Public submissions on proposed amendments to the *Poisons Standard*

Subdivision 3D.2 of the *Therapeutic Goods Regulations 1990* (the Regulations) sets out the procedure to be followed where the Secretary receives an application under section 52EAA of the *Therapeutic Goods Act 1989* (the Act) to amend the current *Poisons Standard* and decides to refer the proposed amendment to an expert advisory committee. These include, under regulation 42ZCZK, that the Secretary publish (in a manner the Secretary considers appropriate) the proposed amendment to be referred to an expert advisory committee, the committee to which the proposed amendment will be referred, and the date of the committee meeting. The Secretary must also invite public submissions to be made to the expert advisory committee by a date mentioned in the notice as the closing date, allowing at least 20 business days after publication of the notice. Such a notice relating to the scheduling proposals initially referred to the March 2017 meetings of the Advisory Committee on Medicines Scheduling (ACMS #20), the Advisory Committee on Chemicals Scheduling (ACCS #19), and the Joint Advisory Committee on Medicines and Chemicals Scheduling (ACMS #15), was made available on the TGA website on 22 December 2016 and 3 February 2017, closing on 10 February 2017 and 3 March 2017 respectively. Public submissions received on or before these closing dates will be published on the TGA website in accordance with regulation 42ZCZL.

Under regulation 42ZCZN of the Regulations, the Secretary, after considering the advice or recommendation of the expert advisory committee, must (subject to regulation 42ZCZO) make an interim decision in relation to the proposed amendment. If the interim decision is to amend the current *Poisons Standard*, the Secretary must, in doing so, take into account the matters mentioned in subsection 52E(1) of the Act (including, for example, the risks and benefits of the use of a substance, and the potential for abuse of a substance) and the scheduling guidelines as set out in the *Scheduling Policy Framework for Chemicals and Medicines* (SPF, 2015), available on the TGA website.

Under regulation 42ZCZP of the Regulations, the Secretary must, among other things, publish (in a manner the Secretary considers appropriate) the scheduling interim decision, the reasons for that decision and the proposed date of effect (for decisions to amend the current *Poisons Standard*, this will be the date when it is expected that the current *Poisons Standard* will be amended to give effect to the decision).

Also in accordance with regulation 42ZCZP of the Regulations, the Secretary must also invite the applicants and persons who made a submission in response to the original invitation under paragraph 42ZCZK(1)(d), to make further submissions to the Secretary in relation to the interim decisions by a date mentioned in the notice as the closing date, allowing at least 10 business days after publication of the notice. Such a notice relating to the interim decisions of substances initially referred to the March 2017 meetings of the Advisory Committee on Medicines Scheduling (ACMS #20), the Advisory Committee on Chemicals Scheduling (ACCS #19) and the Joint Advisory Committee on Medicines and Chemicals Scheduling (ACMS #15) was made available on the TGA website on 17 May 2017 and 15 September 2017, closing on 31 May 2017 and 3 October 2017 respectively.

Public submissions received on or before these closing dates (31 May 2017 and 3 October 2017) are published here in accordance with regulation 42ZCZQ of the Regulations. Also in accordance with regulation 42ZCZQ , the Secretary has removed information that the Secretary considers confidential.

Privacy statement

The Therapeutic Goods Administration (TGA) will not publish information it considers confidential, including yours/other individuals' personal information (unless you/they have consented to publication) or commercially sensitive information. Also, the TGA will not publish information that could be considered advertising or marketing (e.g. logos or slogans associated with products), information about any alleged unlawful activity or that may be defamatory or offensive.

For general privacy information, go to https://www.tga.gov.au/privacy. The TGA is part of the Department of Health and the link includes a link to the Department's privacy policy and contact information if you have a query or concerns about a privacy matter.

The TGA may receive submissions from the public on a proposed amendment to the Poisons Standard where there has been an invitation to the public for submissions on the proposal in accordance with the Therapeutic Goods Regulations 1990. These submissions may contain personal information of the individual making the submissions and others.

The TGA collects this information as part of its regulatory functions and may use the information to contact the individual who made the submissions if the TGA has any queries.

As set out above, the TGA is required to publish these submissions unless they contain confidential information.

If you request for your submission to be published in full, including your name and any other information about you, then the TGA will publish your personal information on its website. However, if at any point in time, you change your mind and wish for your personal information to be redacted then please contact the Scheduling Secretariat at medicines.scheduling@health.gov.au so that the pubic submissions can be updated accordingly.

Please note that the TGA cannot guarantee that updating the submissions on the TGA website will result in the removal of your personal information from the internet.

Please note that the TGA will not publish personal information about you/others without your/their consent unless authorised or required by law.

[redacted]

The proposed Appendix F Part 3 entries for resorcinol also seem out of step with other hair dye substances with similar toxicity profiles, for example:
19 – WARNING Skin contact may be dangerous. Take every precaution to avoid contact - wash off after spillage and after use

This statement is currently only applied to the "chlorinating compounds" entry, and these substances are known to be highly corrosive to skin. Resorcinol has been classified by NICNAS as a low level skin irritant, so this statement does not seem appropriate. The Appendix F entry should be in line with other hair dye substances with similar toxicity profiles.

As noted in our pre-meeting submission, we do not believe that therapeutic uses of resorcinol should be captured in any new schedule entry for resorcinol due to the higher level of regulatory control for therapeutic goods regarding their safety (as compared to consumer products), and given the regulatory status of resorcinol overseas for use in OTC products.

We are pleased to see the Committee and Delegate have taken on board our previous comments in relation to implementation timing for decision, in that that an adequate transition period of at least 12 months should be provided to allow for any labelling changes that may be required. While we appreciate the 12 month implementation period included with recent decisions, feedback from our members indicates that this remains a very tight timeframe within which to implement the required changes, which is why it was indicated as a minimum. Where there is no evidence that would suggest immediate action is required for the risk management of a substance, the implementation period should be 12-24 months. To our knowledge, there is no evidence to suggest immediate action is required for the risk management of this substance.

From:	Cristina Arregui
To:	Chemicals Scheduling; Medicines Scheduling
Cc:	Cristina Arregui
Subject:	Notice under subsection 42ZCZN/42ZCZP of the Therapeutic Goods Regulations 1990 (the Regulations) [SEC=No Protective Marking]
Date:	Wednesday, 31 May 2017 2:50:10 AM
Importance:	High

Dear Sirs,

We would like to like to make the following comments related to the interim decisions by ACCS/ACMS concerning the substances: Anise alcohol, Trans-anethole, Cinnamaldehyde and Benzyl salycilate. (https://www.tga.gov.au/scheduling-decision-interim/scheduling-delegates-interim-decisions-and-invitation-further-comment-accsacms-march-2017)

We represent IFRA, the International Fragrance Association (www.ifraorg.org) and one of the major activities of our Association is to maintain and develop the voluntary regulatory system of the fragrance industry (which is binding for our members) that is known as the IFRA Standards. Within this system we prohibit or restrict the use of certain fragrance ingredients based on safety assessment carried out by the Research Institute for Fragrance Materials (RIFM, www.rifm.org) reviewed and adopted by their Panel of Experts.

In March we were informed about consultations going on regarding measures suggested under the Australian Poisons Standard for Geraniol and Isoeugenol, tow important fragrance ingredients. We now became aware of new proposals for Anise alcohol, trans-Anethole, Cinnamic aldehyde and Benzyl salicylate.

According to our understanding the resulting impact of the Poisons Standard consists mainly in labelling requirements for the products in the scope of the regulation. These labelling requirements seem to go beyond the simple indication of presence (which would be more or less in line with other similar regulations, e.g. the Cosmetic regulation in Europe for a number of 26 materials identified potential skin allergens) and sometimes even resemble hazard warning phrases as e.g. required under the GHS system for harmonized classification and labelling. For Anise alcohol for example a warning statement 'This product contains ingredients which may cause skin sensitization to certain individuals is requested if the leave-on cosmetic product contains 2.5% or less, unless the material is present below 0.001%. The latter is the threshold for labeling the 26 allergens (Anise alcohol is one of the 26) under the EU Cosmetic regulation. But this is a threshold not established for induction – it is established to inform those people having an allergy about the presence so they can prevent using the product to avoid elicitation. Safe induction levels are higher, this is what we establish in our Standard.

We have a long history in better understanding and managing fragrance ingredients with potential adverse effects like e.g. skin sensitizing properties. We are currently in the process of adapting our risk assessment and related risk management system for the third time, moving from what we call Quantitative Risk Assessment or QRA1 into a refined and further improved QRA2. The latter one is the outcome of a process called IDEA (**www.ideaproject.info**), which is a multi -stakeholder dialogue under the auspices of DG Sante of the European Commission. It incorporates as one aspect of major improvement the incorporation of considering aggregate exposure.

Scheduling the above mentioned materials as “Poisons” with severe labelling requirement for household but especially cosmetic products does not seems adequate from a risk management perspective and we wonder whether there is information we can provide that would change the position of the ACCS-ACMS recommendation.

We would be more than happy to also share more information with you on the IDEA project and the further improvement of the QRA.

Thanks very much in advance for considering these comments and remain at your disposal.

Kindest regards,
Cristina Arregui

Cristina Arregui
Director Global Regulatory Affairs

IFRA (International Fragrance Association)

[redacted]

[redacted]

Comment on Scheduling Delegates Interim Decision: In Vitro Diagnostic and Analytical Preparations

Contents

1 Summary

Alere supports the proposed amendment of the Appendix A exemption for in vitro diagnostic and analytical preparations to include Schedule 9 substances.

Schedule 9 contains a range of commonly abused drugs. Laboratory testing for these drugs is critical in a range of domains. Medically, testing is used to determine what drug or combination of drugs have been taken so that correct treatment can be provided. Workplace testing is used to identify and deter drug induced impairment to help keep work sites safe.

Although drugs of abuse diagnostic tests themselves do not typically contain any Schedule 9 substances, laboratory tests require control and calibrator solutions to ensure their analytical performance. In some cases these solutions must contain trace amounts of the Schedule 9 drug that is being tested for.

These control and calibrator solutions are a low risk for diversion. By their nature they are used exclusively in the controlled environment of laboratories. These solutions are also provided at drug concentrations that are relevant to the physiological drug concentration in the specimen (blood, urine, etc.) being tested i.e. the concentration of the drug in the specimen that is being tested.

As an example, the highest concentration calibrator for a phencyclidine (PCP) urine test contains 100 ng/mL of PCP[1]. 20 Litres, or 800 x 25 mL bottles, of the control solution would need to be consumed in order to achieve a relevant dose of 2 mg[2].

Another example of a more potent drug is lysergic acid diethylamide (LSD). For LSD the highest concentration control solution is provided at a concentration of 1.0 ng/mL[3]. 7.5 Litres of this control solution would need to be consumed in order to achieve a relevant dose of 75 μg of LSD[4].

In light of the low-risk posed by IVD solutions, the requirement to obtain and maintain S9 permits as well as comply with permit conditions is a significant impost on both suppliers and laboratories. For IVD suppliers the Schedule 9 classification is significant disincentive to import such tests leading to fewer test brands being available and at higher cost to the laboratories that use them.

[redacted]

2 About Alere

Alere is a global organisation delivering reliable and actionable health information through rapid diagnostics, resulting in better clinical and economic healthcare outcomes. Our high-performance infectious disease, cardiometabolic and toxicology products are designed to meet the growing global demand for accurate and cost-effective tests.

Globally Alere is the largest provider of rapid, point of care tests and a world leader in toxicology testing and specialty toxicology laboratories.

Since 1978, Alere Toxicology has provided substance abuse testing solutions, providing timely and accurate services that deter and detect drug and alcohol abuse.

Alere Toxicology is committed to providing innovative solutions and exceptional support to organisations seeking to detect and deter the abuse of drugs and alcohol in a wide variety of industries, including employers, government agencies, occupational health clinics, pain management practitioners, physician offices, rehabilitation centres, and resellers.

For more information on Alere, please visit www.alere.com.au.

[redacted]

3 Drugs of Abuse Testing in Australia

Drugs of abuse testing or toxicology testing is used in a wide range of contexts.

Medically it is used to identify or exclude drug abuse during an emergency in order to improve treatment. In the workplace it is used to identify and deter impairment stemming from drug abuse, improving site safety. In law enforcement its uses include identifying drivers who may be under the influence of drugs.

When performed in a laboratory, this testing relies on dilute solutions of the target drug (or metabolite) to act as controls or calibrators for the test.

For most commonly tested drugs, such as cocaine or many opiates, the target drugs are in Schedule 8 or lower. As such, the control and calibrator solutions are generally covered by the current Appendix A general exemption for:

IN VITRO DIAGNOSTIC AND ANALYTICAL PREPARATIONS containing 0.001 per cent or less of a poison included in Schedules 1 to 8.

However, Schedule 9 also contains a range of drugs that are abused in Australia. There is still a definite need to test for Schedule 9 drugs, albeit at a lower frequency than Schedule 1 - 8 drugs.

[redacted]

4 In Vitro Diagnostic (IVD) Control and Calibrator Solutions

IVD control and calibrator solutions for drugs of abuse tests are typically solutions containing a low concentration of the target drug or metabolite. They are used to confirm the performance and calibration of a laboratory test such as an ELISA or other assay.

By their nature, laboratories performing the drugs of abuse testing are controlled environments. Laboratories must be secure and have controlled access to ensure the validity of test results. It is considered that the risk of diversion from such environments is relatively low.

Calibrators and controls are provided in concentrations that mirror the diagnostic cut-off or physiological concentration of the drug being tested. The concentration of a control for a very potent drug would be relatively low because the drug would be found at relatively low concentrations in the blood, urine or saliva that is tested. Conversely, the concentration of an analytical control for a less potent drug would be relatively high to reflect the relevant specimen concentrations.

As an example, the analytical cut-off for a PCP urine test is 25 ng/mL[1]. The highest concentration calibrator for this test is provided at a concentration of 100 ng/mL, which is above the cut-off concentration and serves as the high point for a calibration curve. 2 mg is the lower end of a dose of PCP with clinical effects[2]. 20 Litres of the 100 ng/mL calibrator solution would need to be consumed in order to achieve a relevant dose of 2 mg. Controls are typically supplied in individual bottles of 10 - 50 mL. This particular calibrator solution is supplied in 25 mL bottles so the 20 litres corresponds to 800 individual bottles of calibrator solution.

Another example of a more potent drug is lysergic acid diethylamide (LSD). For LSD, the highest concentration control solution is provided at a concentration of 1.0 ng/mL[3]. 7.5 Litres of the control solution would need to be consumed in order to achieve a relevant dose of 75 µg of LSD[4]. The high potency of the drug means that the concentration of the drug found in assay specimens is typically low. As such, the concentration of controls and calibrators associated with the assay is also low.

The combination of the controlled laboratory environment in which they are used and the concentrations/volumes at which they are provided means that there is extremely low potential for diversion for IVD control and calibrator solutions.

5 Need for Change to the Schedule

Alere supports the proposed amendment of the Appendix A exemption for in vitro diagnostic and analytical preparations to include Schedule 9 substances.

It is not viable for many commercial suppliers to import and supply IVD controls and calibrators for Schedule 9 substances under current arrangements. This leads to fewer test brands being available and at higher cost to the laboratories that use them.

In the worst case this may lead to a diagnostic test for particular Schedule 9 substances not being available at all. This is a particular risk for synthetic cannabinomimetics where there may only be a transient demand for testing for a particular compound.

To address some of the specific advice raised by the ACCS-ACMS which the delegate acknowledged in reaching their interim decision:

- *Consideration of Schedule 9 substances on a case by case basis.*
  Proposals for individual Schedule 9 substances are always possible but the resources required to prepare an effective submission and the relatively low commercial returns from an individual assay means that this will generally not be a practical pathway.
- *Potency and risk of diversion.*
  It is acknowledged that some Schedule 9 poisons are extremely potent and must be handled appropriately. However, the combination of use in the laboratory and the fact IVD solutions are supplied in very low concentrations and volumes relative to the potency of the product mean that the risk of diversion is low.
- *An exemption may not automatically apply in all jurisdictions*
  This point is acknowledged but in of itself it should not be a reason for rejecting the amendment.

It is acknowledged that analytical solutions that are not IVDs regulated by the TGA may pose a greater risk due to being supplied in greater volumes or at higher relative concentrations e.g. analytical standards for the forensic chemical analysis of substances as compared to diagnostic specimens (blood, urine, etc.). To mitigate against this risk an alternative exemption could be envisaged such as:

Medical Devices classified as In Vitro Diagnostic Medical Devices (IVDs) as defined in the Therapeutic Goods (Medical Devices) Regulations 2002.

Alere would be pleased to provide additional information regarding these comments, including the use of drugs of abuse in vitro diagnostic and analytical preparations in Australia.

6 References

1. Immunalysis Product Catalogue, https://immunalysis.com/products/, accessed 29/5/2017
2. Bey T, Patel A. Phencyclidine intoxication and adverse effects: a clinical and pharmacological review of an illicit drug. *Cal J Emerg Med.* 2007 Feb;8(1):9-14.
3. Lysergic Acid Diethylamide (LSD) assay information, https://usdiagnostics.roche.com/products/20763284122/PARAM439/overlay.html, accessed 29/5/17.
4. Passie T, Halpern JH, Stichtenoth DO, Emrich HM, Hintzen A. The pharmacology of lysergic acid diethylamide: a review. CNS Neurosci Ther. 2008 Winter;14(4):295-314

[redacted]

The Secretary
Medicines and Poisons Scheduling
Office of Chemical Safety (MDP 88)
GPO Box 9848
CANBERRA ACT
2601

31/05/2017

Dear Sir/Madam,

RE: Comments on Proposed amendments referred by the Delegates to the joint advisory committees on Chemicals Scheduling (ACCS) and the Advisory Committee on Medicines Scheduling (ACMS)

We refer to the notice inviting further comment under subsection 42ZCZP of the Therapeutic Goods Regulations 1990 and would like to provide comment on the Delegate's Interim Decisions arising from the March 2017 meeting of the ACCS/ACMS. The comments submitted below address matters raised in s.52E of the *Therapeutic Goods Act 1989.*

Anise alcohol, benzyl salicylate, cinnamaldehyde

Johnson & Johnson notes the Delegate's interim decision to defer the interim decision for Anise alcohol, benzyl salicylate, cinnamaldehyde.
Johnson and Johnson also notes the committees have recommended that therapeutic goods be excluded from scheduling, and recommended very low cut-offs for cosmetic/personal care products (unless a warning statement is included).
Johnson & Johnson believes that the same scheduling decisions should be applied to both topical therapeutic products and cosmetics due to the same skin contact administration and fragrance ingredients involved.

Johnson & Johnson has the following comments:

1. We note the widespread use of these ingredients in fragrances commonly used in cosmetic and therapeutic goods.
   It is difficult for sponsors to obtain detailed information on the presence of ingredients found within fragrances; often the ingredient is present within a range and the manufacturers will not provide quantitative ingredient information to sponsors of a cosmetic good. As such it will be difficult to ascertain if the label will need to include the warning statements if the cut-off level is exceeded.

2. Johnson & Johnson requests that the TGA engages in transparent consultation with industry regarding fragrances and proprietary ingredients, noting that there are significant commercial implications and long lead times needed if re-formulation is required.

[redacted]

3. Realistic implementation dates (18-24 months) should be proposed, providing industry with adequate lead times to implement changes to labelling or formulations. Changes to formulation require long lead times for product development and stability testing.

4. IFRA standards already exist for these ingredients and therefore scheduling is not required. An Appendix B listing should be considered for these ingredients. If scheduling is to proceed, any scheduling decisions should align with IFRA standards

Yours faithfully,

[redacted]

[redacted]