9,10-Anthracenedione: Human health tier II assessment

24 April 2015

CAS Number: 84-65-1

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

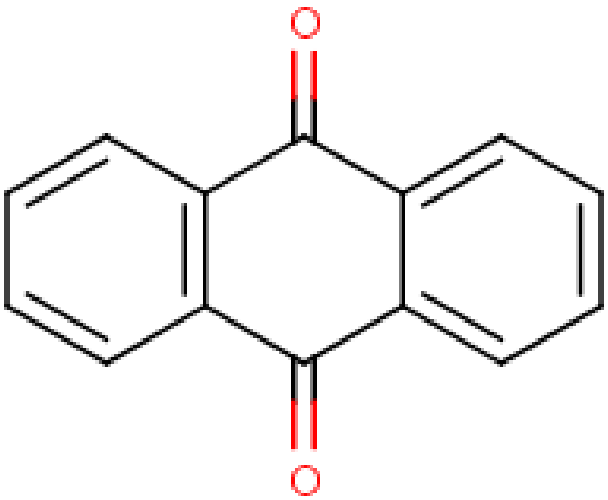
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:www.nicnas.gov.au

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	anthraquinone 9,10-anthraquinone anthracene, 9,10-dihydro-9,10-dioxo- bis-alkylamino anthraquinone 9,10-dioxoanthracene
Structural Formula	
Molecular Formula	C14H8O2
Molecular Weight (g/mol)	208.22
Appearance and Odour (where available)	Light yellow crystals.
SMILES	c12C(=O)c3c(C(=O)c1cccc2)cccc3

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

International

The following international uses have been identified through:

- Galleria Chemica;
- the Substances and Preparations in Nordic countries (SPIN) database;
- United States (US) National Library of Medicine's Hazardous Substances Data Bank (HSDB);
- European Union (EU) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) dossiers; and
- various international assessments (NTP, 2005; IARC, 2012).

The chemical has reported site-limited uses as an:

- intermediate for dyes and pigments in fabrics;
- additive in tyre manufacturing;
- additive and accelerator in chemical alkaline pulp processes in the paper and pulp industry; and
- accelerant in nickel electroplating.

The chemical has reported domestic use as an ingredient in scented candles (HPD). However, based on information on the product manufacturer website (Reckitt Benckiser), the ingredient in the candles is likely to be a dye derived from anthraquinone. In addition, these products have been discontinued.

The chemical is also also used as bird repellent. In 22 August 2008, the EU phased out the use of anthraquinone as a repellent and attractant (IARC, 2012).

The chemical occurs naturally and can be found in certain plants (e.g. aloe latex, senna and rhubarb) fungi, lichens and some insects (HSDB).

Restrictions

Australian

No known restrictions have been identified.

International

The chemical is listed on the following (Galleria Chemica):

- Chile: List of Dangerous Substances;
- Costa Rica: Prohibited and Restricted Pesticides;

- China: Catalogue of Hazardous Chemicals;
- India: Manufacture, Storage and Import of Hazardous Chemical Rules—Schedule: List of hazardous and toxic chemicals;
- Sweden: Restricted Substances; and
- United Arab Emirates: Restricted chemicals.

Food packaging

Previously, Germany's Federal Institute for Risk Assessment (BfR) has listed the chemical in the BfR Recommendations XXXVI and XXXVI/2 for use in paper, cardboard, and paperboard intended for food-contact and for baking purposes. 'The substance may be used at a maximum quantity of 0.15 % of the finished paper. Dry paper must not contain more than 30 mg of anthraquinone per kilogramme' (BfR, 2013). However, it has recently removed the chemical from this list due to its reported carcinogenic potential shown in animal studies and following the European Food Safety Authority's (EFSA) review on the maximum residue level for anthraquinone (EFSA, 2012). In this review, EFSA could not determine whether the maximum residue level of 0.01 mg/kg of the chemical in food is sufficient to protect the consumers. BfR is of the opinion that contamination of the chemical in paper and paperboard products can exceed the permitted level (BfR, 2013). As a result, BfR has recently submitted a proposal for classification and labelling according to the Classification, Labelling and Packaging Regulation (CLP) as a 'Category 1B carcinogen' (ECHA, 2015).

In the US, the chemical (at a purity of >98 %) is permitted 'for use only as a pulping aid in alkaline pulping of lignocellulosic material at levels not to exceed 0.1 percent by weight of the raw lignocellulosic material' (US FDA, 2014).

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Substances Information System (HSIS)(Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica).

An occupational exposure limit of 5 mg/m^3 time weighted average (TWA) in Bulgaria and Latvia.

Health Hazard Information

Toxicokinetics

Anthraquinone (AQ) can enter the body via oral, dermal and inhalation routes. Data from a radiolabelling study in Fischer 344 (F344) rats indicated that the chemical is well-absorbed by the body as demonstrated by the >99 % absorption of the orally-

administered ^{14}C-AQ (doses: 0.35 to 350 mg/kg bw (ECHA, 2015; REACH). It is rapidly and completely absorbed from the gastro-intestinal tract and is distributed throughout the body. High concentrations of AQ were found in the adipose tissue, liver, kidneys and blood (ECHA, 2015; REACH). Bioaccumulation of the chemical in tissues has not been reported. The majority of the chemical (90–97 % of the administered dose) is eliminated in the urine and faeces usually within 24–48 hours from dosing. Biliary excretion has also been reported to be an important pathway leading to faecal excretion of the chemical (ECHA, 2015).

In the liver, the chemical can undergo aromatic ring hydroxylation facilitated by cytochrome P450 enzymes (CYP1A2 and CYP2B1), with subsequent formation of sulfate and glucuronide conjugates (Doi et al., 2005; ECHA, 2015). The results from a National Toxicological Program (NTP) 32-day study suggested that these enzymes could play a role in forming active metabolites (NTP, 2005). In this study, F344 rats showed treatment- and dose-related elevations of CYP1A1 (2 to 3-fold increase above control) and CYP2B1 (80-fold increase above controls in males, 40-fold above control in females) in the liver (NTP, 2005).

Amakura et al. (2014) reported that anthraquinones are aryl hydrocarbon receptor (AhR) agonists.

Metabolically, quinones can also undergo one-electron reduction by oxidoreductases (NADPH-cytochrome P450, NADH dehydrogenase, or xanthine oxidase) to produce a semi-quinone free radical. Upon auto-oxidation, this free radical can produce cytotoxic reactive oxygen species (Doi et al., 2005).

The compounds 1-hydroxyanthraquinone (1-OH-AQ) and 2-hydroxyanthraquinone (2-OH-AQ) have been detected as AQ metabolites in several rats studies, with 2-OH-AQ considered as the major metabolite (NTP, 2005; IARC, 2012; ECHA, 2015). Sulfate and glucuronide conjugates of 2-hydroxyanthraquinone, 9,10-dihydroxyanthracene, and 2,9,10-trihydroxyanthracene were also identified as urinary metabolites in rats (ECHA, 2015).

The chemical is considered to be able to interact directly with DNA via intercalation, because of the size and planarity of the ring system (ECHA, 2015).

The chemical is manufactured using various processes and, as a result, impurities or contaminants might be present. For example, the chemical can be synthesised by anthracene oxidation, which yields isomers of nitroanthracene (e.g. 9-nitroanthracene) as impurities (Butterworth et al., 2001). It is suggest that the impurities can contribute to the toxicity of AQ.

Acute Toxicity

Oral

The chemical has low acute toxicity based on results from animal tests following oral exposure. The reported median lethal dose (LD50) in Wistar and albino rats is >2000 mg/kg bw. No significant pathological changes were reported (REACH).

Dermal

Limited data are available. In a single dermal study in New Zealand White rabbits, the chemical was found to have low acute toxicity. The reported LD50 is >3000 mg/kg bw. No significant pathological changes were reported (REACH).

Inhalation

Limited data are available. In a non-guideline study, rats were exposed to the chemical in dust form for approximately four hours. No mortalities or toxic effects were observed. The median lethal concentration (LC50) was reported as >244 mg/m^3 (REACH). In another study in rats, an LC50 of >1.3 mg/L was reported. No study details were available.

Corrosion / Irritation

Skin Irritation

In a skin irritation study in rabbits which was performed in accordance with the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 404, no signs of irritation were reported (REACH).

Eye Irritation

In an OECD TG 405-compliant eye irritation study, AQ was reported to be a slight eye irritant in New Zealand White rabbits (REACH). The effects observed one hour after AQ exposure included lacrimation (shedding tears) and swelling and red conjunctivae. The effects had resolved 48 hours after exposure and, therefore, were not sufficient to warrant a hazard classification.

Sensitisation

Skin Sensitisation

The chemical is considered to be a skin sensitiser based on the positive result observed in a single mouse local lymph node assay (LLNA). Classification for skin sensitisation is considered warranted (refer to **Recommendation** section).

In a guideline-compliant mouse LLNA study, 25 µL of a solution containing either 0.3 %, 3 % or 30 % AQ suspended in a vehicle composed of dimethylacetamide, acetone and ethanol was applied to the back of the ear of female Balb/c mice once daily for three consecutive days. Dinitrochlorobenzene was used as the positive control (REACH). The effects were evaluated by measuring the stimulation index (SI) (cell proliferation with stimulation divided by without stimulation) and changes in ear weight. The result showed a dose-dependent increase in ear weight and at the 30 % concentration, the chemical elicited a positive sensitisation reaction with a reported SI of 6.53 (REACH).

Repeated Dose Toxicity

Oral

The chronic oral toxicity of the chemical was investigated in F344 rats,Wistar rats and B6C3F1 mice in several subchronic and long-term studies. Whilst effects in the liver and spleen were observed at relatively low doses, the available data are neither sufficient nor adequately comprehensive for classification.

In a guideline-compliant study, male and female Wistar rats were given 135, 275, 555, 1130 or 2350 mg/kg bw/day of AQ for 14 weeks (NTP, 2005; ECHA 2015). The following effects were observed at all doses:

- increased kidney and liver weights;
- minimal to moderate centrolobular liver cell hypertrophy;
- changes in the haematological profile;
- nephropathy (kidney damage) in all male rats; and
- extramedullar haematopoiesis and iron-positive pigmentation in the spleen.

Minimal follicular cell hypertrophy in the thyroid and inflammation and transitional epithelial hyperplasia of the urinary bladder were observed at higher doses. A no observed adverse effect level (NOAEL) could not be established in this study.

In this study, mice also showed treatment-related changes after exposure to the chemical in the diet at doses of 250, 500, 1050, 2150, or 4300 mg/kg for males and 300, 640, 1260, 2600, or 5300 mg/kg for females. Effects included mild to moderate

hypertrophy of centrolobular liver cells, minimal to severe intracellular or cytoplasmic changes in the urinary bladder, and mild to severe haematopoiesis and pigmentation in the spleen (NTP, 2005; ECHA 2015).

Similar pathological changes were observed in a two-year feeding study (see **Carcinogenicity** section) at daily doses of 20–200 mg/kg bw for rats and 80–825 mg/kg bw for mice (NTP, 2005; IARC, 2012).

In non-guideline compliant studies, rats were exposed to 2–250 mg/kg bw/day AQ in the diet for 28 or 90 days. The results indicated that exposure to 10–20 mg/kg bw/day for 28–90 days caused changes in body weight and organ weight, in particular of the liver and spleen (ECHA, 2015; REACH). At this dose, rats also showed liver hypertophy and congestion of the spleen. These changes became prominent in animals exposed to higher doses of the chemical. Although effects were observed at low doses of AQ, these studies lacked important experimental details.

Dermal

No data are available.

Inhalation

Limited data are available on the chronic inhalation toxicity of the chemical. In one reported study, rats (unspecified strain) were exposed to dust (whole body exposure) containing either 5.2 or 12.2 mg/m^3 of the chemical, for five to six hours daily for four months. At a concentration of 12.2 mg/m^3, animals displayed chemically-related changes in body weight, and pathological changes in the blood (slight anaemia) and lungs (emphysema and collapsed lungs) (ECHA, 2015; REACH). However, this study lacked experimental details.

Genotoxicity

Based on the limited data available, it is not possible to draw a definite conclusion regarding the genotoxicity of the chemical. Although available data are neither sufficient nor adequately comprehensive for classification, a genotoxic mode of action cannot be ruled out. Limited in vivo data are available.

A number of in vitro bacterial reverse mutation assays tested the mutagenic potential of the chemical in *Salmonella typhimurium* strains TA98, TA1537, TA100 and TA1535, TA1538 and *Escherichia coli* WP2 uvrA strain. Whilst the majority of these tests gave negative results with or without metabolic activation, some gave positive or weakly positive results (Butterworth et al., 2001; ECHA, 2015). The positive results observed could be due to impurities that are known to be mutagenic (IARC, 2012; ECHA, 2015). The chemical did not show mutagenicity or genotoxicity in an L5178Y mouse lymphoma forward mutation assay, chromosomal aberrations in Chinese hamster ovary cells (CHO) or gene mutation in a test with h1A1v2 cells (Butterworth et al., 2001; ECHA, 2015). A weak, positive effect was observed in a micronucleus assay in Syrian hamster embryo (SHE) cells, although the purity of the test substance was not known (ECHA, 2015).

The chemical showed inconclusive results when tested for in vivo mutagenicity.

In test guideline-compliant bone marrow micronucleus assays in Crl:CD-1 (ICR) and B6C3F1 mice, negative results were obtained.

However, in non-guideline micronucleus assays, increases in the frequency of micronucleated normochromatic erythrocytes in the peripheral blood were observed in a 14-week study in B6C3F1 mice. Strand breaks were also reported in the liver and kidney cells of CD-1 mice treated intraperitoneally with 250 mg/kg bw of AQ (DNA damage assay) (IARC, 2012; ECHA, 2015).

Results from the bacterial gene mutation tests for the metabolite of the chemical, 1-OH-AQ, showed equivocal results, while 2-OH-AQ tested positive with and without metabolic activation (ECHA, 2015). The potential impurity, 9-nitroanthracene, gave weakly positive results in bacterial gene mutation tests and mammalian cell cultures (ECHA, 2015). In a rodent hepatocyte DNA repair assay, 1-OH-AQ gave positive results.

Carcinogenicity

Data from a robust and test guideline-compliant study demonstrated that long-term exposure of rats and mice to AQ induced benign and malignant multi-organ tumours. The available data support the recommendation for classification (see **Recommendation** section).

The carcinogenic potential of AQ has been investigated in F344 rats and B6C3F1 mice in a long-term (105 weeks) feeding study conducted by the NTP. The doses of AQ tested were 0, 469, 938 or 1875 ppm for rats (equivalent to average daily doses of 20, 45, 90 and 180 mg/kg bw/day for males and 25, 50, 100 and 200 mg/kg bw for females). In mice, the doses tested were 0, 833, 2500 or 7500 ppm for mice (equivalent to average daily doses of 90, 265 or 825 mg/kg bw/day for males and 80, 235 or 745 mg/kg bw/day for females).

The results demonstrated clear evidence of carcinogenicity in female rats with the target organs being the kidneys, urinary bladder and liver; and both sexes of mice with the target organs being the liver and the thyroid gland (NTP 2005; IARC, 2012). There was some evidence of carcinogenicity in male rats (kidney and urinary bladder). The following neoplastic effects were observed in rats:

- renal tubule adenoma or carcinoma;
- urinary bladder transitional epithelial papilloma or carcinoma; and
- hepatocellular adenoma or carcinoma (equivocal in males).

The incidences of mononuclear cell leukaemia were significantly reduced in all chemically-exposed rats.

In mice, hepatocellular adenomas and carcinoma were reported in both sexes, while hepatoblastoma was only observed in males. The findings of follicular cell adenoma and carcinoma in the thyroid gland were equivocal.

No specific epidemiological data are available to evaluate the carcinogenity of AQ in humans. However, statistically significant risks for lung and central nervous system cancers were reported in workers in a manufacturing plant that produced AQ and its intermediates, azo dyes and epichlorohydrin. These studies had a number of limitations including the small study size, the lack of exposure measurements and exposure to multiple chemicals. Therefore, no conclusion could be drawn (IARC, 2012).

The International Agency for Research on Cancer (IARC) has classified the chemical as ‘Possibly carcinogenic to humans’ (Group 2B), based on inadequate evidence for carcinogenicity in humans, but sufficient evidence for carcinogenicity in animal testing. Tumours of the kidney and urinary bladder, and hepatoblastomas are rare spontaneous neoplasms in laboratory animals (IARC, 2012).

The mechanism of action for the carcinogenicity of AQ is still not fully understood. Intercalation of DNA or a one electron reduction of AQ to semiquinone radicals causing peroxidative damage have been suggested as potentially contributing to its carcinogenicity (see **Toxicokinetics** section). In addition, the enzyme-mediated formation of active metabolites (see **Toxicokinetics** section) and the impurities produced during AQ synthesis could also play a role in tumour induction in rats and mice (Doi et al., 2005; ECHA, 2015). A genotoxic mode of action cannot be ruled out.

Germany has recently submitted a proposal to label the chemical as carcinogenic (Category 1B carcinogen, H350 (May cause cancer)) (ECHA, 2015).

Reproductive and Developmental Toxicity

Based on the limited data available, the chemical does not show specific reproductive or developmental toxicity. Any reproductive or developmental effects were only observed at high doses and are likely to be secondary to maternal toxicity.

The potential reproductive or developmental toxicity of the chemical was tested in an OECD Test Guideline 421-compliant study in Sprague Dawley (SD) rats. In this study, rats were exposed to the chemical, by oral gavage, at doses of 150, 600, 2400 mg/kg, once daily for eight weeks (REACH).

In the parental animals, decreased body weight and urine discolouration was observed at all doses. Several deaths were reported in females in the 600 and 2400 mg/kg groups during the gestation and lactation periods. In addition to a number of

mortalities, the pathological and histological changes in the stomach and the liver observed in these doses included female rats with a glandular stomach containing black or red foci; females with erosion and oedema of the glandular stomach; erosion or ulcers in the pyloric stomach; and minimal focal necrosis and moderate periportal vacuolation of hepatocytes (REACH).

Mating, fertility, and fecundity indices (male and female) in all treatment groups were comparable with controls. Exposure to the chemical at 600 mg/kg daily caused significant lengthening of the oestrus cycle in females. Pup survival was poor at the highest two doses. Pup viability at 150 mg/kg bw was not affected. Decreases in body weights were noted in the pups at all treatment levels (REACH).

Lengthening of the oestrus cycle was observed in the 14-week repeated dose oral toxicity study (refer **Repeated dose toxicity** section for details of study) but only at the higher doses (1130 or 2350 mg/kg bw/day) (ECHA, 2015).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (carcinogenicity) and local effects (skin sensitisation). Whilst the mechanism of action for the carcinogenicity of AQ is still not fully understood, a genotoxic mode of action cannot be ruled out.

Public Risk Characterisation

Domestic products

Based on the available data (refer to **Import, manufacture and use** section) widespread use of the chemical in domestic chemical products is not expected and hence the risk is not considered to be unreasonable.

Paper products

The chemical is used as a processing aid in paper manufacturing. The chemical has been detected in an unbleached Kraft linerboard sample from a pizza delivery box. Experimentally, the chemical was found to migrate out of the box to the pizza crust at the equivalent of 3.6 % migration (IARC, 2012). Based on the limited information contained in this report, there is potential for exposure due to its use in food packaging and migration into food. The chemical is recommended for Tier III assessment to further characterise the likelihood of exposure via this route. The Tier III report would be provided to Food Standards Australia New Zealand (FSANZ) for consideration as to whether further action is required.

In addition, if the chemical is used in paper products, infants could suck on these, resulting in another potential route of exposure. The risk from this route of exposure is uncertain. Therefore, the Tier III assessment would also include further characterisation of exposure and risks from the chemical being used in paper products. This assessment should be aligned with the recommended Tier III assessment for other carcinogenic chemicals potentially present in paper (NICNASa; NICNASb) and focus on the exposure and the risks from carcinogenic chemicals being used in paper products.

Occupational Risk Characterisation

During product formulation, workers could be exposed to the chemical, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long-term and local health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise exposure are implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

The *Guidance on the interpretation of workplace exposure standards for airborne contaminants* advises that 'exposure to carcinogens should be eliminated or minimised so far as is reasonably practicable' (Safe Work Australia, 2012).

The data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (refer to **Recommendation** section).

NICNAS Recommendation

The data available support an amendment to the hazard classification in the HSIS.

Based on the limited information contained in this report, there is potential for exposure due to its use in food packaging and migration into food. The chemical is recommended for Tier III assessment to further characterise the likelihood of exposure via this route. The Tier III report would be provided to FSANZ for consideration as to whether further action is required.

The Tier III assessment would also include further characterisation of exposure and risks from the chemical being used in paper products. This assessment should be aligned with the recommended Tier III assessment for other carcinogenic chemicals potentially present in paper (NICNASa; NICNASb) and focus on the exposure and the risks from carcinogenic chemicals being used in paper products.

Regulatory Control

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)
Carcinogenicity	Carc. Cat 2 - May cause cancer (T; R45)	May cause cancer - Cat. 1B (H350)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal, ocular and inhalation exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;

- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

References

Amakura Y, Yoshimura M, Takaoka M, Toda H, Tsutsumi T, Matsuda R, Teshima R, Nakamura M, Handa H, Yoshida T 2014. Characterization of natural aryl hydrocarbon receptor agonists from cassia seed and rosemary. Molecules 19(4) pp. 4956-4966.

Bundesinstitut fur Risikobewertung (BfR) (2013). BfR opinion No. 005/2013. Accessed March 2015 at http://www.bfr.bund.de/cm/349/bfr-removes-anthraquinone-from-its-list-of-recommandations-for-food-packaging.pdf

Butterworth BE, Mathre OB, Ballinger K 2001.The preparation of anthraquinone used in the National Toxicology Program cancer bioassay was contaminated with the mutagen 9-nitroanthracene. Mutagenesis 16(2) pp. 169-167.

ChemIDPlus Advanced. Accessed March 2015 at http://chem.sis.nlm.nih.gov/chemidplus/

Doi AM, Irwin RD, Bucher JR 2005. Influence of functional group substitutions on the carcinogenicity of anthraquinone in rats and mice: analysis of long-term bioassays by the National Cancer Institute and the National Toxicology Program. Journal of Environmental Health, Part B Critical Reviews 8 (2) pp. 109-126.

ECHA 2015. CLH Report Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2. Substance name: anthraquinone (CAS No. 84-65-1). Accessed February 2015 at http://www.echa.europa.eu/documents/10162/13626/clh_proposal_anthraquinone_en.pdf

European Food Safety Authority (EFSA) 2012. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for anthraquinone according to Article 12 of Regulation (EC) No 396/2005. Accessed March 2015 at http://www.efsa.europa.eu/en/efsajournal/pub/2761.htm

Galleria Chemica. Accessed March 2015 at http://jr.chemwatch.net/galeria/

Hazardous Substances Data Bank (HSDB). National Library of Medicine. Accessed March 2015 at http://toxnet.nlm.nih.gov.

International Agency for Research on Cancer (IARC) 2012. IARC monographs on the evaluation of carcinogenic risks to humans. Anthraquinone. Volume 101. Some chemicals present in industrial and consumer products, food and drinking-water. Accessed February 2015 at http://monographs.iarc.fr/ENG/Monographs/vol101/mono101-001.pdf

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (NICNASa). Inventory Multi-tiered Assessment and Prioritisation (IMAP) Human Health Tier II Assessment for acetamide, n-[4-[(2-hydroxy-5-methylphenyl)azo]phenyl]- (CAS No 2832-40-8). Available at http://www.nicnas.gov.au

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (NICNASb). Inventory Multi-tiered Assessment and Priorisation (IMAP): Human health Tier II assessment for chrysoidine base and its salts. Accessed March 2015 at http://www.nicnas.gov.au

National Toxicology Program (NTP) 2005. Technical report on the toxicology and carcinogenesis studies of anthraquinone (CAS No. 84-65-1) in F344/N rats and B6C3F1 mice (feed studies). US Department of Human Health Services, Public Health Service, National Institutes of Health. Accessed March 2015 at http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr494.pdf

REACH Dossier (REACH). Anthraquinone (CAS No. 84-65-1). Accessed February 2015 at http://echa.europa.eu/information-on-chemicals

Reckitt Benckiser North American Product Listing. Accessed March 2015 at http://www.rbnainfo.com/productpro/ProductSearch.do?brandId=2&searchType=CAT&template=1

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed March 2015 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance.

The Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP)(2002) Opinion on the Safety Review of the Use of Certain Azo-Dyes in Cosmetics Products. SCCNFP/0495/01, final. Accessed February 2015 at http://ec.europa.eu/health/archive/ph_risk/committees/sccp/documents/out155 _en.pdf

US Department of Health and Human Services, Household Products Database (HPD), health and safety information on household products. Accessed February 2015 at http://householdproducts.nlm.nih.gov/

US Food& Drug Administration (US FDA) Code of Federal Regulations; Title 21, Volume 3; Revised as of April 1, 2014, Accessed Mar 2015 at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=176.170

US National Library of Medicine. Information on Hazardous Chemicals and Occupational Diseases. Haz-Map. Accessed February 2015 at http://hazmap.nlm.nih.gov/index.php

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