a substance;

(e) the potential for abuse of a substance;

(f) any other matters that the Secretary considers necessary to protect public health.

The Act directs that the matters to have regard to must be read in conjunction with the AHMAC guidelines. The AHMAC guidelines make clear that "*poisons include medicines for human therapeutic use, veterinary medicines, agricultural, domestic and industrial chemicals where there is a potential* **risk** *to public health and safety*" and that "*Poisons are scheduled according to* **the risk of harm** *and the level of access control required to protect consumers*" [emphasis added].

The guidelines also make clear that scheduling may need to be reconsidered where knowledge ***or practice*** changes. Thus, scheduling is a risk-based process and submissions for scheduling should be required to provide the information necessary to support a risk assessment and consideration by the delegate and the ACCS of the matters the legislation require should be had regard to..

2.4 Presence at low levels

The SUSMP allows impurities of substances included in schedules 1 to 6 at a concentration not exceeding 10 mg per litre or 10 mg per kilogram (0.001%, 10 ppm), unless that substance is also included in Schedule 7 or 8, and any substance present as an impurity in a pesticide, at a concentration at or below the maximum content for that substance, specified for the pesticide in the *Standards for Active Constituents*, as published by the APVMA. No allowance is made for any impurity from schedules 7 to 10 regardless of how low the level. The sophistication of modern analytic instruments and techniques is such that impurities can be detected and identified at levels in the parts per billion (ppb) or trillion (ppt).

The absence of a cut off level for impurities in cosmetic and domestic chemicals to exempt low levels of chemical impurities included in schedules 7 to 10 does not reflect the advances in analytical techniques and creates substantial unintended regulatory compliance burdens for industry. ACCORD give the example of ethylene oxide which is an S7 substance with no cut-off or use exemption. Ethylene oxide is used in the manufacture of poly ethoxylated surfactants and is consequently a low level residue of manufacturing commonly used surfactants e.g. alkylphenol ethoxylates. A strict application of the SUSMP would make products using these surfactants S7 and require the stipulated controls and labelling. This is clearly not the intent of Scheduling process.

Similarly, 1,4-Butanediol in Schedule 10 is used industrially as a solvent and in the manufacture of some types of plastics, elastic fibers and polyurethanes. This compound is in Schedule 10 primarily because it is a drug of abuse. Low levels of the compound however would be expected to remain in materials and products manufactured using it. Under the current no impurity threshold arrangements these products are also technically Schedule 10. Again this is unlikely to be the intent of the scheduling process.

These examples also raise the question as to whether these ethoxylated surfactants and 1,4 butanediol polymers are "derivatives" of ethylene oxide and 1,4 butanediol. Although chemically speaking, these compounds are reagents the vagueness of the definition of derivative creates uncertainty, even though the toxicological profile of the surfactant/polymer is significantly different to scheduled compounds. There's some difficulty interpreting what is intended by "on balance of consideration" in the Poisons Standard, as this has not been clarified by any regulator.

If the definition of "derivative" is not interpretable to the average chemist, then there would at least be some doubt as to the legal enforceability of scheduling of derivatives. Advice should be sought on this matter and the definition of "derivative" reviewed.

2.4.1 APPENDIX G DILUTE PREPARATIONS

2.5 Derivatives

The introduction to the SUSMP indicates that:

> *"a Schedule entry includes preparations containing the poison in any concentration and all salts and derivatives of the poison unless it specifically states otherwise. (See Part 1, Interpretation, subparagraph 1(2)).*
>
> *It is important to note that a substance is not classed as a derivative on the basis of a single, prescriptive set of criteria. Classification of a substance as a derivative of a scheduled poison relies on a balanced consideration of factors to decide if a substance has a similar nature (e.g. structurally, pharmacologically, and toxicologically) to a scheduled poison or is readily converted (either physically or chemically) to a scheduled poison."*

"a Schedule entry includes preparations containing the poison in any concentration and all salts and derivatives of the poison unless it specifically states otherwise. (See Part 1, Interpretation, subparagraph 1(2)).

It is important to note that a substance is not classed as a derivative on the basis of a single, prescriptive set of criteria. Classification of a substance as a derivative of a scheduled poison relies on a balanced consideration of factors to decide if a substance has a similar nature (e.g. structurally, pharmacologically, and toxicologically) to a scheduled poison or is readily converted (either physically or chemically) to a scheduled poison."

To be eligible for use in a listed medicine an ingredient, among other conditions (TGA 2018);

> ingredients must not be subject to a Schedule of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) also known as the Poisons Standard.

All essential oils consist of a mixture of a range of terpenoids and related compounds, Figure 1 & Figure 2 (Chizzola 2013). The vagueness of the definition of derivative potentially means that the scheduling of a small number of terpenoids could result in all essential oils being barred from being included in listed and complementary medicines.

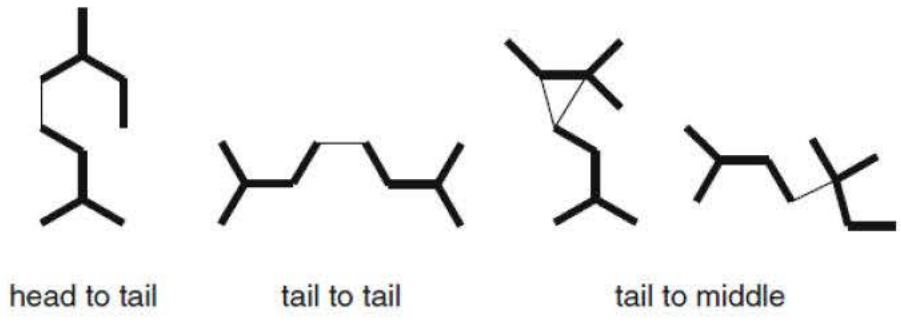

Figure 1. Terpenoids are combinations of isoprene units

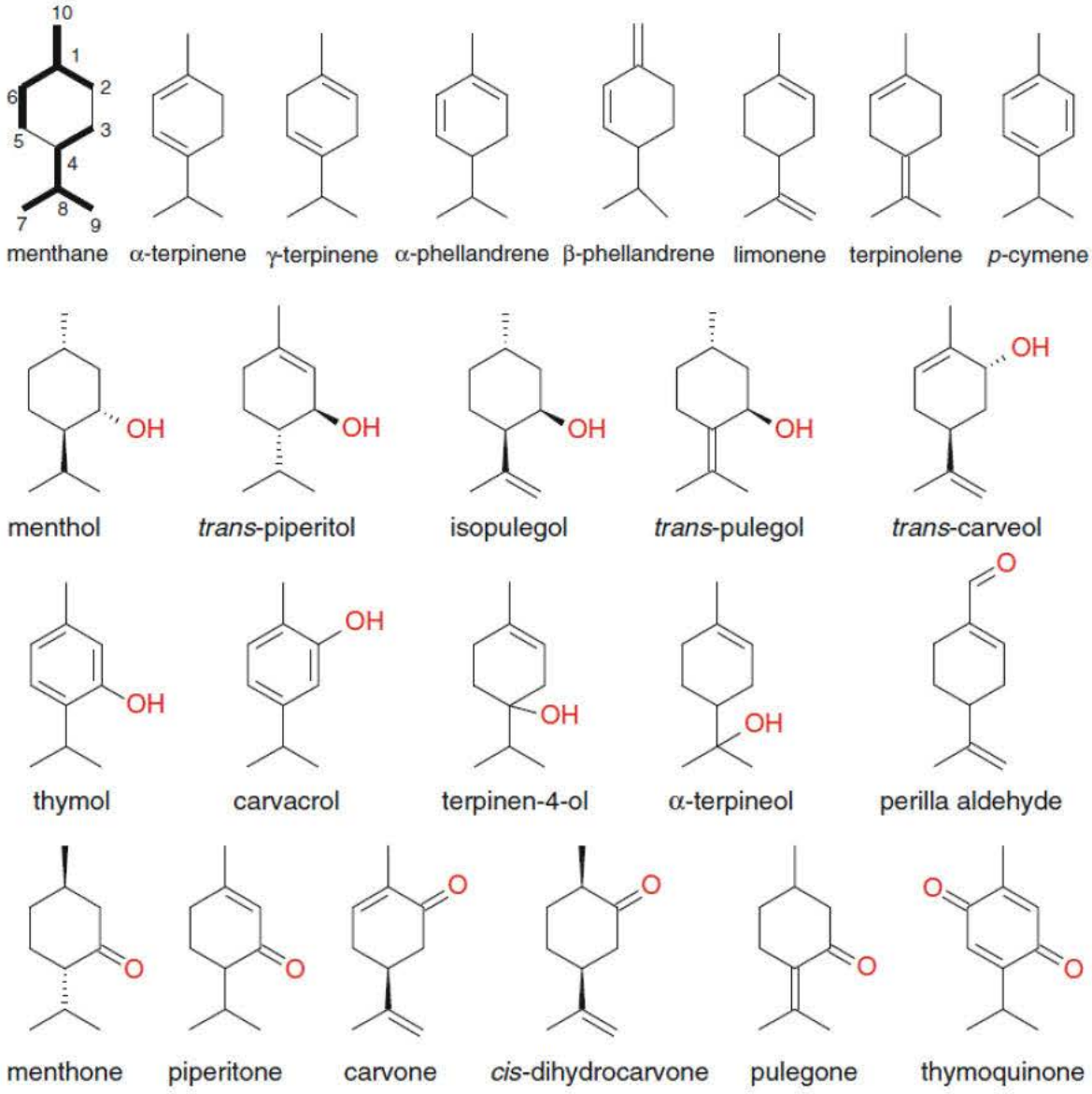

Figure 2. Monoterpenes with a menthane core structure

2.6 Structuring the Review

In order to ensure sufficient opportunity for relevant stakeholders to adequately consider and comment on the outcomes of the review and to ensure final recommendation of options for consideration fully incorporate the views and needs of the relevant stakeholders, the review has been conducted in stages. These stages reflect the discussion above which identified a number of factors that clearly impact the Scheduling decision making process including;

- Is there a discordance in the hazard assessments conducted by NICNAS with those conducted by comparable international agencies?
- Is the analysis being presented to the ACCS sufficient to enable the members to provide adequate advice on all matters that the Delegate to the Secretary is required to have regard to?
- Are the risk management options of the SUSMP suitable for cosmetics and fragrance substance or should some other mechanism be considered?
- Are the analyses supporting the EU cosmetics Directive and the IFRA standards being adequately considered to ensure compatible regulatory outcomes where appropriate?

- Are there administrative, procedural, or organizational policy changes that can be readily implemented that would improve the alignment of Scheduling outcomes with those of major trading partners?
- Are there structural changes that are required to achieve better alignment?
- Could a mechanism for direct adoption or referencing of European standards be practicable?

2.6.1 STAGING

To address the relevant issues this review has been staged into the following components

1. Consideration of the adequacy of the information and analysis of the Scheduling application provided to the ACCS for cosmetic and fragrance materials to support consideration of the relevant matters.
2. A review of the regulatory environment for cosmetics in Australia
3. A review of the regulatory Requirements for Cosmetics in Europe
4. Identification of the nature and sources of practical difficulties arising from current procedures, processes and mechanisms and development of options to mitigate or remove these difficulties.

This preliminary draft touches on many of these issues and seeks to identify those that are likely with further consideration to yield substantial improvements in the efficiency of scheduling considerations of cosmetic ingredients.

2.6.2 RECOGNITION OF INTERNATIONAL STANDARDS – PRECEDENCE

There are precedences for recognizing international regulatory requirements for flavours and fragrances. The Food

Permitted flavouring substances, for the purposes of Standard 1.3.1, are

Flavouring substances which are listed in at least one of the following publications –

- Generally Recognised as Safe (GRAS) lists of flavouring substances published by the Flavour and Extract Manufacturers' Association of the United States from 1960 to 2011 (edition 25); or
- Chemically-defined flavouring substances, Council of Europe, November 2000; or
- 21 CFR § 172.515; or

- Flavouring substances obtained by physical, microbiological, enzymatic, or chemical processes from material of vegetable or animal origin either in its raw state or after processing by traditional preparation process including drying, roasting and fermentation; or
- Flavouring substances obtained by synthetic means which are identical to any of the flavouring substances described in subparagraph (b).

Standards Code of FSANZ for example recognises international approvals or safety assessments of flavouring agents in standard 1.3.1, see break out box above.

For prescription medicines changes to Formulation involving a change relating to colouring agent, flavour or fragrance are Self-Assessable Requests (SARs) - lower risk variations for which the sponsor can provide an assessment of their own data for the TGA to verify (TGA 2017). This provision recognises the low risk associated with flavouring and fragrance materials ***at the levels they are used in such products***. Additionally, the TGA utilises the monographs of recognised Pharmacopoeia's and for colourings:

- the Food and Agriculture Organization (FAO)/World Health Organization (WHO) Combined compendium of food additive specifications
- the European Union regulations - Laying down specifications for food additives No. 231/2012 (pdf,2.95Mb)

Consequently, there are a number of directly analogous precedents that would support recognition of International regulations and non-government standards as a basis for exempting fragrance materials from scheduling.

3 REVIEW OF SCHEDULING APPLICATION ADEQUACY

Neither the Advisory Committees nor the Secretariat have the resources or the depth and breadth of expertise to compensate for incomplete applications.

3.1 Introduction

In order to explore any differences between the outcome of Scheduling decisions and the provisions of the European Cosmetics Directive, a direct comparison of cosmetic ingredients proposed for scheduling has been undertaken focusing initially on perfume ingredients. Comments provided by accord and the secretariat have identified a number of specific substances that have proved problematic and these are examined below.

The ACCS, ACMS and Secretariat rely on the information provided in the scheduling application to provide the basis for balanced, consistent and robust recommendations. Although the Secretariat is able to add further information, particularly in terms of scheduling history and collation of public comments, neither the Secretariat nor the Advisory Committees have the resources or range of expertise to compensate for inadequate or incomplete scheduling applications. The quality of the advice provided by the Advisory committees is therefore dependent on the quality of the Scheduling Request and in particular whether the request adequately addresses each of the matters to which the ACCS and delegate must have regard in formulating their advice and decisions respectively.

In considering the adequacy of the Scheduling requests provided to the ACCS therefore the content of the advice is compared to the matters the legislation requires to be considered ('have regard to').

3.1.1 BASIS FOR SCHEDULING RECOMMENDATIONS

Cosmetic ingredients by intent are generally of low systemic toxicity via the dermal route. Frank Carcinogens or reproductive toxicants for example are unlikely to be knowingly used in cosmetic products. Consequently, acute toxicity end points tend to be the primary drivers of scheduling recommendations.

The primary risk determinants of scheduling recommendations by ACCS for cosmetic ingredients therefore, are the acute oral and dermal toxicity, skin and eye irritation and skin sensitization. Each of these toxicological effects exhibits classical dose response relationships with a threshold for effects occurring at some dose (acute systemic toxicity) or level of dilution (irritation) or dose per unit area (sensitization). Determination of the likely threshold for effect is a critical aspect of scheduling decisions and a key requirement for acceptable scheduling applications. Acute systemic toxicity through oral and dermal exposure is relatively straight forward to extrapolate across dilutions. For a product containing 10 % of a substance with an oral LD50 of 1000 mg/kg bw, the product as a whole will have an LD50 of 10,000 mg/kg bw (10 x 1000 mg/kg) provided other ingredients do not contribute significantly to the toxicity of the product. Arguably however the dose that results in death of 50% of animals (LD_{50}) is not an especially appropriate dose metric for consumer risk assessments. A more appropriate metric might be the highest non-toxic or highest non-lethal dose which give a more usable estimate of risk.

Similarly, for most direct eye and skin irritants, irritation will decline directly with increased dilution, although calculating a specific dilution with low to negligible irritancy generally requires experimental data. Nonetheless low concentrations, below say 0.5 %, are very unlikely to be severe irritants. Chlorocresol for example is a severe eye

irritant at high concentrations (ECHA 2018) but is approved for use as a preservative in eye drops at 0.2 % in the EU (Cosmetic Ingredient Review Panel 1997).

For skin sensitization the situation is somewhat more challenging. Allergic contact dermatitis (ACD) depends primarily on the activation of allergen-specific T cells. A clear distinction needs to be made between elicitation of a skin sensitization reaction in previously sensitized persons, versus induction of sensitization in naive individuals. The EU cosmetic directive is intended to address the former and the IFRA guidance the latter. Thus, the IFRA standard for anisyl alcohol sets limits for 11 product use categories that range from 0.04% for category 1 (lip products) to 2.5% for category 11 (candles). Hand creams, in category 5, have a limit of 0.36% for safe use. The EU Cosmetics Regulation however sets lower limits of 0,001 % in leave-on products and 0,01 % in rinse-off products but requires only that where concentrations greater are than these values the product must be labelled with a statement of the presence of the ingredient. The two standards work in combination to ensure that products compliant with the IFRA standard will not induce sensitization in naïve individuals and that sensitive individuals will have the necessary information to be able to avoid a product that might illicit sensitization. Although these limits are expressed as a percentage of the ingredient in products, those percentages, particularly for the IFRA standard, are based on a consideration of the amount of the various types of product applied and the area of application compared to the Weight of Evidence (WoE) No Expected Sensitization Induction Level (NESIL) expressed as µg/cm^2. This approach reflects the principle dose metric for skin sensitization of dose per unit area of skin. Neither total dose nor concentration in a preparation provide a usable basis for ***risk*** estimation. The entire process of the induction phase requires ca. 10 days to several weeks, whereas an elicitation phase reaction develops within 1–2 days.

Thus, the purpose of labelling is to alert a sensitive person to the presence of the ingredient and to enable anyone having a reaction to identify the ingredient(s) that might be responsible. The purpose of the IFRA standard conversely is to ensure products do not contain sufficient of an ingredient to induce sensitization in a naïve individual.

The dose per unit area, generally µg/cm^2, is a function of;

1. concentration of the substance in a product,
2. amount of product applied,
3. area of skin product is applied to.

Various reliable sources of information are available to estimate these parameters. Skin sensitization is a threshold effect. Sufficient of a substance must be applied per cm^2 of skin to initiate an effective immune response to lead to induction of sensitisation. A key concept that does not appear to have been addressed in any of the NICNAS scheduling submissions to ACCS is that of the Dermal Sensitisation Threshold (DST). The DST has been derived utilising an analogous approach to that used for the derivation of threshold of toxicological concern – widely used internationally and within the TGA and APVMA for consideration of the toxicological significance of impurities in pharmaceuticals and pesticides.

In order to understand the basis for the threshold approach and understanding of the underlying mechanism of dermal sensitisation is required.

> Most contact allergens are small, chemically reactive compounds. As these compounds are too small to be directly immunogenic, they act as haptens; i.e. they react with higher molecular weight epidermal and/or dermal biomolecules to form immunogenic adducts. It is usually considered that the biomolecules involved are free or membrane bound proteins, which react via nucleophilic thiol, amino, and hydroxyl groups. Dendritic cells (DCs) and the local tissue microenvironment are crucial factors in the development of ACD. Langerhans cells (LCs), as epidermal DCs, and dermal DCs are pivotal for the sensitisation and the elicitation phases of ACD. During sensitisation, DCs react with the immunogenic complexes by interaction with neighbouring keratinocytes, migration to the local draining lymph nodes and the priming of naïve T-cells. These reactions are mediated by inflammatory cytokines, chemokines and adhesion molecules. Antigen

specific effector T-cells are then recruited into the skin upon contact with the same hapten (elicitation). Following their recruitment these T-cells are activated by antigen-presenting skin cells, including LCs, dermal DCs and keratinocytes, and macrophages. Although most allergens can form hapten–carrier complexes directly, some need activation, e.g. by enzyme-induced metabolic conversion or abiotic oxidation. Such compounds are termed prohaptens and prehaptens, respectively. Well known examples of prehaptens and prohaptens are limonene and eugenol. Reduced enzyme activity in certain individuals, related to genetic enzyme polymorphisms, may give an increased or reduced risk of sensitisation to prohaptens (that need enzymatic activation) in certain individuals or populations.

Table 1. EU Cosmetics Regulation ((EC) No 1223/) Annex III Entries for fragrance Materials Considered in this Review

Reference No	Chemical Name	Common Name	CAS No	EC No	Product type, body part	Maximum concentration in ready for use preparation	Other	Wording of conditions of use and warnings
80	4-Methoxybenzyl alcohol	Anise Alcohol	105-13-5	203-273-6	-	-	The presence of the substance must be indicated in the list of ingredients referred to in Article 19(1)(g) when its concentration exceeds: 0,001 % in leave-on products — 0,01 % in rinse-off products	[none]*
75	Benzyl Salicylate	Benzyl Salicylate	115-58-1	204-261-9			The presence of the substance must be indicated in the list of ingredients referred to in Article 19(1)(g) when its concentration exceeds: 0,001 % in leave-on products — 0,01 % in rinse-off products	[none]
73	Phenol, 2-methoxy-4-(1-propenyl)-	Isoeugenol	97-54-1	202-590-7			The presence of the substance must be indicated in the list of ingredients referred to in Article 19(1)(g) when its concentration exceeds: 0,001 % in leave-on products — 0,01 % in rinse-off products	[none]
78	2,6-Octadien-1-ol, 3,7-dimethyl-, (2E)-	Geraniol	106-24-1	203-377-1			The presence of the substance must be indicated in the list of ingredients referred to in Article 19(1)(g) when its concentration exceeds: 0,001 % in leave-on products — 0,01 % in rinse-off products	[none]
87	2-Benzylideneoctanal	Hexyl Cinnamal [alpha hexyl cinnamaldehyde]	101-86-0	202-983-3			The presence of the substance must be indicated in the list of ingredients referred to in Article 19(1)(g) when its concentration exceeds: 0,001 % in leave-on products —	[none]

Reference No	Chemical Name	Common Name	CAS No	EC No	Product type, body part	Maximum concentration in ready for use preparation	Other	Wording of conditions of use and warnings
							0,01 % in rinse-off products	
76	2-Propenal, 3-phenyl-	Cinnamal [Cinnamaldehyde]	104-55-2	203-213-9			The presence of the substance must be indicated in the list of ingredients referred to in Article 19(1)(g) when its concentration exceeds: 0,001 % in leave-on products — 0,01 % in rinse-off products	[none]
67	2-Benzylideneheptanal	Amyl Cinnamal [alpha Amyl Cinnamaldehyde]	122-40-7	204-541-5			The presence of the substance must be indicated in the list of ingredients referred to in Article 19(1)(g) when its concentration exceeds: 0,001 % in leave-on products — 0,01 % in rinse-off products	[none]

* entries in square brackets [] in the table do not appear in the EC Annex III and have been added for clarity

Table 2. Assessment of the Adequacy of Scheduling Submission to Enable Consideration of Matters that should be had Regard to.

Relevant Matter	Cinnamaldehyde	Iso-eugenol	Anise Alcohol	Geraniol	Benzyl Salicylate	Comments
Chemical Characterisation Substance Identification	√	√	√	√	√	Generally adequate
Isomer and analogue consideration	χ	χ	χ	√	χ	Not or partially addressed – unclear if an isomer is a derivative
Definition of relevant derivatives	χ	χ	χ	χ	χ	Not or only partially addressed. Which derivatives are likely to share the toxicity driving the Scheduling outcome
Natural occurrence and related materials	χ	χ	χ	χ	χ	Not addressed. Many fragrance chemicals occur in essential oils also scheduled. These need to be identified and considered in conjunction
Class definition	χ	χ	χ	χ	χ	Not or only partially addressed. Consideration of related molecules likely to share the pivotal toxicological end point
Hazard Identification Acute Oral Toxicity	√	√	√	√	√	Straight forward
Acute Dermal Toxicity	√	√	√	√	√	Straight forward
Acute inhalation toxicity	√	-	√	√	√	Straight forward
Skin irritation	√	√	√	√	√	Straight forward
Eye irritation	√	√	√	√	√	Straight forward
Skin sensitization	√	√	√	√	√	Straight forward
Hazard Characterisation Acute Oral Toxicity	√	√	√	√	√	
Acute dermal toxicity	√	√	√	√	√	Straight forward
Acute inhalation		-				
Skin irritation	√	√	√	√	√	Greater consideration of concentration/effect relationship would improve assessments
Eye irritation	χ	χ	χ	χ	χ	Inadequate attention to dose response
Sensitisation	χ	χ	χ	χ	χ	Incorrect dose metrics used (pivotal dose metric is µg/cm² (not % or quantity applied)
Exposure	χ	χ	χ	χ	χ	Cursory

Concentrations in use						
Amount applied		χ	χ	χ	χ	Cursory
Where and how applied	χ	χ	χ	χ	χ	Cursory
Frequency of application	χ	χ	χ	χ	χ	No discussion
Product presentation	χ	χ	χ	χ	χ	No discussion
	χ	χ	χ	χ	χ	No discussion
Risk Charaterisation	χ	χ	χ	χ	χ	Cursory
Risk / Benefit Considerations	χ	χ	χ	χ	χ	No discussion
Regulatory impact	χ	χ	χ	χ	χ	No discussion
Potential impacts on other regulatory schemes	χ	χ	χ	χ	χ	**No discussion**

√ Assessment adequate for delegate decision making, - No data, χ Assessment inadequate for delegate decision making

General Comments

The NICNAS Scheduling submissions are essentially hazard based classification proposals, reflecting the hazard based regulatory regime for which NICNAS is responsible. The proposals have not adequately explored the other critical aspects that the ACCS would be expected to consider for scheduling recommendations. Specifically NICNAS has not considered likely risks of these substances;

- at the levels used
- in the types of products in the market
- the packaging and presentation of the product
- any existing labelling
- where each type of product is used on the body
    - how much is applied
    - over what surface area
    - how frequently

The NICNAS assessment also does not adequately consider the dose response pattern for the hazards they are seeking to control and have not used appropriate dose metrics for skin sensitization. No consideration of dermal sensitization thresholds has been included in their assessments and the regulatory impact on industry of the collective scheduling proposals for cosmetic chemicals has not been addressed.

3.2 Isoeugenol

The key decision points for scheduling for this compound were eye irritation, severe skin irritation, and skin sensitization (Various 2 % weighted mean from over 40 tests).

ACCS Interim Decision

Schedule 6

ISOEUGENOL except:

when included in Schedule 5; or

in preparations intended for contact with skin containing 0.5 per cent or less of isoeugenol.

Schedule 5

ISOEUGENOL in preparations not intended for skin contact containing 25 per cent or less of isoeugenol except in preparations intended for contact with skin containing 0.5 per cent or less of isoeugenol.

3.3 Anise Alcohol

In contrast to the NICNAS Scheduling proposal the published RIFM risk assessment for Anisyl alcohol (anise alcohol) on which the IFRA Standard is based utilizes an exposure-based quantitative risk assessment. This assessment considers the types of products the substance is used in, the range of concentrations, where and how those products are used, how frequently, how much and over what surface area they are used. From this assessment typical worst case exposures are

identified and form the basis of a model risk assessment. For substances with skin sensitisation potential, acceptable levels of use reflect the best available science if dermal sensitization, utilize DST where appropriate and identify levels which will not result in induction of sensitization in consumers. The IFRA standard provides appropriate product type specific restrictions for anise alcohol:

- acceptable levels of use between 0.04% (lip products) and 5% (rinse-off hair conditioners) depending on the intended use and resulting exposure scenario of the finished product.
- There are no concentration restrictions for use in products with no intended, or only incidental, skin contact as the basic exposure pre-requisites for skin sensitisation is absent for these products.

The EU Cosmetics Regulation established concentration levels for 26 identified fragrance allergens to inform consumers with a known allergy (i.e. those already sensitised) of the presence of these ingredients so they can choose to avoid certain products. They are not reflective of levels that would result in induction. The EU requirements for anise alcohol in cosmetics are:

- products containing greater than or equal to 0.001% anise alcohol in leave-on products, and greater than or equal to 0.01% anise alcohol in rinse-off products must include "anise alcohol" in the ingredient list on the product label.
- There are no restrictions on the concentration of this substance that may be used in products, and no further warnings or label statements are required on finished products.

The delegate's interim decision for anise alcohol appeared to be an attempt to combine the 2 different risk management approaches of addressing sensitisation (elicitation vs induction) despite their very different bases, and to include additional warning statements, even for products where no skin contact was expected (and hence no skin sensitization risk).

The primary determinants of the recommended scheduling were expected eye irritation (based on benzyl alcohol data) and skin sensitization in an LLNA assay (EC3 is 5.9 %, 1475 µg/cm^2).

Taking a hand cream as an example, the typical area of application is 890 cm^2 and that approximately 2.2 g is applied (SCCS 2016). This equates to an exposure of 24.3 µg/cm^2, well below the likely Dermal Sensitisation threshold for reactive chemicals of 64 µg /cm^2 (Safford et al. 2015) and is discordant with the Scheduling recommendations for Anise alcohol. The IFRA standard (IFRA 2015) for anise alcohol sets a concentration limit for anise alcohol in category 5 products (hand creams) of 0.36% reflecting their use of safety factors.

The interim ACCS decision is as follows:

Schedule 6 - New Entry

ANISE ALCOHOL except:

a) in preparations intended for therapeutic use; or

b) in domestic preparations not intended for direct skin contact containing 5 per cent or less of anise alcohol when declared on the label; or

c) in leave-on cosmetic and personal care preparations containing more than 0.001 and up to 2.5 per cent of anise alcohol when declared on the label and labelled with the following statement:

WARNING – This product contains ingredients which may cause skin sensitisation to certain individuals.

written in letters not less than 1.5 mm in height; or

d) in rinse-off cosmetic and personal care preparations containing more than 0.01 and up to 5 per cent or less of anise alcohol when declared on the label and labelled with the following statement:

WARNING – This product contains ingredients which may cause skin sensitisation to certain individuals.

written in letters not less than 1.5 mm in height; or

e) in leave-on cosmetic and personal care preparations containing 0.001 per cent or less of anise alcohol; or

f) in rinse-off cosmetic and personal care preparations containing 0.01 per cent or less of anise alcohol.

Appendix E, Part 2 – New Entry

ANISE ALCOHOL

Standard Statement: A (For advice, contact a Poisons Information Centre (e.g. phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor (at once)).

Appendix F, Part 3 – New Entry

ANISE ALCOHOL

Warning Statement: 28 ((Over) (Repeated) exposure may cause sensitisation).

Safety Direction: 4 (Avoid contact with skin).

3.4 Geraniol

The IFRA Standard for geraniol sets specific cut-offs for a range of different product categories. There are no restrictions for products that are not intended for skin contact (category 11) e.g. air fresheners, candles, machine dishwashers or laundry detergents, and higher than 5% concentration cut-off for some products (categories 4 and 6) including oral care products and body lotions, creams (except baby products), foot care products and body sprays.

The acyclic terpene alcohols geraniol, linalool, and citronellol are the most important terpene alcohols used as fragrance and flavor substances. Geraniol and linalool are, in addition to nerol and lavandulol, primary products in terpene biosynthesis. Geraniol [106-24-1], (2E)-3,7-Dimethyl-2,6-octadien-1-ol Geraniol [106-24-1], (2E)-3,7-Dimethyl-2,6-octadien-1-ol occurs in nearly all terpene-containing essential oils

Palmarosa oil, citronella oil and geranium oil are all included in Appendix B for any use (7.1) for reasons of low toxicity (a). Geraniol (and its isomer nerol), a major ingredient in palmarosa oil (approx. 65%) and citronella oil (10-20%) and rose oil, and a minor ingredient in geranium oil, is included in Schedule 6 if in preparations at greater than 5%. Technically speaking all these essential oils are both not scheduled (Appendix B) and schedule 6 according to the Poisons

Standard. The second major ingredient in palmarosa oil is geranyl acetate (approx. 20%), a condensation product of geraniol and acetic acid and therefore a derivative, and presumably captured by the geraniol schedule entry as it does not exclude derivatives (and it readily converts to geraniol by hydrolysis) i.e. palmarosa oil is approx. 85% geraniol and its derivative.

3.5 Cinnamaldehyde

3.6 Benzyl Salicylate

4 CONCLUSIONS

No obvious need for, or benefit in, de novo assessment of fragrance materials and cosmetic ingredients has been identified except where they are unique to Australia or are produced in Australia.

NICNAS does not have the relevant skills or corporate experience, or has not committed suitable resources, to conduct risk assessments of the standard suitable for scheduling decisions on these types of substances. The assessments are less useful for scheduling than the RIFM and SCCP assessments and these would provide a beter basis for scheduling considerations.

4.1 Options for Consideration

The following options are based on a preliminary assessment of the difficulties arising from the current approach to consideration of scheduling for cosmetic and domestic product ingredients. Most of the options identified require further analysis to determine their viability and suitability. More specifically the complex interaction between the many agencies with responsibility for these substances both in Australia and in major trading partners (EU and North America) is required to validate underlying assumptions and preliminary conclusions.

Alternative Approaches

- consider alternative regulatory arrangements for cosmetic and consumer goods
- Consider alternative mechanisms for regulating fragrance substances and other chemicals present at low levels in cosmetic products
    - Establishment of an Australian standard that references the IFRA and EU standards/requirements
    - Establish an onus on industry to ensure their products are safe and provide appropriate safety advice to consumers
        - Give the EU cosmetic directive requirements and IFRA standards as examples of adequate and sufficient compliance.
    - Adopt by reference the EU Cosmetics directive (as FSANZ have done for flavours)

- Create an Appendix B entry for perfumes and flavours when used and labelled in accordance with EU cosmetics Regulation at levels below the limits proposed by the IFRA Standards
  - Insert an amendment to the interpretation section of the SUSMP to exempt fragrance and flavor materials when in appendix B.
- Consider a review of the European and US regulatory regimes to determine the extent to which the respective regimes can be adopted or leveraged by Australia to reduce resources required to manage the relatively minor risks presented by cosmetic ingredients as used in commercial practice

Identify the most appropriate Regulatory Environment for Cosmetics

- NICNAS is a ***hazard*** assessment agency, but cosmetics scheduling is a ***risk***-based regime
- Review the interaction of the multiple regulatory schemes impacting ingredients of cosmetics, consumer and household goods in Australia
  - TGA all types of therapeutic goods, APVMA all pesticides and veterinary medicines but especially insect repellents, FSANZ, ACCC, NICNAS, others ?

Improved Guidance to Committees and Applicants

- Prepare for the ACCS and ACMS improved, science based, guidance for estimating acute ***risk*** of dilute preparations to provide a sound foundation for consistent decision making
- Improve the scheduling application form to require broader assessment of the impact of scheduling decisions on industry and to ensure that all affected preparations (such as essential oils) are considered

Improved Processes

- Consider implementing a revision of the previous review of the scheduling of essential oils to include their constituents.
- Conduct a regulatory impact assessment on the costs and benefits of utilizing the scheduling mechanism for the regulation of cosmetic ingredients present at low levels in consumer products.
- If cosmetic ingredients are to continue to be routinely considered for scheduling then;
  - Consideration of the resources required to support greater input from the Secretariat may be required, or
  - Better use might be made of existing, and higher quality, risk assessments (RIFM/IFRA, FEMA, SCCP etc)
  - Improved engagement of industry and recognition of the costs of that engagement to industry
  - Better consideration of the impact of regulation across multiple industries that use these types of substances (listed and OTC medicines, AgVet chemicals, food ingredients etc)
  - Grouping of related substances in a class review rather than ad hoc, piecemeal assessments
  - Address the Regulatory impact in scheduling submissions even if a formal RIS is not indicated.

5 GLOSSARY

Acronym	Expansion
ACCORD	The national industry association representing manufacturers and suppliers of hygiene, cosmetic and specialty products, their raw material suppliers and service providers.
ACCC	Australian Competition and Consumer Commission
ACCS	Advisory Committee on Chemical Scheduling
ACD	Allergic Contact Dermatitis
ACCM	Advisory Committee on Complimentary Medicines
ACMS	Advisory Committee on Medicines Scheduling
AICS	Australian Inventory of Chemical Substances
CMEC	Complimentary Medicines Evaluation Committee
CORs	Comparable Overseas Regulators
DST	Dermal Sensitisation Threshold
FSANZ	Food Standards Australia New Zealand
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
IMAP	Inventory Multi-tiered Assessment and Prioritisation process
IFRA	International Fragrance Association
LOAEL	Lowest Observed Adverse Effect Level
NESIL	No Expected Sensitisation Induction Level
NICNAS	National Industrial Chemicals Assessment Scheme
NOAEL	No Observed Adverse Effect Level
OBPR	Office of Best Practice Review
OECD	Organisation for Economic Cooperation and Development
PMC	Department of Prime Minister and Cabinet
PPE	Personal Protective Equipment
RIS	Regulatory Impact Statement
SPF	Scheduling Policy Framework
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TGA	Therapeutic Goods Agency
WoE	Weight of Evidence

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