# Formamide: Human health tier III assessment

**1 July 2016**

## CAS Number: 75-12-7



## 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 III because the Tier II assessment indicated that it needed further investigation. The report should be read in conjunction with the Tier II assessment.

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

Acronyms & Abbreviations

## Synopsis

The human health Tier II assessment of the chemical under the Inventory Multi-tiered Assessment and Prioritisation (IMAP) Framework determined that further work is required to fully assess the carcinogenicity data for the chemical formamide. Therefore, a human health Tier III assessment was recommended.

In this Tier III assessment, the available data are considered insufficient to demonstrate that a proposed mode of action (MOA) for non-genotoxic haemangiosarcoma formation (consisting of an upstream initiating event such haemolysis or oxidative stress, and ultimately leading to dysregulated erythropoiesis and/or angiogenesis) occurs in female mice, as well as male and female rats. Tumours were only present in male mice; evidence of disrupted erythropoiesis existed in mice and rats of both sexes; however, clear effects on angiogenesis were lacking in female mice, as well as male and female rats. On this basis, the haemangiosarcomas induced by the chemical are not considered relevant to a human health risk assessment. However, the disrupted erythropoiesis with repeated oral exposure to the chemical is relevant to a human health risk assessment and NICNAS has made a recommendation for risk mitigation through hazard classification of the chemical for repeated dose toxicity.

The human health Tier II IMAP report for the chemical is available at: http://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessment-details?assessment_id=3 and contains detailed assessment information that remains valid (NICNAS). New or updated information is included in the Tier III human health report, in the relevant sections. The Tier II and Tier III reports for this chemical should be read together.

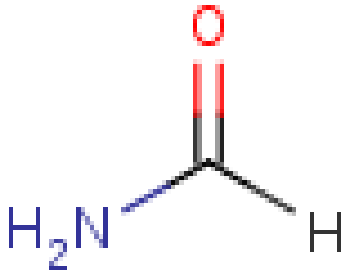
## Rationale for Tier III Assessment

In order to determine if a recommendation for carcinogenicity classification of formamide in the Hazardous Substances Information System (HSIS, Safe Work Australia) is warranted, NICNAS reviewed the current information on formamide exposure and provided an analysis of the adverse effects observed in animal studies.

The three-month and two-year gavage studies in rodents conducted by the United States (US) National Toxicology Program (NTP, 2008) were considered critical for evaluation of carcinogenicity potential of formamide. In the two-year studies, carcinogenicity was unequivocally reported in one sex, in one species of rodent—the male B6C3F1 mouse (NTP, 2008). The primary purpose of this assessment is a more thorough evaluation of all data available from the NTP and other relevant studies, to determine if there is mechanistic evidence supporting potential for carcinogenicity, or other adverse effects, in both sexes of mice and/or multiple species of rodents, of relevance to human health.

## Chemical Identity

| | |
|---|---|
| Synonyms | carbamaldehyde<br>methanamide<br>methanoic acid, amide<br>formic acid, amide<br>formimidic acid |
| Structural Formula | |



| | |
|---|---|
| Molecular Formula | CH3NO |
| Molecular Weight (g/mol) | 45.04 |
| Appearance and Odour (where available) | Slightly viscous, colourless liquid with a faint ammonia odour |
| SMILES | C(N)=O |

## Restrictions

### Australian

The following information is *additional* to that provided in the Tier II report for this chemical.

The chemical is listed in the Code of Practice for Supply Diversion into Illicit Drug Manufacture—Category II: Illicit Drug Precursors/Reagents. An end-user declaration is required when the chemical is sold to non-account customers (Galleria Chemica).

The following state-specific restrictions have been identified (Galleria Chemica):

- Victorian Occupational Health and Safety Regulations—Schedule 9: Materials at Major Hazard Facilities (and their threshold quantity) Table 2. A threshold quantity of 20 tonnes for 'materials that meet the criteria for very toxic in Table 3 except materials that are classified as infectious substances (Class 6.2) or as radioactive (Class 7)' applies;
- Victorian Drugs, Poisons and Controlled Substances (Precursor Chemicals) Regulations 2007—Schedule 1: Precursor Chemicals and Quantities. The chemical is a prescribed precursor chemical and a quantity of 50 mL applies; and
- Queensland *Drugs Misuse Regulation 1987*. The chemical is a controlled substance (Schedule 6) with a permitted gross weight of 0.1 g (Schedule 8A).

### International

The following information is an *update* to that provided in the Tier II report for this chemical.

The chemical is listed on the EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products, which replaced the EU Cosmetic Directive 76/768/EEC Annex II—List of Substances which must not form part of the Composition of Cosmetic Products (Galleria Chemica).

The following information is *additional* to that provided in the Tier II report for this chemical.

The entry for the chemical in Annex II to Directive 2009/48/EC of the European Parliament and of the Council on the safety of toys was amended in Commission Directive (EU) 2015/2115 of 23 November 2015—a specific limit value when used in toys is to be adopted by member states by 24 May 2017 to comply with Appendix C to Annex II of this directive. A limit value of '20 µg/$m^3$ (emission limit) after a maximum of 28 days from commencement of the emission testing of foam toy materials containing more than 200 mg/kg (cut-off limit based on content)' applies.

## Existing Work Health and Safety Controls

### Hazard Classification

Following the human health Tier II IMAP assessment of this chemical, it is listed on the Hazardous Substances Information System (HSIS) with the following risk phrases for human health (Safe Work Australia):

- R61 Repr. Cat. 2 (developmental toxicity); and
- R62 Repr. Cat. 3 (reproductive toxicity).

A skin notation (Sk) applies—'Absorption through the skin may be a significant source of exposure' (Safe Work Australia).

## Health Hazard Information

Carcinogenicity was the key focus for this Tier III assessment. However, when evaluating data from range-finding studies undertaken to inform the carcinogenicity study, it was reported that doses ≥312 mg/kg bw/day were not tolerated by mice or rats, resulting in death as early as day two (NTP, 2008). This conflicts with the extensively documented low acute oral toxicity of the chemical, with reported median lethal dose (LD50) values ranging 3150–7932 mg/kg bw/day in rodents (OECD, 2007; EC-HC, 2009). Therefore, in addition to carcinogenicity, a re-evaluation of acute oral toxicity of the chemical is also considered necessary. Repeated dose oral, dermal and inhalation toxicity studies were re-evaluated to determine if there is supporting evidence for a mechanism and a threshold dose that may cause carcinogenicity, or other adverse health effects.

### Acute Toxicity

Oral

It was previously concluded that the chemical has low acute oral toxicity (NICNAS), based on animal studies conducted in the 1960s, where information on the purity of the chemical was not available (OECD, 2007; EC-HC, 2009). Based on the available data from sub-acute (two or four week) rodent studies conducted similarly to or according to the Organisation of Economic Co-operation and Development (OECD) Test Guideline (TG) 407, and with chemical purity stated as >99.5 %, there is evidence that the chemical may have moderate acute oral toxicity (LD50 <2000 mg/kg bw). However, as information on the actual days of animal death is lacking, confirming the proportion of deaths that occurred following a single oral dose in these short-term studies is not possible; therefore, hazard classification is not recommended.

In dose range-finding studies conducted by the NTP, B6C3F1 mice (n = 5/sex/dose) and Fischer 344 (F344)/N rats (n = 5/sex/dose) were administered the chemical at 0, 160, 312, 625, 1250 or 2500 mg/kg bw/day five days per week for 16 days. Male mice exposed at 2500 mg/kg bw/day and female mice exposed at ≥1250 mg/kg bw/day were euthanised moribund on day two. It is unclear if the deaths occurred after a single dose of the chemical or after two doses. There was also 100 % mortality before the end of the study in male mice exposed at 1250 mg/kg bw/day and all mice exposed at 312 and 625 mg/kg bw/day, but the exact days of death are not available. In rats exposed to the chemical at ≥312 mg/kg bw/day, there was 100 % mortality before the end of the study, but the exact days of death were also not available (NTP, 2008).

The above findings are in line with the previously reported (NICNAS) repeated dose oral gavage study in Sprague Dawley (SD) rats (n = 20/sex/dose). Rats were administered the chemical at 0, 34, 113, 340 or 1130 mg/kg bw/day five days per week for four weeks. There was 100 % mortality in rats exposed at 1130 mg/kg bw/day within the first week of study and 50 % mortality in rats exposed at 340 mg/kg bw/day during the course of the study, but again the exact days of death were not available (OECD, 2007).

### Repeated Dose Toxicity

Oral

Based on the available data, the chemical is considered to cause haematological effects following repeated oral exposure, warranting hazard classification (see **Recommendation** section).

Three-month studies conducted by the NTP using the chemical at 0, 10, 20, 40, 80 or 160 mg/kg bw/day in B6C3F1 mice (n = 10/sex/dose) and F344/N rats (n = 10/sex/dose) included haematology analysis at the end of the study in mice; and on days 4, 23 and at the end of the study in rats. In both three-month studies, mortality rates were similar compared with control animals. Overall, mean body weights were generally reduced in male and female rodents exposed at ≥40 mg/kg bw/day compared with control animals (NTP, 2008).

Dysregulated erythropoiesis was confirmed in the three-month mouse studies with the observation of small but significant reductions in haematocrit values and erythrocyte concentrations in male mice treated at 160 mg/kg bw/day. A similar, but not significant trend, was observed in female mice. The authors of the NTP report stated that 'the minimal nature [of these changes] would suggest that the clinical significance is questionable' (NTP, 2008). However, there was a positive trend for increased segmented neutrophils, a marker of inflammation, in exposed male mice and this was significantly increased at 160 mg/kg bw/day. A similar positive trend in segmented neutrophil counts was observed in all treated female groups (NTP, 2008). Chemical-induced oxidative stress may have contributed to the disrupted erythropoiesis observed in these studies, although more definitive examination of this is lacking.

In the three-month rat studies, dose-dependent changes in haematocrit values, haemoglobin and erythrocyte concentrations were observed from as low as 10 mg/kg bw/day and these were significantly increased compared with controls at doses ≥40 mg/kg bw/day at the end of the study. Segmented neutrophils were also increased at the end of the study in all male groups exposed at ≥80 mg/kg bw/day and in female rats at 160 mg/kg bw/day (NTP, 2008).

In two repeated dose gavage studies, it was reported that SD rats exposed to the chemical at ≥113 mg/kg bw/day for four weeks and rabbits exposed at 227 mg/kg bw/day for five weeks had increased red blood cell count, increased haemoglobin or increased haematocrit. Deaths occurred in both studies at higher doses, at 340 and 1130 mg/kg bw/day in rats (50 and 100 % mortality, respectively) and 567 mg/kg bw/day (100 % mortality) in rabbits. The haematological effects following four weeks' exposure were reversible in SD rats after a two-week recovery period—they were 'less frequent and almost completely absent' at the 340 and 113 mg/kg bw/day doses, respectively (OECD, 2007; EC-HC, 2009).

### Dermal

Based on the available data, the chemical is considered to cause haematological effects following repeated dermal exposure at high doses.

In two repeated dose dermal studies in Wistar rats exposed to the chemical at up to 3000 mg/kg bw/day for 90 days (the second being a follow-up study using lower doses), exposure at ≥300 mg/kg bw/day was associated with increased red blood cell count, increased haemoglobin and increased haematocrit in males only; females were similarly affected at 3000 mg/kg bw/day (OECD, 2007; EC-HC, 2009).

### Inhalation

Based on the available data, the chemical is considered to cause haematological effects following repeated inhalation exposure at high doses.

Observations in a two-week repeated dose inhalation toxicity study in male Crl:CD BR rats exposed (nose-only) to the chemical at up to 1500 ppm (2.8 mg/L) included mild thrombocytopaenia (reduced platelets) and statistically significant lymphopaenia (reduced lymphocytes or white blood cells) that persisted even after a two-week recovery period (OECD, 2007; EC-HC, 2009).

## Carcinogenicity

Based on the available animal data, there is insufficient evidence to make a conclusion on the carcinogenic potential of the chemical. Liver haemangiosarcomas observed in male mice at doses ≥40 mg/kg bw/day were the only overt indications of carcinogenicity. However, female mice and all rats in the carcinogenicity study, and both rats and mice in the three-month studies have shown effects due to dysregulated erythropoiesis (red blood cell production) at doses ≥40 mg/kg bw/day. Dysregulated erythropoiesis is one factor which can lead to uncontrolled endothelial cell proliferation and stimulate the development of haemangiosarcomas (Cohen et al., 2009). Liver Kupffer cell pigmentation—a marker of hepatic haemosiderosis (iron overload) resulting from haemolysis (red blood cell rupture), that is highly correlated with haemangiosarcoma formation (Nyska et al., 2004)—was not identified in the carcinogenicity studies for the chemical. Therefore, the presence of isolated mechanistic-related events was not considered adequate to indicate a carcinogenicity risk from long-term exposure to the chemical.

### *Carcinogenicity studies*

The NTP conducted carcinogenicity studies (OECD TG 451) in B6C3F1 mice (n = 50/sex/dose) and F344/N rats (n = 50/sex/dose), by administering the chemical in deionised water via gavage at doses of 0, 20, 40 or 80 mg/kg bw/day for 104–105 weeks. It was concluded that there was '*clear evidence of carcinogenic activity* of formamide in male B6C3F1 mice based on increased incidences of hemangiosarcoma of the liver'; '*equivocal evidence of carcinogenic activity* of formamide in female B6C3F1 mice based on increased incidences of hepatocellular adenoma or carcinoma (combined)'; and '*no evidence of carcinogenic activity* of formamide in male or female F344/N rats' (NTP, 2008).

The incidences of liver haemangiosarcoma observed in male mice increased in a dose-dependent manner, with the increases being statistically significant at 40 and 80 mg/kg bw/day, suggesting that this effect may be treatment-related. Spleen haemangiosarcomas were also observed in all male mouse groups, but incidences were not different between control and treated animals, suggesting that this effect was spontaneous. In mice that received the highest dose, splenic haematopoiesis was altered—cell proliferation was significantly increased in male mice, but significantly decreased in female mice. The increased incidence of splenic haematopoietic cell proliferation in male mice was attributed to physical damage of the red blood

cells passing through the liver haemangiosarcomas (NTP, 2008). Haematological analysis was not undertaken for the 2-year carcinogenicity studies in mice.

In female mice, the incidence of combined hepatocellular adenoma or carcinoma was increased in all exposed groups compared with controls, with the increase being statistically significant at the highest dose only. However, this increase was within the historical control ranges (NTP, 2008).

The only treatment-related effect in the 104–105 week carcinogenicity study in rats was significantly increased incidence of bone marrow hyperplasia in males exposed at 80 mg/kg bw/day. This is a non-neoplastic change and was attributed to 'a response to erythrocyte damage' but the reason for the erythrocyte damage was not available (NTP, 2008). Haematological analysis was not undertaken for the 2-year carcinogenicity studies in rats.

#### *Information related to the potential mechanism of carcinogenicity*

Haemangiosarcomas are malignant tumours of endothelial cells. Since endothelial cells are continuously proliferating (in the process of angiogenesis—blood vessel formation), they are susceptible to neoplastic changes. Spontaneous haemangiosarcomas are rare in humans (<0.001 % incidence), but they can occur in rodents, with a higher incidence in mice (2–5 %) than in rats (0.1–2 %) (Cohen et al., 2009). In mice, the incidence is higher in males than females, with particularly high incidence in the B6C3F1 strain. The relevance of rodent haemangiosarcomas to human carcinogenicity is unclear, particularly in response to non-genotoxic chemicals (like formamide) where there can be a number of initiating factors, such as haemolysis or oxidative stress. However, dysregulated erythropoiesis and/or angiogenesis are common factors which can lead to uncontrolled endothelial cell proliferation and ultimately stimulate the development of haemangiosarcomas (Cohen et al., 2009).

An analysis of 130 carcinogenicity studies conducted by the NTP, identified liver Kupffer cell pigmentation, arising from erythrocyte haemolysis and resultant hepatic haemosiderosis, as highly associated with liver haemangiosarcoma formation in male mice. Proposed mechanisms by which iron overload may contribute to tumour development include oxidative stress and stimulation of cell proliferation (Nyska et al., 2004). These features are overlapping with the features of the MOA described by Cohen et al. (2009) above.

Dysregulated erythropoiesis (reduced haematocrit values and erythrocyte concentrations) and the presence of circulating inflammatory markers (increased segmented neutrophils) was confirmed in the three-month mouse and rat studies conducted by the NTP (see **Repeated dose toxicity: Oral** section for details).

In other repeated dose oral, dermal and inhalation toxicity studies, effects on haematological parameters were also noted (see **Repeated dose toxicity: Oral or Dermal or Inhalation** sections for details). These included increased red blood cell count, increased haemoglobin, increased haematocrit, thrombocytopaenia (reduced platelets) or lymphopaenia (reduced lymphocytes or white blood cells). Some effects were reversible, and some persisted, after a two-week recovery period (OECD, 2007; EC-HC, 2009).

Markers of altered angiogenesis or haemosiderosis were not reported in the above studies.

The authors of the NTP studies reported that 'there was no evidence of ... Kupffer cell pigmentation in the liver consistent with red cell hemolysis' (NTP, 2008). This is in line with the absence of haemangiosarcoma formation in more than one sex and more than one species of rodent in these studies, suggesting that the liver haemangiosarcoma observed in male B6C3F1 mice only may have been spontaneous and not necessarily relevant for human health.

## Risk Characterisation

### Critical Health Effects

The critical health effects for risk characterisation include reproductive toxicity and developmental toxicity, as well as haematological effects following repeated exposure through the oral route (systemic long-term effects).

The chemical may also cause harmful effects following a single exposure through the oral route.

Data are insufficient to derive a conclusion on the carcinogenicity potential of the chemical.

### Public Risk Characterisation

The total volume introduced into Australia reported under previous mandatory and/or voluntary calls for information was low. No specific Australian use information has been identified, except that the chemical may be released from play mats and toys for children. Testing undertaken by the Australian Competition and Consumer Commission (ACCC) has shown that the amount of chemical released by these articles is very small and that there is no evidence that these products present any risk to children. The outcome of the ACCC testing does not change with the addition of a classification for repeated dose oral toxicity due to haematological effects (or the uncertainty of the carcinogenicity potential). The dose at which haematological effects have been shown to occur (40–160 mg/kg bw/day) is similar to the lowest observed adverse effect level (LOAEL) reported for developmental toxicity (79 and 100 mg/kg bw/day in rabbits and rats, respectively) (EC-HC, 2009) which was used by the ACCC in their exposure calculation (ACCC). Any domestic use of the chemical is considered to be limited based on overseas surveys (EC-HC, 2009). Hence, the public risk from this chemical is not considered to be unreasonable.

### Occupational Risk Characterisation

During product formulation, oral, dermal, ocular and inhalation exposure may occur, 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 health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise oral, dermal, ocular and inhalation exposure are implemented. The chemical 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 data available support an amendment to the hazard classification in the HSIS (Safe Work Australia) (see **Recommendation** section).

## NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

### 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 |
|---|---|---|
| Repeat Dose Toxicity | Harmful: danger of serious damage to health by prolonged exposure if swallowed (Xn; R48/22) | May cause damage to organs through prolonged or repeated exposure through the oral route - Cat. 2 (H373) |
| Reproductive and Developmental Toxicity | Repro. Cat 3 - Possible risk of impaired fertility (Xn; R62)* Repro. Cat 2 - May cause harm to the unborn child (T; R61)* | May damage the unborn child. Suspected of damaging fertility - Repr. 1B (H360Df) |

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

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

### Advice for industry

The advice provided in the human health Tier II IMAP report remains unchanged.

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

## References

Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)]. Third edition [NOHSC:1008 (2004)]. Accessed at http://www.safeworkaustralia.gov.au/sites/swa/about/publications/Documents/258/ApprovedCriteria_Classifying_Hazardous_Substances_NOHSC1008-2004_PDF.pdf

Australian Competition and Consumer Commission (ACCC). Alert on 'Testing of foam play mats show no safety risk to children'. Available at http://www.productsafety.gov.au/content/index.phtml/itemId/989496

Cohen SM, Storer RD, Criswell KA, Doerrer NG, Dellarco VL, Pegg DG, Wojcinski ZW, Malarkey DE, Jacobs AC, Klaunig JE, Swenberg JA, Cook JC 2009. Hemangiosarcoma in Rodents: Mode-of-Action Evaluation and Human Relevance. Toxicological Sciences 111(1) pp. 4–18.

Environment Canada-Health Cananda (EC-HC) 2009. Screening Assessment for the Challenge Formamide (CAS No. 75-12-7). Available at http://www.ec.gc.ca/ese-ees/default.asp?lang=En&xml=5E549DF6-45F0-D775-70E2-58B9A1034213

Galleria Chemica. Accessed February 2016 at http://jr.chemwatch.net/galleria/

Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Accessed at http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

National Industrial Chemical Notification and Assessment Scheme (NICNAS). Human health Tier II assessment for Formamide (CAS No. 75-12-7). Australian Government Department of Health. Accessed at http://www.nicnas.gov.au

National Toxicology Program (NTP) 2008. Technical Report Series No. 541 - Toxicology and Carcinogenesis Studies of Formamide in F344/N rats and B6C3F1 mice (Gavage Studies). US Department of Health and Human Services. Available at https://ntp.niehs.nih.gov/results/pubs/longterm/reports/longterm/tr500580/listedreports/tr541/index.html

Nyska A, Haseman JK, Kohen R& Maronpot RR 2004. Association of liver hemangiosarcoma and secondary iron overload in B6C3F1 mice–the National Toxicology Program experience. Toxicol Pathol 32(2) pp. 222–8.

Organisation for Economic Cooperation and Development (OECD) 2007. SIDS Dossier on Formamide (CAS No. 75-12-7). Available at http://webnet.oecd.org/hpv/ui/SIDS_Details.aspx?id=4de35fc9-1932-4800-99c3-a3e9f7a59332

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed February 2016 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

*Last update 1 July 2016*