Australian Government
Department of Health, Disability and Ageing
Australian Industrial Chemicals Introduction Scheme

# Urea, *N*'-(3,4-dichlorophenyl)-*N*,*N*-dimethyl- (Diuron)

## Evaluation statement (EVA00170)

**3 October 2025**

**Draft**

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# AICIS evaluation statement (EVA00170)

## Subject of the evaluation

Urea, *N*′-(3,4-dichlorophenyl)-*N*,*N*-dimethyl- (Diuron)

## Chemical in this evaluation

| CAS name | CAS number |
|---|---|
| Urea, *N*′-(3,4-dichlorophenyl)-*N*,*N*-dimethyl- | 330-54-1 |

## Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health and environmental risk.

## Parameters of evaluation

The chemical is listed on the Australian Inventory of Industrial Chemicals (the Inventory).

This evaluation statement includes a human health and environmental risk assessment for all identified industrial uses of urea, *N*′-(3,4-dichlorophenyl)-*N*,*N*-dimethyl- (Diuron).

The risks posed to the environment associated with the industrial uses of the chemical have been evaluated with the following parameters:

- Industrial uses listed in the '**Summary of introduction, use and end use**' section.
- Measured concentrations in urban surface waters, including stormwater and sewage treatment plant (STP) effluent.
- Estimated concentrations in soils following STP sludge application.

The use of diuron in agricultural products is not assessed in this evaluation because this is not an industrial use.

## Summary of evaluation

### Summary of introduction, use and end use

Based on international information, the chemical has functional use as a preservative. The chemical is used in domestic and commercial products (adhesive and sealants, paints and coatings, renders) at concentrations of 0.2-2.5%.

The chemical also has reported site limited functional use as an intermediate in polymer and rubber production.

The chemical has non-industrial use in agricultural products.

# Human health

## Summary of health hazards

The identified health hazards are based on available data for the chemical. Based on the available data the chemical:

- has low acute oral, dermal and inhalation toxicity
- is at most slightly irritating to skin and eyes
- is not a skin sensitiser
- does not cause specific adverse effects on fertility/sexual function and foetal development
- is not likely to have genotoxic potential.

Diuron is listed on the Hazardous Chemical Information System (HCIS) with hazard classification for acute toxicity: acute tox 4. However, based on the weight of evidence from the available data, the chemical is expected to have low acute oral toxicity. In the majority of available studies, including those conducted according to, or similar to, the Organisation for Economic Co-operation and Development (OECD) Test Guidelines, the median lethal dose (LD50) was > 2000 mg/kg bw/day. Therefore, the available data supports removing the existing hazard classification for acute oral toxicity.

The repeat dose toxicity studies indicate that the chemical can produce adverse health effects following repeated exposure. Changes in haematological parameters were consistently observed in 28 day, 90 day and chronic studies conducted in different species. Effects indicative of haemolytic anaemia were observed by all routes of exposure (oral, inhalation, dermal). The chemical is classified as hazardous in the HCIS with hazard category ‘Specific target organ toxicity repeated exposure (STOT RE)—Category 2’ on HCIS. (SWA n.d.). The available data supports this classification. Although the effects were observed in females in oral studies at doses corresponding to a higher classification, based on the severity of haematological changes the existing classification is supported.

Diuron is classified as hazardous in the HCIS (SWA n.d.) as ‘Carcinogenicity – Category 2; H351 (Suspected of causing cancer). The weight of evidence from animal studies including neoplasms observed in 2 species (mice and rats), different types of neoplasms with evidence of progression to malignancy and mechanistic evidence for bladder carcinogenesis support amending this classification to the hazard category ‘Carcinogenicity – Category 1B’.

Mammary gland adenocarcinoma and benign ovarian luteoma were observed in female mice. In rats, neoplastic lesions were found in the urinary bladder in both sexes. In addition, renal carcinomas were observed in males and uterus adenocarcinomas in females.

A threshold mode of action is likely for urinary bladder tumours. This is based on data suggesting diuron or its metabolised products have cytotoxic effects on urothelial cells which leads to regenerative hyperplasia and urinary bladder tumours. The mode of action for other observed tumours is uncertain and the availability of mechanistic data is limited. However, genotoxicity studies are negative.

For further details of the health hazard information see **Supporting information**

## Hazard classifications relevant for worker health and safety

The chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for work health and safety as follows. This evaluation does not consider classification of physical hazards.

The chemical is already listed in listed in the HCIS (see **Supporting information**). This evaluation supports removal of an acute toxicity classification, retaining the specific target organ toxicity (repeated exposure) classification and amending the carcinogenicity classification from Carc. 2 to Carc. 1B.

| Health hazards | Hazard category | Hazard statement |
|---|---|---|
| Specific target organ toxicity (repeated exposure) | STOT Rep. Exp. 2 | H373: May cause damage to organs through prolonged or repeated exposure |
| Carcinogenicity | Carc. 1B | H350: May cause cancer |

## Summary of health risk

### Public

Based on the available use information, the chemical may be present in some products that could be used in a domestic setting. These products include adhesives and sealants, paint and coatings, and renders.

Therefore, the public may be exposed to the chemical:

- at concentrations up to 2.5%
- via incidental skin and eye contact with the chemical during use of domestic products
- via inhalation from spray products.

However, the frequency and duration of use of such products is considered to be sufficiently low that exposure to the chemical would be intermittent. The post-application dermal and inhalation exposures are expected to be minimal when used as preservative in paints because of diuron's low vapour pressure and dermal absorption.

The chemical may cause adverse effects on the haemopoetic system. A quantitative risk assessment conducted by the US EPA (US EPA 2020) indicated that risks of effects on the haemopoetic system from using paints preserved with diuron are not a concern with estimated margins of exposure ranging from 140 to 135 000.

The chemical is carcinogenic with evidence indicating a threshold mode of action. There is uncertainty regarding the extrapolation from continuous exposure studies in animals to repeated, intermittent human exposures. Although high frequency consumer use cannot be ruled out, and such use could possibly be at risk for chronic health effects, it is considered unlikely.

Therefore, there are no identified risks to the public that require management.

### Workers

During product formulation and packaging, dermal, inhalation and ocular exposure might 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 a risk to workers. Control measures to minimise dermal and inhalation exposure are needed to manage the risk to workers (see **Proposed means for managing risk** section)

## Environment

### Summary of environmental hazard characteristics

Based on the information presented in this evaluation and according to the environmental hazard thresholds stated in the Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals (DCCEEW n.d.) the chemical is:

- Persistent (P)
- Not Bioaccumulative (Not B)
- Toxic (T).

### Environmental hazard classification

This chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for environmental hazards as follows (UNECE 2017). This evaluation does not consider classification of physical hazards. This is the existing classification listed on the HCIS. The available data support these classifications.

| Environmental hazards | Hazard category | Hazard statement |
|---|---|---|
| Hazardous to the aquatic environment (acute / short-term) | Aquatic Acute 1 | H400: Very toxic to aquatic life |
| Hazardous to the aquatic environment (long-term) | Aquatic Chronic 1 | H410: Very toxic to aquatic life with long-lasting effects |

### Summary of environmental risk

Diuron is expected to be introduced in Australia for industrial use as a preservative in paints and coatings, adhesives and sealants, and renders. Diuron will be slowly released from treated surfaces via rainfall, resulting in releases to urban waterways.

Diuron is persistent and toxic but is not expected to bioaccumulate. Emerging evidence indicates that diuron can cause chronic toxic effects in fish at low concentrations. It is unclear whether these effects are due to endocrine activity or another mode of action.

Based on measured concentrations in urban stormwater, urban STP effluent, and urban estuaries, and estimated concentrations in soil, diuron is expected to be present in Australian urban surface waters and soil below levels of concern. The estimated risk quotient (RQ) for

these compartments is less than 1. Therefore, current industrial use of these chemicals is not expected to pose a significant risk to the environment.

# Proposed means for managing risk

## Workers

### Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include classifications relevant to work health and safety.

### Information relating to safe introduction and use

The information in this statement including recommended hazard classifications, should be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Recommended control measures that could be implemented to manage the risk arising from dermal and inhalation exposure to the chemical include, but are not limited to:

- using closed systems or isolating operations
- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

These control measures may need to be supplemented with:

- conducting health monitoring for any worker who is at significant risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health

Measures required to eliminate, or manage risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used.

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.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

# Conclusions

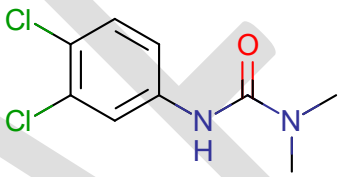
The Executive Director proposes to be satisfied that the identified risks to human health and the environment from the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under *section 100 of the Industrial Chemicals Act 2019* apply.
2. A person introducing this chemical should be aware of their obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory

# Supporting information

## Chemical identity

| | |
|---|---|
| **CAS number** | 330-54-1 |
| **CAS name** | Urea, *N*′-(3,4-dichlorophenyl)-*N*,*N*-dimethyl- |
| **Molecular formula** | $C_9H_{10}Cl_2N_2O$ |
| **Associated names** | Diuron |
| | DMCU |
| **Molecular weight (g/mol)** | 233.09 g/mol |
| **SMILES (canonical)** | O=C(NC1=CC=C(Cl)C(Cl)=C1)N(C)C |
| **Structural formula** |  |



## Relevant physical and chemical properties

| | |
|---|---|
| **Physical form** | White crystalline solid |
| **Melting point** | 156 °C at 1013 hPa (ECHA 2024) |
| **Boiling point** | 355 - 357 °C at 1013.3 hPa (ECHA 2024) |
| **Vapour pressure** | 7.6x10-9 hPa at 20 °C (ECHA 2024) |
| **Water solubility** | 28.8 mg/L (20°C, pH 7.01) (ECHA 2024) |
| **Henry's law constant** | - |
| **Ionisable in the environment?** | Stable under normal conditions (ECHA 2024) |
| **p$K_a$** | - |
| **log $K_{ow}$** | 2.89 (20 °C, pH 7.01) (ECHA 2024) |

# Introduction and use

## Australia

Based on information reported to the former National Industrial Chemicals Notification and Assessment Scheme (NICNAS) under previous mandatory and/or voluntary call for information, the annual introduction volume for industrial uses of diuron was <100 tonnes.

The chemical has non-industrial uses in agricultural products including herbicides, defoliants, antifouling paints, and pond and aquarium products.

## International

The following international uses have been identified through:

- Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH n.d.)
- PubChem (NCBI n.d.)
- Screening Assessment for the Challenge Urea, *N*'-(3,4-dichlorophenyl)-*N*,*N*-dimethyl- (Diuron**)** (Government of Canada 2011)
- North American data reporting initiatives and product databases (DeLima Associates n.d.; Government of Canada 2017; US EPA 2016; US EPA 2020).

The chemical has reported commercial uses as a preservative in:

- adhesives and sealants
- paints and coatings
- renders.

Some of these commercial uses may also have consumer use applications. The chemical is reported as an ingredient in several paint and coating products up to a concentration of 1% (DeLima Associates n.d.) The reported concentration of diuron in paints, sealants and adhesives is 0.2 to 2.5%. Less than 1% of all paints were reported to contain diuron (US EPA 2003). Consumer uses in these types of products was reported as part of Government of Canada inventory update reporting (Government of Canada 2017). No consumer uses are registered under REACH or for these type of products under the US Chemical Data Reporting (CDR) under the Toxic Substances Control Act (US EPA 2016; US EPA 2020).

The chemical has site limited use as an intermediate in polymer and rubber production.

The US EPA CDR report for 2020 indicates that the national aggregated production volume for the chemical was 39,888 lbs. (approximately 18 tonnes) (US EPA 2020). It is also noted that the chemical is listed in United States High Production Volume Challenge (HPVC) Program List. Chemicals considered to be HPV are those that are manufactured in or imported into the USA in amounts equal to or greater than one million pounds per year (Chemwatch n.d.).

This chemical is registered under the REACH Regulation and is manufactured in and/or imported to the European Economic Area, at ≥100 to <1000 tonnes per annum (ECHA n.d.). Additionally, it has been identified as an HPV chemical under the OECD Cooperative Chemicals Assessment Programme (Chemwatch n.d.).

# Existing Australian regulatory controls

## AICIS

The chemical is listed on the Australian Industrial Chemicals Introduction Scheme (AICIS) − List of chemicals with high hazards for categorisation.

## Public

No specific public controls have been identified for industrial uses of the chemical.

## Workers

The chemical is listed on the Hazardous Chemical Information (HCIS) with the following hazard categories and statements for human health (SWA n.d)

| Health hazards | Hazard category | Hazard statement |
|---|---|---|
| Acute toxicity | Acute Tox. 4 | H302: Harmful if swallowed |
| Specific target organ toxicity (repeated exposure) | STOT Rep. Exp. 2 | H373: May cause damage to organs through prolonged or repeated exposure |
| Carcinogenicity | Carc. 2 | H351: Suspected of causing cancer |

The chemical is listed on the HCIS with a workplace exposure standard of 10 mg/m$^3$ (8 hour time weighted average (TWA) (SWA n.d.). From 1 December 2026 and following implementation into the work health and safety laws of the Commonwealth, states and territories, new Workplace Exposure Limits (WEL) for airborne contaminants (WEL list) will be adopted throughout Australia. The WEL for the chemical is the same as the Workplace Exposure Standards (WES) (TWA 10 mg/m$^3$).

## Environment

The industrial use of diuron is not subject to any specific national environmental regulations.

The chemical is listed on the HCIS with the following hazard categories and statements for environment (SWA n.d)

| Environmental hazards | Hazard category | Hazard statement |
|---|---|---|
| Hazardous to the aquatic environment (acute) | Aquatic Acute 1 | H400: Very toxic to aquatic life |
| Hazardous to the aquatic environment (chronic) | Aquatic Chronic 1 | H410 (Very toxic to aquatic life with long-lasting effects) |

The Australian Pesticides and Veterinary Medicines Authority (APVMA) regulates agricultural and veterinary (AGVET) chemical products to ensure they are effective and safe for people, animals, plants, and the environment. In accordance with the AGVET legislative framework,

APVMA's regulatory controls include evaluation and product registration, permit approval, chemical reconsideration, recalls and compliance monitoring. APVMA does not monitor or enforce the correct use of AGVET products – state and territory governments are responsible for control of use beyond the point of retail sale in Australia.

The APVMA completed a detailed reconsideration assessment of agricultural and related uses of diuron in November 2012. A summary of the outcomes of that review is available on APVMA's website (APVMA 2012). The APVMA considered the very high sensitivity of freshwater and marine aquatic plants and organisms (e.g., algae and coral) to the chemical as the main issue of concern.

The current uses of diuron in non-industrial settings are subject to a range of restrictions including:

- Maximum permitted application rates in specified crops and geographic regions.
- Restrictions on permissible associated farming practices, requirements for associated physical controls (e.g., retention of potentially contaminated water and use of buffer zones to protect non-target vegetation).
- Geographic exclusions from use in very high rainfall areas (e.g., the wet tropics) and calendar based exclusions on use where seasonal rainfall patterns may lead to issues with contaminated run-off.

Non-industrial use in anti-fouling paints on water-borne vessels is subject to a maximum permitted application rate consistent with permissible limits on the estimated leaching rate into surrounding waters. Further, suitable label instructions including protection and disposal statements are provided on registered diuron product labels to minimise hazards to non-target species (e.g., aquatic life) and mitigate risks to environment.

# International regulatory status

## Exposure standards

The following exposure standards were identified (Chemwatch n.d.):

- TWA (Time weighted average): - 10 mg/m$^3$ in Argentina and Canada
- TWA: - 5 mg/m$^3$ in Austria.

## Canada

The screening assessment on the chemical concluded that it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health (Government of Canada 2011).

## European Union

The chemical is listed on 'EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products - Annex II - List of Substances Prohibited in Cosmetic Products' (EC).

## New Zealand

The chemical is listed on approved hazardous substances with controls on New Zealand Inventory of Chemicals (NZIoC**)**. It is also listed on New Zealand Cosmetic Products Group Standard, as a component cosmetic products must not contain (NZ EPA 2024).

## Asia

The chemical is listed in ASEAN Cosmetic Directive Annex II Part 1: List of substances which must not form part of the composition of cosmetic products (HAS 2025)

# Health hazard information

## Toxicokinetics

Diuron is rapidly absorbed, widely distributed, metabolised and rapidly eliminated following oral administration.

There are no specific toxicokinetic data available on dermal or inhalation absorption of diuron. However, clinical effects were reported in acute inhalation toxicity studies (see **Acute toxicity – Inhalation**) and repeated dose toxicity studies (see **Repeated dose toxicity – inhalation**), indicating absorption via inhalation. Although the molecular weight and log Kow value indicate favourable dermal absorption, dermal absorption is expected to be low based on absorption of the structurally similar chemical linuron (CAS No. 330-55-2), which has an estimated dermal absorption factor of 6% (US EPA 2020; US EPA 2023).

In oral studies using radiolabelled diuron, more than 80% of the chemical was rapidly absorbed and eliminated from the body primarily via the urine and faeces. The majority was excreted as metabolites with 3,4-dichlorophenyl urea (DCPU) identified as the major metabolite. Smaller amounts of 1-(3,4- dichlorophenyl)-3-methylurea (DCPMU) and 3,4-dichloroaniline (DCA) were also excreted in the urine. A small amount was excreted unchanged in faeces (ECHA 2024).

Another study using radiolabelled phenyl diuron demonstrated a similar rapid absorption and excretion pattern. Diuron was excreted mainly via urine within 72 hours. The highest residues were observed in haematopoietic organs including blood, metabolism and excretion related organs, and female ovaries. However, no accumulation potential was observed (ECHA 2024, REACH n.d.). In a subacute inhalation study in rats, DCPU, DCPMU and 3,4-dicholoaniline (DCA) were excreted in urine with DCPU as the main metabolite (APVMA 2011; ECHA 2024).

Based on available *in vitro* data, diuron is expected to undergo similar metabolism as that observed in animals via partial or complete demethylation and hydroxylation. An *in vitro* study using human liver homogenate identified DCPMU as the major metabolite.

In a study which investigated toxicokinetics of diuron in *ex vivo* human placental perfusion, diuron was found to cross the placenta. This study also investigated metabolism *in vitro* using human placental microsomes and human trophoblastic cancer cells. Metabolism to DCPMU was detected but only with the highest used diuron concentration (ECHA 2024).

## Acute toxicity

### Oral

Diuron is listed on the HCIS with hazard classification for acute toxicity: acute tox 4 (H302:Harmful if swallowed). However, based on the weight of evidence from the available data, the chemical is expected to have low acute oral toxicity. In the majority of available studies, including those conducted according to, or similar to, OECD Test Guidelines, the median lethal dose (LD50) was > 2000 mg/kg bw/day. In addition, the ECHA risk assessment committee concluded that no classification for acute oral toxicity is warranted (ECHA 2021a). Therefore, the available data supports removing the existing hazard classification for acute oral toxicity.

In a GLP-compliant, acute oral toxicity study similar to OECD TG 401, 5 male and 5 female Sprague Dawley(SD) rats were administered a single dose of diuron (98.5% in propan-1,2-diol) at 2000 mg/kg bw by oral gavage. The LD50 was > 2000 mg/kg bw. No further study details were reported (ECHA 2021b).

In a non GLP-compliant, acute oral toxicity study similar to OECD TG 401, 10 female Wistar rats were administered a single dose of diuron (in Cremophor EL and distilled water) at 25, 50, 100, 2500, 5000 or 7100 mg/kg bw by oral gavage. The LD50 was 4150 mg/kg bw. Reported signs of toxicity included behavioural, respiratory and motility disorders, staggering/spastic gait, lying on lateral or prone position, and a narcosis-like state. Mortalities were reported at the 2500 mg/kg bw dose and higher within 2 days of dosing (APVMA 2011; ECHA 2021b; REACH n.d.).

In a GLP-compliant, acute oral toxicity study reported to be conducted in accordance with OECD TG 420, 5 female -SD caesarean-derived (CD) rats were treated with 2000 mg/kg bw of the chemical by oral gavage. The median lethal dose (LD50) was > 2000 mg/kg bw. No further study details were reported.(REACH n.d.).

In a non-guideline, non GLP-compliant, acute oral toxicity study, 10 male Wistar rats were treated with the chemical in cotton seed oil (no dose information) by oral gavage. The following LD50 values were reported based on the type of diet fed before treatment:

- LD50 =1017 mg/kg bw (Normal laboratory diet)
- LD50 = 437 mg/kg bw (Protein deficient diet)
- LD50 = 2390 mg/kg bw (Normal protein diet).

Reported clinical signs of toxicity included:

- drowsiness
- ataxia
- abnormal reflexes
- irritability diarrhoea
- diuresis
- shedding of bloody tears
- bleeding from the nose
- significant weight loss (with decreased food and water intake).

Hypothermia, glucosuria, proteinuria, and aciduria were detected 24 hours after exposure. Animals that eventually died were prostrate and had bradypnoea (abnormally slow breathing). The main cause of death was respiratory failure. Investigators determined that cotton seed oil as a vehicle increased the lethality of diuron compared with diuron in watery

preparations. A protein deficient diet was associated with higher susceptibility of Wistar rats to diuron toxicity. In this study, weanling rats were included (acquired as weanlings or 2 weeks after weaning) instead of 8 to 12 week old rats as recommended in the OECD TG (ECHA 2021a; ECHA 2021b; REACH n.d.)

Several other non-guideline, non GLP-compliant oral acute toxicity studies have reported LD50 > 2000 mg/g bw (APVMA 2011; ECHA 2021b; REACH n.d.).

### Dermal

Based on the available data, the chemical is expected to have low acute dermal toxicity (LD 50 > 2000 mg/kg bw/day).

In a GLP-compliant acute dermal toxicity study (reported as OECD TG 402), SD CD rats (5/sex/dose) were applied a single dose of 2000 mg/kg of the chemical under semi-occlusive conditions. The LD50 was reported as >2000 mg/kg bw. No further study details were reported (ECHA 2021b; REACH n.d.).

In a non-GLP-compliant acute dermal toxicity study (reported as OECD TG 402), Wistar rats (5/sex/dose) were applied a single dose of the chemical at 2500 or 5000 mg/kg bw under occlusive conditions. The dermal LD50 was > 5000 mg/kg. Reported sublethal signs of toxicity included reduced motility and apathy at 5000 mg/kg bw. No macroscopic lesions were observed either on the skin or in any other organs at termination (APVMA 2011; REACH n.d,).

Several other non-guideline, non GLP-compliant dermal acute toxicity studies have reported LD50s > 2000 kg/g bw (APVMA 2011; REACH n.d.).

### Inhalation

Based on the available data, the chemical is expected to have low acute inhalation toxicity (no mortality observed below 5 mg/L).

In a GLP-compliant, acute inhalation toxicity study (reported as OECD TG 403), SD rats (10/sex/dose) were exposed to the chemical as an aerosol, with mass median aerodynamic diameter (MMAD) of up to 3.59 µm via nose-only inhalation for 4 hours at a mean concentration of 5.05 mg/L. Sub-lethal effects included increased respiratory rate, hunched posture, pilo-erection and wet fur (ECHA 2021; REACH n.d.). One female died on day 1 post exposure. Necroscopy revealed abnormally dark lungs and an accentuated lobular pattern in the liver. Abnormally dark lungs were also observed in another treated male upon necroscopy. A median lethal concentration (LC50) value of > 5.05 mg/L was determined (ECHA 2021; REACH n.d.).

In a GLP-compliant acute inhalation toxicity study similar to OECD TG 403, Wistar rats (10/sex/dose) were exposed to diuron via nose-only inhalation as a dust at 0, 7 or 7.1 mg/L for 4 hours. No animal mortality was observed. Sub-lethal effects observed during exposure included red nasal discharge, lethargy and partially closed eyes. Some animals also showed signs of hair loss, red ocular or oral discharges, stained perineum, and stained or discoloured fur and weight loss during post exposure period. No gross abnormalities were detected at necropsy. An LC50 value of > 7.1 mg/L was determined (APVMA 2011; ECHA 2021).

In a non GLP-compliant, acute inhalation toxicity study similar to OECD TG 403, Wistar rats (10/sex/dose) were exposed to the chemical (in ethanol:lutrol (1:1) vehicle) as an aerosol,

with MMAD of up to 2.7 ± 1.8 µm only for 4 hours at concentrations of 73, 195 or 223 mg/m$^3$. An LC50 value of > 223 mg/m$^3$ (0.223 mg/L) was determined. Sub-lethal effects included non-specific behavioural changes. No mortality was observed. No organ lesions were observed at necropsy (APVMA 2011, REACH n.d.).

In a non-guideline, non-GLP acute inhalation toxicity study, Wistar rats (9/sex/dose) were exposed to the diuron as a dust at 0 or 6200 mg/m$^3$ for 4 hours. Only 50% of the test substance produced in the dynamic inhalation system fell into the respirable range (< 7 µm). No mortality was observed. Sub-lethal effects included bloody discharge in the nose/eyes, balance impairment, ataxic movement and decreased motility. Lower body weights were observed in treated males. No macroscopic changes were seen at necropsy. An LC50 value of > 6.2mg/L was determined (APVMA 2011).

In a GLP-compliant, acute inhalation toxicity study similar to OECD TG 403, Wistar rats (10/sex/dose) were exposed to diuron dust at 0 or 2139 mg/m$^3$ for 4 hours. The MMAD was 6.16 µm with 58% of the particles generated < 4.45 µm. No mortalities or sublethal effects were observed as a result of exposure. Diffused pneumonic foci or emphysema was seen in 3 treated rats at necropsy. An LC50 value of > 2139 mg/m$^3$ (2.139 mg/L) was determined (APVMA 2011).

### Observation in humans

No data on cases of human poisoning are available. The probable oral lethal dose in humans was reported to be in the range of 500 to 5000 mg/kg. However, where information was available the data were confounded as incidents involving diuron also included other substances (APVMA 2011; ECHA 2021a).

## Corrosion/Irritation

### Skin irritation

Based on the available data, the chemical is at most a slightly irritating to skin.

In a GLP-compliant skin irritation study conducted in accordance with OECD TG 404, 3 female New Zealand White (NZW) rabbits were topically treated with 0.5 g of the chemical for 4 hours on intact skin under semi-occlusive conditions. Observations were recorded at 1, 24, 48, and 72 hours after patch removal. No signs of erythema (mean score = 0) or oedema (mean score = 0) were reported during the observation period (REACH n.d.).

In a GLP-compliant skin irritation study conducted in accordance with OECD TG 404, 3 NZW rabbits were topically treated with 0.5 g of the chemical for 4 hours on shaved skin under semi-occlusive conditions. Observations were recorded at 24, 48, and 72 hours after patch removal. The mean score for erythema at these intervals was reported as 0.3. No signs of oedema (mean score = 0) were reported during observation period (REACH n.d.).

In a GLP-compliant skin irritation study similar to OECD TG 404, 3 rabbits were topically treated with 0.5 g of the chemical for 4 hours on intact skin. Observations were recorded at 1, 24, 48, and 72 hours. No signs of skin irritation were reported (all scores = 0) (APVMA 2011).

In a non-guideline, non GLP-compliant study, 6 NZW rabbits were treated with 0.5 g of the chemical on intact and scarified skin (treatment duration not reported). Observations were

recorded at 24, 48, 72, 168 hours and 2 weeks. Mild erythema (score = 1) was reported in 2/6 intact skin sites, and in 3/6 scarified skin sites at 24 hours, but had recovered after 2 days. Parchment like skin necrosis (score 1 or 2) occurred in 3/6 intact skin sites, and in all scarified skin sites followed by skin peeling off within 3–5 days. The skin recovered completely from all effects within 7 days (APVMA 2011).

In a non-guideline, non GLP-compliant skin irritation study, 0.05 g of the chemical was applied to the intact skin under occlusive condition for 3–6 days. No signs of irritation were reported. No further study details are available (APVMA 2011).

### Eye irritation

Based on the available data, the chemical is likely to be at most slightly irritating to the eye.

In a GLP-compliant eye irritation study, conducted in accordance with OECD TG 405, 0.1 g of the chemical was instilled into 1 eye each of 3 NZW rabbits. The eyes were observed at 24, 48 and 72 hours after treatment. The following mean scores were reported based on observations at 24, 48 and 72 hours: corneal opacity 0/4, iritis 0/2, conjunctival redness 0.22/3, chemosis 0.33/4. The conjunctival redness and chemosis was reversible in animals within 72 hours and 48 hours, respectively. Individual animal data were not provided (REACH n.d.).

In a GLP-compliant eye irritation study conducted in accordance with OECD TG 405, 0.1 g of the chemical was instilled into 1 eye each of 3 NZW rabbits. The eyes were observed at 24, 48 and 72 hours after treatment. The following mean scores were reported based on observations at 24, 48 and 72 hours: corneal opacity 0/4, iritis 0/2, conjunctival redness 0.2/3, chemosis 0/4. The conjunctival redness was reversible in all animals 48 hours. Individual animal data were not provided (REACH n.d.).

In a GLP-compliant eye irritation study similar to OECD TG 405, 0.1 g of the chemical was instilled into 1 eye each of 6 male NZW rabbits. The eyes were observed at 1, 24, 48 and 72 hours after treatment. Slight redness (score 1) was observed in 5/6 treated eyes at 1 hour, and partial erosion (1/4 area) of corneal epithelium was in 2/6 treated eyes at 24 hours. No signs of irritation were observed at 48 and 72 hours. No further study details were available (APVMA 2011).

In a non-guideline, non-GLP-compliant eye irritation study, 0.05 g of the chemical was instilled into 1 eye each of 9 NZW rabbits. The eyes were rinsed with water 5 minutes after instillation in 3 animals. The eyes of 6 animals were not rinsed. The eyes were observed at 24, 48, 72, 168 hours and 2 weeks after treatment. Hyperaemia of the conjunctive developed immediately after dosing (no score was recorded) and had resolved within 24 hours. No further study details are available (APVMA 2011).

## Sensitisation

### Skin sensitisation

Based on the available data, the chemical is not a skin sensitiser.

#### In vivo

In a GLP-compliant *in vivo* skin sensitisation study conducted in accordance with OECD TG 406 (Buehler test), Dunkin-Hartley (DH) guinea pigs (20/sex) were induced twice

with diuron at 10% (intradermal) and 50% (topical) in saline. The animals were challenged with the chemical at 50%. After the challenge, none of the treated animals showed skin reactions. The chemical was reported to be non-sensitising in this study (REACH n.d.).

In a GLP-compliant *in vivo* skin sensitisation study reported to be conducted in accordance with OECD TG 406 (Buehler test), 20 male DH guinea pigs were induced twice with diuron at 1% (intradermal) and 100% (dermal) in 1% methyl cellulose. The animals were challenged with the chemical at 75% and 37.5% concentrations. Two animals showed positive reactions 24 hours after challenge. However, none of the animals showed skin reactions 48 hours after the challenge. No further study details are available. The chemical was reported to be non-sensitising in this study (REACH n.d.).

Several other GLP-compliant guideline and non-guideline studies have reported that the chemical is non-sensitising (APVMA 2011).

**In silico**

The parent chemical has no structural alerts for protein binding based on the mechanistic (and endpoint-specific) profiling functionality of the Organisation for Economic Co-operation and Development (OECD) QSAR Application Toolbox (OECD QSAR Toolbox). However, when skin metabolism is simulated, several metabolites have mechanistic (and endpoint-specific) alerts for protein binding and skin sensitisation via Schiff base formation or an SN2 reaction.

The knowledge based expert system Deductive Estimation of Risk from Existing Knowledge (DEREK) Nexus version 6.3.0 was utilised to estimate the skin sensitisation potential of the chemical. The chemical was predicted negative for skin sensitisation with no misclassified or unclassified features.

The chemical was out of domain in OASIS-TIMES (Optimised Approach based on Structural Indices Set–Tissue Metabolism Simulator) version 2.31.

## Repeat dose toxicity

Diuron is classified as hazardous in the HCIS with hazard category ‘Specific Target Organ Toxicity Repeated Exposure (STOT RE)—Category 2’ on HCIS. (SWA n.d.). The available data supports this classification. Effects indicative of haemolytic anaemia were observed by all routes of exposure (oral, inhalation, dermal). Signs of regenerative haemolytic anaemia have been observed in rats, mice and dogs. The rat was the most sensitive species to the chemical.

In a 90 day oral study in rats (see below), a significant increase in haemosiderosis was noted in the spleen of females at 23 mg/kg bw/d in combination with significant haematological findings (Hb reduction ≥ 10%, increased methaemoglobin formation). Although some effects were observed at doses below 10 mg/kg bw/day (criteria for GHS classification as Category 1 (UNECE 2017) these were not severe enough for classification. The Category 2 classification is supported by effects (pigment deposits in the spleen and kidney) seen in a 1 year dog study at 11 mg/kg bw/day and haematological effects observed at in rat inhalation studies.

### Oral

Evidence of haemolytic anaemia in rats, mice and dogs were observed in multiple oral (feed and gavage) studies, including 28 day, 90 day, 6 month and 2 year studies (APVMA 2011, ECHA 2021a; ECHA 2021b). The critical oral studies for GHS classification are a 90 day guideline study in rats and a 1 year study in dogs. These are summarised below.

In a GLP-compliant 90 day study conducted in accordance with OECD TG 408 Wistar rats 20/sex/dose were administered the chemical in feed 7 days/week at 0, 100, 250 or 2500 ppm (equivalent to 0, 6.7, 17, 176 mg/kg bw (males) and 0, 8.7, 23.3, 214 mg/kg bw (females). No mortality was observed in any of the dose groups. Body weight was decreased (14% males and 9% females) at highest dose.

The main targets of the chemical were the blood cells and the urinary system.

Effects related to haemolytic anaemia included:

- A dose dependent increase in absolute and relative spleen weight in all treated females. Absolute and relative spleen weights were also increased in high dose males.
- An increase in extramedullary haematopoiesis and congestion in the spleen at all doses in females.
- An increase in bone marrow haematopoiesis in both sexes at concentrations 250 ppm and above.
- Hepatic extramedullary haematopoiesis and increase in hepatic pigments were observed at 2500 ppm in both sexes.
- A decrease in red blood cell count (RBC), haemoglobin (Hb) concentration and haematocrit in females from 250 ppm and in males at the 2500 ppm. The decrease in Hb was > 10% for females from 250 ppm.
- Increased bilirubin in both sexes at 2500 ppm.
- An increase in reticulocyte count at concentrations ≥100 ppm, methaemoglobin at concentrations ≥250 ppm and sulfhaemoglobin at concentrations ≥100 ppm.
- An increase incidence of pigmentation due to haemosiderin storage with pigments seen in the liver in males and females at 2500 ppm and in the spleen in males at 2500 ppm and all females from 250 ppm.

The majority of the histopathological and haematological effects were reversible within a 90-day recovery period.

Effects related to the urinary tract included reversible urinary bladder and kidney mucosal hyperplasia in both sexes at doses 250 ppm or above. Transitional cell hyperplasia seen in the urothelium are considered adaptive effects with no adverse consequences on cessation of exposure except possible development of neoplasia. This effect is addressed in the **carcinogenicity** section.

The No Observed Adverse Effect Level (NOAEL) was determined to be 6.7 mg/kg bw/day for males. An NOAEL could not be established for females. The Lowest Observed Adverse Effect Level (LOAEL) was 17.0 mg/kg bw in males and 8.7 mg/kg bw in females based on the effects described above (ECHA 2021a; ECHA 2021b; REACH n.d.).

In a GLP-compliant, non-guideline study similar to OECD TG 452, Beagle dogs (6/sex/dose) were administered the chemical in feed at 0, 50, 300 and 1800 ppm (equivalent to 1.8, 11,

64 mg/kg bw). Body weights and body weight gain were decreased in both sexes in the highest dose group. These effects did not appear to be related to food intake.

The main target of the chemical was the red blood cells with findings related to hypochromic anaemia (loss of Hb in red blood cells). The main observed effects included decreases in RBC and Hb (>10 % at highest dose) and increases in MCV, reticulocytes and Heinz bodies at highest dose. Spleen weights a were increased at the highest dose. Pigment deposits in the liver (from at 1800 ppm) and kidney and spleen (from 300 ppm).

### Dermal

In a GLP-compliant, repeated dose dermal toxicity study, similar to OECD 411, SD rats (12/sex/dose) were treated with the chemical at 0, 250, 500 or 1000 mg/kg bw, 6 hours/day, 5 days/week under occlusive conditions for 13 weeks. Changes in haematological parameters were observed at all treatment doses including a decrease in RBC, Hb (14-16%) and haematocrit and an increase in MCV and MCH. However, statistical significance was not reported. Increase in blood bilirubin was observed in females at 250 mg/kg bw. Mild haemosiderosis of the spleen and signs of extramedullary haemopoiesis could be demonstrated in the red pulp of in all treated rats but this was also seen in controls. The LOAEL of 250 mg/kg bw was reported based on haematological changes (APVMA 2011; ECHA 2021b, ECHA 2024).

In a GLP-compliant repeated dose dermal toxicity study, similar to OECD TG 410, NZW rabbits (5/sex/dose) were treated with the chemical at 0, 50, 500 or 1200 mg/kg bw/day, 6 hours daily on shaved intact skin for 3 weeks. No changes in organ weights or pathology were observed at any doses. As there were no effects observed at any dose level, a no observed effect level (NOEL) of 1200 mg/kg bw was reported (APVMA 2011, ECHA 2021b).

In a GLP-compliant, repeated dose dermal toxicity study, similar to OECD TG 410, NZW rabbits (3/sex/dose) were treated with the chemical at 0, 50 or 250 mg/kg bw for 6 hours/day (5 days/week) on intact or abraded skin for 3 weeks. Signs of skin irritation were observed at 250 mg/kg bw No significant signs of systemic toxicity were observed. Therefore, the NOAEL was reported to be 250 mg/kg bw (APVMA 2011; REACH n.d.; ECHA 2024).

### Inhalation

In a GLP-compliant, repeated dose inhalation toxicity study, similar to OECD 412, Wistar rats (5/sex/dose) were exposed (head/nose) to chemical as an aerosol at concentrations of 0, 4.1, 37.4 or 268.1 mg/m$^3$, 6 hours per day, 5 days per week for 4 or 8 weeks.

No mortality was reported. Effects indicative of haemolytic anaemia were observed in females from 37.4 mg/m$^3$ and in males at the highest dose. The most significant haematological effects included: decreases in Hb (at 268.1 mg/m$^3$ in both sexes, >10% in females), erythrocytes (from 37.4 mg/m$^3$ females and 268.1 mg/m$^3$ males), and increases in Heinz bodies and reticulocytes (from 37.4 mg/m$^3$ in both sexes). The spleen was dark and enlarged in both sexes at the highest dose and had evidence of iron accumulation (haemosiderin staining).

There were no marked differences between the 4 and the 8 week timepoint. Clinical chemistry was mostly normal apart from a decrease in plasma protein and albumin from 37.4 mg/m$^3$ in males and in both sexes at the highest dose. Thyroid hormones were decreased, T4 levels at 268.1 mg/m$^3$ in males, and T3 levels only in females at 37.4 mg/m$^3$.

Thyroxine binding capacity was significantly increased in females at 268.1 mg/m$^3$. There were no histopathological findings in the thyroid. The lowest no observed adverse effect concentration (NOAEC) was 37.4 mg/m$^3$ (males) and 4.1 mg/m$^3$ (females) based on the haematological (ECHA 2021a; ECHA 2021b).

In a GLP-compliant, repeated dose inhalation toxicity study, similar to OECD TG 412, Wistar rats (10/sex/dose) were exposed (head/nose) to the chemical as an aerosol at concentrations of 0, 6.6, 47.6 or 311 mg/m$^3$ for 6 hours (5 days /week for 3 weeks). No mortality was reported.

The main haematological findings were a dose-related increase in Heinz body formation and an increase in MCV, MCH and reticulocyte formation (Hb levels were not reported). Spleen weight was increased from 47.6 mg/m$^3$ in females and at all doses in males. The spleens were swollen and congested at the highest dose in both sexes. There were significant reductions in T4 levels at 311 mg/m$^3$ in both sexes and T3 levels only in males at 311 mg/m$^3$. Thyroxine binding capacity was significantly increased in both males and females at 47.6 mg/m$^3$ and higher doses. There were no marked changes in thyroid weight or histopathology. The no observed adverse effect level (NOAEC) was 6.6 mg/m$^3$ based on consistent haematological effects at 47.6 mg/m$^3$ in both sexes (ECHA 2018, ECHA 2021b, ECHA2024).

## Genotoxicity

Based on the weight of evidence, diuron is not likely to be genotoxic. The majority of the *in vitro* studies were negative with one study providing equivocal evidence of clastogenic effects. There was no evidence of chromosome aberrations in somatic or germ cells *in vivo*. Two out of 3 mouse micronucleus were negative with the positive result not replicated at higher doses. A direct genotoxic effect was not identified in an *in vivo* unscheduled DNA synthesis (UDS) test.

### In vitro

Negative results were reported in:

- Several bacterial reverse mutation assays (Ames tests) (OECD TG 471) in *Salmonella typhimurium* TA 1535, TA 1537, TA 98, TA 100 and *Escherichia coli* WP2 uvrA with and without metabolic activation (S9) at concentrations up to 5000 µg/plate (APVMA 2011; ECHA 2021a).
- Two mammalian gene mutation assay (similar to OECD TG 476) in the hypoxanthine-guanine phosphoribosyl transferase (Hprt) locus in Chinese hamster ovary (CHO) cells with and without metabolic activation (REACH n.d.).
- Mammalian chromosome aberration test (OECD TG 473) in CHO cells with and without metabolic activation at concentrations up to 360 µg/plate (REACH n.d.).
- Sister chromatid exchange (SCE) assay (OECD TG 479) in CHO cells with and without metabolic activation at concentrations 0.001-0.1 µg/mL (APVMA 2011).
- In a non-guideline UDS assay in rat hepatocytes at concentrations 0.1-20mM. Although a significant dose-related increase in net grain count was observed, this was determined to be due to cytotoxicity rather than DNA repair synthesis (APVMA 2011; ECHA 2021a).

Positive results were reported in a non-guideline cytogenetic study in human lymphocyte cells at concentrations up to 1000 and 500 µg/plate with and without metabolic activation, respectively. It was reported that the effects were observed at cytotoxic concentrations, but

the extent of the decrease in mitotic index was not reported (APVMA 2011; ECHA 2021a; REACH n.d.).

### In vivo

Negative results were reported in:

- GLP-compliant mammalian erythrocyte micronucleus test reported to be conducted in accordance with OECD TG 474, NMRI mice (5/sex/dose) were treated with the chemical by intraperitoneal injection at a single dose of 700 mg/kg bw/day. The incidence of micronuclei in bone marrow polychromatic erythrocytes did not increase in any of the treated groups, indicating a lack of clastogenicity (APVMA 2011; ECHA 2021b; REACH n.d.).
- Non-guideline mammalian erythrocyte micronucleus test in which Bor:NMRI mice (5/sex/dose) were treated with the chemical by oral gavage at single dose of 2500 mg/kg bw/day. The incidence of micronuclei in bone marrow polychromatic erythrocytes did not increase in any of the treated groups, indicating a lack of clastogenicity (REACH n.d.).
- GLP-compliant, mammalian bone marrow chromosome aberration test reported to be conducted in accordance with OECD TG 475 but with deviation on number of metaphases counted. Rats (strain not specified, n=15/sex/dose) were treated with the chemical by oral gavage, at single doses of 50, 500 or 5000 mg/kg bw. Bone marrow sampling (n=5/sex/dose) occurred at 6h, 24h and 48h post treatment. The incidence of chromosome aberrations in bone marrow cells did not increase in any of the treated groups, indicating a lack of clastogenicity. Cytotoxicity to the bone marrow and systemic toxicity were observed in high dose animals providing evidence that the target tissue had been reached by the test substance (ECHA 2021a; ECHA 2021b).
- GLP-compliant, mammalian bone marrow chromosome aberration test reported to be conducted in accordance with OECD TG 475 but with deviation on number of metaphases counted. Chinese hamster inbred stain (n=6–10/sex/group depending on dose and sampling time) were treated with the chemical orally, at single doses of 500 and 1670 (sampling at 24 hour post-treatment only) and 5000 mg/kg bw (sampling at 6h, 24h and 48h post treatment). The incidence of chromosome aberrations in bone marrow cells did not increase in any of the treated groups, indicating a lack of clastogenicity (ECHA 2021b; REACH n.d.).
- GLP-compliant, mammalian spermatogonial chromosome aberration test reported to be conducted in accordance with OECD TG 483 but with deviation on number of metaphases counted. Male NMRI mice (6/dose) were orally administered the chemical with a single dose at 5000 mg/kg bw at single doses of 500 and 1670 (sampling at 24 hour post-treatment only) and 5000 mg/kg bw (sampling at 6h, 24h and 48h post treatment). Chromosomal aberrations were not observed in spermatogonial cells (APVMA 2011; ECHA 2021b; REACH n.d.).
- GLP-compliant, *in vivo* SCE assay conducted in accordance with EPA guidelines, Chinese hamster inbred strain (n=6/sex/dose) administered the chemical by oral gavage with a single dose at 500, 1670 or 5000 mg/kg bw. No increased number of SCEs in preparations made 24 hours post treatment were observed (ECHA 2021b; REACH n.d.)

Positive results were reported in a non-guideline, non-GLP micronucleus assay in which Swiss mice (6/sex/dose) were treated with the chemical by intraperitoneal injection at single doses of 85,170 or 340 mg/kg bw. The incidence of chromosome aberrations in bone marrow increased after 30 and 48 hours but not after 72 hours (APVMA 2011; ECHA 2021b).

Contradictory results were observed in 2 dominant lethal tests in male mice. However, due to the absence of positive controls these tests were not considered reliable (APVMA 2011; ECHA 2021a; ECHA 2021b).

Equivocal results were reported in a non-guideline, non GLP-compliant, UDS assay, female BOR:WISW rat were treated with a chemical at 25, 250 or 2500 ppm in feed (equivalent 1.25, 12.5 or 125 mg/kg bw). The purity of the test chemical was unknown. The study reported an increase in the portion of S phase cells, an increase in the number of cells with induced UDS and a decrease in DNA repair in bladder urothelial cells at 25 and 250 ppm. These effects were considered mitotic rather than genotoxic (ECHA 2021a; ECHA 2021b; REACH n.d.).

### In silico

The chemical has a structural alert for DNA binding based on the mechanistic functionality of the Organisation for Economic Co-operation and Development (OECD) QSAR Application Toolbox (OECD QSAR Toolbox). However, there are no alerts in end point specific profiling for *in vitro* mutagenicity (AMES test), *in vivo* mutagenicity (Micronucleus)

QSAR modelling using OASIS-TIMES (Optimised Approach based on Structural Indices Set–Tissue Metabolism Simulator) version 2.3 predicted that the chemical is positive for *in vitro* (AMES mutagenicity, chromosomal aberration (CA) and mouse lymphoma thymidine kinase assay (MLA)). However, the chemical structure was only in domain for Ames mutagenicity assay but this was due to the chemical being the part of the training set (non-guideline study in single strain). The chemical structure is out of domain for CA and MLA. Similarly chemical structure was out of domain for *in vivo* genotoxic predictions.

## Carcinogenicity

Diuron is classified as hazardous in the HCIS (Safe Work Australia) as ‘Carcinogenicity – Category 2; H351 (Suspected of causing cancer). The weight of evidence from animal studies including neoplasms observed in 2 species, different types of neoplasms with evidence of progression to malignancy and mechanistic evidence for bladder carcinogenesis support amending this classification to the hazard category ‘Carcinogenicity – Category 1B’ and hazard statement ‘H350 – May cause cancer’.

Diuron exposure via diet resulted in tumours in both rats and mice at different sites. In rats, carcinogenicity studies reported increase in urinary tract tumours in both sexes. In addition, pre-neoplastic urinary bladder lesions ware reported after 90 days exposure in both sexes (See **Repeat Dose Toxicity section**). A treatment related increase in uterine adenocarcinomas was also observed in female rats. In mice, a significant increase in incidences of malignant mammary gland tumours and benign ovarian luteoma were observed. A mechanistic study indicated that the bladder tumours were induced primarily via the intrinsic chemical cytotoxicity of diuron and not due to an increase in precipitates. These findings provide sufficient evidence of carcinogenic potential of diuron in animals.

In a 2 year combined chronic toxicity and carcinogenicity study reported to be similar to OECD TG 453, Wistar rats (50/sex/dose) received the chemical via their feed at 0, 25, 250 or 2500 ppm (equivalent to 0, 1, 10 and 111 mg/kg bw/day and 0, 1.7, 17 and 203 mg/kg bw/day in males and females, respectively). The mortality rate was low throughout the study. Urinary bladder carcinoma was observed at 2500 ppm in both males (67% vs 2% in controls) and females (22% vs 0% in controls). These lesions were preceded by bladder hyperplasia. One high dose male had transitional cell papilloma and 2 high dose males had transitional cell carcinoma in the renal pelvis. Transitional carcinoma incidence

was determined as statistically significant. Uterine adenocarcinoma was observed in females (20% vs 10% in controls) at the highest dose. The historical control data for this type of tumour was reported to be 2–20%; hence, the tumour incidence at the at the highest dose was at the upper bounds of the historical controls. No treatment related neoplasia was observed in other organs (ECHA 2021a; ECHA 2021b; ECHA 2024).

In a 2 year combined chronic toxicity and carcinogenicity study conducted similar to OECD TG 453, NMRI mice (50/sex/dose) received the chemical via their feed at 0, 25, 250 or 2500 ppm (equivalent to 0, 5.4, 50.8, 640.1 mg/kg bw/day and 0, 7.5, 77.5, 867 mg/kg bw/day in males and females, respectively). The mortality rate increased throughout the study; however, a clear relationship between treatment and mortality was not established. Statistically significant increases in the incidence of mammary gland adenocarcinoma (15.4% vs 5.1% in controls) were observed in females at the highest dose. Rare benign ovarian luteomas (15.9% vs 6.7% in controls) were also observed at this dose. Ovarian luteoma did not progress to malignancy and no increase in combined sex cord stromal tumours were noted. Therefore, this observation is not considered a strong indication of carcinogenicity (ECHA 2021a; ECHA 2021b; ECHA 2024).

**Mechanistic studies**

In a non-guideline study, male Wistar rats received the chemical via feed at 0 or 2500 ppm (equivalent to 0 and 130 mg/kg bw/day) with or without 10,000 ppm ammonium chloride for 15, 25, or 30 weeks. Diuron-fed rats had urinary amorphous precipitate and magnesium ammonium phosphate crystals similar to control animals. Groups treated with diuron and ammonium chloride showed decreased urinary pH and reduced amounts of urinary crystals and precipitate. Urothelial necrosis and hyperplasia were observed by light microscopy and scanning electron microscopy both in diuron- and in diuron and ammonium chloride-treated groups. Cytotoxicity and proliferative changes were mostly reversible. A modified comet assay developed *in vitro* with CHO cells showed that diuron did not induce DNA cross-links. These data suggest that cytotoxicity with consequent regenerative cell proliferation is a plausible mode of action for diuron rat urothelial carcinogenesis. It also demonstrates that the cytotoxicity is chemically induced and not due to urinary solids (Da Rocha 2010; ECHA 2021b)

In a non-GLP compliant study, male Wistar rats received the chemical by feed at 0 or 2500 ppm (equivalent to 0 or 295 mg/kg bw/day, respectively) for up to 8 weeks across various groups. The study demonstrated urothelial cell swelling began on day 1, and by day 28, extensive necrosis, exfoliation and piling up of cells suggestive of hyperplasia were observed. Significant cell proliferation was observed at 8 weeks. The study suggested that cell proliferation follows urothelial cytotoxicity (ECHA 2021b)

Another published study investigating the diuron metabolites in urine, DCPU was found to be a metabolite with highest concentration when exposed to high doses of diuron. DCPU was considered to be main metabolite responsible for cytotoxicity (ECHA n.d.-b).

Limited mechanistic data were available for the mammary tumours. There was reported to be no evidence of a promoting potential of diuron for mammary gland tumours in a 2-stage carcinogenesis model initiated with 7,12 -dimethylbenz(a)anthracene (DMBA) in female SD rats and Swiss mice (ECHA 2021a; ECHA 2024). In a developmental study aimed at examining effect of the early life stage exposure on susceptibility to mammary carcinogenesis (see **Reproductive and developmental toxicity** section) no mammary gland related changes were observed.

## Reproductive and development toxicity

Based on the available data, the chemical is not expected to cause adverse effects on fertility, sexual function or development following oral exposure. Developmental effects were mostly observed secondary to maternal toxicity.

**Reproductive toxicity studies**

In a GLP-compliant 2 generation reproductive toxicity study similar to OECD TG 416, Crl:CD BR rats (30/sex/dose) were administered the chemical in diet at 0, 10, 250 or 1750 ppm, starting 73 days prior to mating. Parental (P) males were dosed during mating and P females were dosed during mating, pregnancy and weaning. The F1 and F2 generations were dosed during growth, mating, pregnancy and up until weaning of the F2 generation (105 days after weaning for F1 generation). No treatment-related clinical signs of toxicity were observed in either P or F1 generations. In both P and F1 generations receiving 1750 ppm of the chemical, there were significant reductions in terminal body weights, body weight gain, food efficiency and food consumption, compared to the control group. The NOAEL for general toxicity was 250 ppm (approximately 15–25 mg/kg bw/day) based on decreased body weight gain in P and F1 adults. No effects were observed on reproductive performance (fertility index, mating index or length of gestation) in either the P or F1 generation. Reproductive functions (oestrous cycle and sperm measures) were not examined in P animals. There were no significant changes in histopathology of examined reproductive organs in any generation. The relative testes weight of P and F1 males were significantly increased, but this is likely to be due to decreases in absolute body weight. Additionally, there were no significant changes in the absolute weight or histopathology of the testes. For the P and F1 generations, the NOAEL for fertility and development was reported as 1750 ppm (APVMA 2011; ECHA 2024; REACH n.d.).

In a non-guideline 3 generation study (GLP status unknown) in rats (strain unknown), animals (16 females and 8 males) received diuron in the diet at 0 and 125 ppm (mg kg bw/day equivalent not provided). The exposure period for the first mating (F1a) was not stated but animals were reported to be 100 days of age, with a second mating (F1b) 10 days after weaning of first litter. Selected 16 females and 8 males from the second litters of each dose group (F1b) continued on their respective diets from weaning and mated (F2a) at 100 days of age and again (F2b) 10 days after weaning the first litter. F3 generation was produced from F2b using the same approach. 10 males and 10 females from the 2 F3 litters (F3a & F3b) of each dose group were euthanised at the age of 21 days and studied histologically for abnormalities. Limited result data were available. Reproductive performance was reported to be comparable for treated rats (125 ppm) and control. There were some reported effects on reduced body weights in litters of all generations. There were no treatment related effects on organ weights and histology (but it was not reported which organs were examined) (APVMA 2011).

In a non-GLP compliant non-guideline reproductive toxicity study, male Wistar rats (18/dose) were administered the chemical by gavage at 0, 125 or 250 mg/kg bw/day. The first group of males (9–10) were euthanised after 30 days of exposure. The second group of males were mated with untreated females. The dams were euthanised on gestation day (GD) 20.

In the first group, there were no significant changes in body weight during the study. However, terminal body weights were reduced by 5% in animals dosed at 250 mg/kg bw/day compared to the control group. No significant differences in absolute or relative weights of the reproductive organs were reported between treated and control groups. There were no significant differences in plasma testosterone concentration and sperm counts or morphology. Sexual behaviour assessment revealed slight and dose-responsive increase in

latencies to first ejaculation and first post-ejaculatory intromission. In addition, latencies to the first mount and first intromission were apparently higher for the 125 mg/kg per day group than either of the other groups. In the females mated with the 125 mg/kg bw/day group, there were significant decreases in maternal weight, uterus weight with foetuses and the number of foetuses in litters compared to controls. However, these effects were not observed in the females mated with 250 mg/kg bw/day group. Overall, none of the effects on sexual behaviour, fertility, pregnancy outcome, reproductive organ weights, sperm parameters or testosterone concentrations were considered consistent or dose dependent (ECHA 2024).

**Developmental toxicity studies**

In a GLP-compliant prenatal developmental toxicity study similar to OECD TG 414, pregnant Crl:SD BR rats (25/dose) were administered the chemical by gavage once daily at 0, 16, 80 or 400 mg/kg bw/day on presumed GD 6–15. Dams were euthanised on GD 20 and the foetuses examined. The NOAEL for maternal toxicity was 16 mg/kg bw/day based on significantly decreased body weight gain and food consumption in the higher dose groups. No treatment related effects on the pregnancy rate, litter size, foetal sex ratios or number of corpora lutea were reported. At 400 mg/kg bw/day, average foetal body weights were significantly decreased by 9% compared to controls. In this group, there was a significantly increased incidence of foetuses with skeletal alterations and delayed ossifications of the vertebrae and sternum. No visceral changes were reported in the foetuses from this group. Higher resorption rate was also observed at the highest dose level. The NOAEL for developmental effects was 80 mg/kg bw/day (APVMA 2011; ECHA 2024; REACH n.d.).

In a GLP-compliant prenatal developmental toxicity study similar to OECD TG 414, pregnant NZW rabbits (25/dose) were administered the chemical by gavage once daily at 0, 2, 10 or 50 mg/kg bw/day on presumed GD 7–19. Dams were euthanised on GD 29 and the foetuses examined. The NOAEL for maternal toxicity was 10 mg/kg bw/day based on decreased body weight gain and food consumption in the higher dose groups. One dam dosed at 50 mg/kg bw/day was aborted on GD 26 and showed weight loss and reduced food consumption. There were no treatment related clinical signs or gross lesions in any group. There were no significant changes in mean foetal weights, number of corpora lutea, number of implantations or the number of live, resorbed or dead foetuses. There were no significant increases in the incidences of external, soft tissue or skeletal alternations in any dosed group when compared to the controls. The NOAEL for developmental effects was reported as 50 mg/kg bw/day (APVMA 2011; ECHA 2024; REACH n.d.).

In a non-guideline non-GLP developmental toxicity study aimed at examining the effect of diuron on male reproductive organs, pregnant SD rats (12/dose) were administered the chemical in diet at 0, 500 or 750 ppm from GD 12 until the end of the lactation period (post-natal day (PND) 21). After weaning, male offspring received the chemical in feed at 0, 500 or 750 ppm until PND 42 (peripubertal age). No significant effects on the dams were reported. Compared to the controls, male offspring dosed with the chemical at 750 ppm exhibited a significantly reduced body weight gain throughout the study. In the offspring at PND 90 (48 days after cessation of treatment), there were no significant effects on reproductive organs (weights of testis, epididymis, vas deferens, ventral prostrate and seminal vesicles), sperm parameters (daily sperm production, sperm number, transit time in epididymis, sperm motility and morphology) and plasma testosterone levels. The NOAEL for developmental effects was 750 ppm (equivalent to 67 mg/kg bw/day) (ECHA 2024; Fernandes et al. 2012).

In a non-guideline non-GLP developmental toxicity study – aimed at examining effect of the early-life stage exposure on susceptibility to mammary carcinogenesis – pregnant SD rats (n=12/dose) were administered the chemical in diet at 0, 500, 750 or 1250 ppm from GD 12

until the end of the lactation period (PND 21). After weaning, female offspring received the chemical in diet at 0, 500, 750 or 1250 ppm until PND 51. At PND 51, female offspring received a single dose of 50 mg/kg bw/day 7,12- dimethylbenz(a)antrachene (DMBA) for initiation of mammary carcinogenesis. Female offspring were euthanised on PND 51 or 75 or 25 weeks (PND 226–233). In the pregnant dams, food consumption and body weight gain were reduced at 1250 ppm compared to the controls. There were no changes in gestational length and litter size.

In the F1 generation:

- Pup body weights were significantly reduced at all dose levels on PND 21 when compared to controls. Significant pup body weight differences were also observed on PND 10 in the 750 and 1250 ppm groups and PND 51 in the 1250 ppm group.
- Reproductive parameters indicative of sexual maturation (time of vaginal opening and oestrous cycle) were not significantly altered in the dosed groups.
- No significant differences were observed in the relative weight of ovaries and uterus in the treated groups when compared to controls. In the offspring at PND 75, absolute ovary weights were significantly decreased in the 1250 ppm dose group and the mean number of corpora lutea were significantly reduced in the 750 and 1250 ppm dose groups.
- No significant differences in hormone concentrations (serum oestrogen and progesterone at PND 51 and follicular stimulating hormone and luteinising hormone on PND 75) were observed between the treated and control groups.
- No mammary gland related changes were observed (ECHA 2024; Grassi et al. 2011).

## Endocrine effects

Based on the weight of evidence, the available data does not provide evidence of an adverse effect of the chemical from an endocrine mode of action. There is some evidence of endocrine activity based on *in vitro* studies. Results from *in vivo* studies are inconclusive but no effects on reproductive function were observed (ECHA 2024).

***Endocrine activity***

Several *in vitro* assays demonstrate that diuron has anti-androgenic activity (ECHA 2024; Kojima et al. 2004; Vinggaard et al. 1999; Orton et al. 2009; Bauer et al. 1998) and potential to be an agonist of the aryl hydrocarbon receptor (AhR) (Noguerol et al. 2006; Zhao et al. 2006, ECHA 2024). It is reported that diuron may have weak interaction with the oestrogen receptor (ECHA 2024).

As per US EPA ToxCast dashboard, *in vitro* assays investigating thyroid pathways involved in endocrine disruption indicate that diuron does not activate the agonism and antagonism of the thyroid receptor signalling pathway. Diuron induced a downregulation in rat thyroid tissue derived thyroid peroxidase catalytic activity by 50% at 40 µM compared to DMSO in the ToxCast assay NCCT_TPO_AUR_dn (ECHA 2024). Diuron exposure in 2 subacute inhalation studies in rats led to effects on thyroid hormones levels (T3 and T4) and thyroxin-binding capacity (TBC) indicating reduced thyroid function.

***Adverse effects***

Reproductive toxicity studies show diuron treatment has no effects on reproductive organs. In a chronic repeat dose toxicity study in dogs, increased relative testicle weight at the highest dose was considered due to reduced body weight and there were no corresponding histopathological changes. The available OECD 416 study (see **repeated dose toxicity** section) was conducted before the guideline was updated. Therefore, it did not include a number of investigations including effects on spermatogenesis (semen quality: sperm numbers, morphology and motility), changes in oestrus cyclicity and on ovaries (corpora lutea, follicles). However, the lack of effects in reproductive organs in repeated dose toxicity, chronic toxicity and carcinogenicity studies, as well as data from open literature are relevant for reducing the uncertainties related to the missing endpoints in the reproductive toxicity studies associated with endocrine disruption (ECHA 2024).

Carcinogenicity studies report increases in the incidence of tumour types that may have endocrine-mediated modes of action, including uterine adenocarcinomas in rat, and mammary gland adenocarcinoma and ovarian luteomas in mice. The WHO/IPCS framework for assessing endocrine disruptors requires a causal link between observed effects and an endocrine mode of action (WHO/IPCS 2002). Currently, there is not sufficient evidence to indicate that these adverse effects are due to an endocrine mode of action (ECHA 2024).

In available *in vivo* studies, there was no remarkable effects on relative thyroid weights and histopathology did not reveal any adverse effects on the thyroid. Effects on thyroid functioning in subacute inhalation studies were observed in the presence of systemic toxicity (hematology and spleen) (see **Repeated dose toxicity** section). Further studies are required to evaluate if changes in thyroid are due to endocrine mode of action (ECHA 2024c).

# Environmental exposure

Industrial uses of diuron are expected to result in both diffuse and point source emissions into the environment.

The main industrial use of diuron is as a preservative in sealants, adhesives, paints, coatings and renders. In these products, diuron will slowly move to the product surface to provide long term protection from algae and other biotic sources of damage. Diuron may slowly leach from painted surfaces and from treated construction materials that are exposed to rainfall (Burkhardt et al. 2012; Paijens et al. 2020; Schoknecht et al. 2009; The Danish Environmental Protection Agency 2018). The resulting run-off containing this chemical will then be discharged directly onto soil or into surface waters through the stormwater drainage systems. These sources may contribute to cumulative diffuse releases of diuron into the environment.

Additional diffuse releases of diuron may occur from the domestic use of diuron containing products through washing and disposal processes. Examples include the cleaning of paint brushes or other painting equipment. These releases will occur to stormwater, sewer, or to the soil around buildings.

Factories that manufacture industrial products involving diuron, such as paint formulation facilities or polymer manufacturers, may release diuron to municipal STPs. The release of trade waste in this way is regulated by local council, state authorities and water management utilities and typically requires permits prior to the disposal of such residues. Depending on the degradation and partitioning processes of diuron in STPs, the release of diuron in treated

effluent to rivers or oceans is expected. Emissions to soil through application of biosolids to agricultural land are also possible.

Diuron also has significant uses in Australia in agricultural and related products. Agricultural uses commonly involve application onto plants or into soils, with associated potential for partial run-off into surface waters. As noted above, an extensive suite of regulatory restraints intended to minimise environmental effects, including run-off occurrence, is in operation (see **Existing Australian regulatory controls** section). It is likely that a significant proportion of diuron releases to the environment originate from non-industrial sources.

## Environmental fate

### Partitioning

Diuron partitions mainly to soil and the water compartments when released into the environment.

Diuron is moderately soluble in water and is not expected to ionise at environmentally relevant pH. Diuron is very slightly volatile and is not expected to volatilise to air from surface waters or moist soils.

Measured organic carbon adsorption coefficients ($K_{OC}$) for diuron range from 366–1,750 L/kg (APVMA 2011b). Diuron is expected to have low to moderate mobility in soils. In water/sediment systems, diuron is expected to partition mostly into the aqueous fraction rather than absorb to sediments.

Fugacity modelling (Level III) suggests that diuron released to soil is expected to stay in soil (> 97%) with minor partitioning to the water compartment (< 3%). Diuron directly released to water is predominately expected to stay in water (> 96%), with minor partitioning to sediment (< 4%). Volatilisation to air is negligible in both scenarios (US EPA 2017).

### Degradation

Diuron is persistent in soil and water. Some degradants of diuron are also persistent.

Notable degradants of diuron include:

- N-(3,4-dichlorophenyl)-N′-methylurea (DCPMU; CAS RN 3567-62-2)
- N-(3,4-dichlorophenyl)-urea (DCPU; CAS RN 2327-02-8)
- 3,4-dichloroaniline (3,4-DCA; CAS RN 95-76-1).

#### *Degradation in soil*

Studies investigating the biodegradation of diuron in soils indicate low overall mineralisation of diuron. Two soil studies that included an analysis of diuron in soil found mineralisation rates of 31.8% after 101 days (European Food Safety Authority 2005) and 8.9% after 365 days (REACH n.d.). These studies indicate that diuron will have an ultimate half life in soil greater than 182 days (Environment Canada 2011). While other soil studies reported field dissipation half lives shorter than this value, those half lives include losses from runoff, leaching, and from the transformation of diuron to other persistent degradants (Gooddy et al. 2002; Guzzella et al. 2006).

Degradation of diuron in soil likely occurs through the aerobic demethylation pathway to eventually form 3,4-DCA (Stasinakis et al. 2009; Tixier et al. 2001; Vroumsia et al. 1996). Soil degradation studies on 3,4-DCA show that this chemical has a soil mineralisation half life of greater than a year (European Chemicals Bureau 2006).

***Degradation in water and sediments***

A ready biodegradability test using sludge inoculation (OECD TG 301F) found no degradation of diuron after 28 days incubation (REACH n.d.). Another ready biodegradation study using STP effluent inoculation (OECD TG 301D) found no biodegradation of diuron after 28 days based on theoretical oxygen demand (Hensen et al. 2018). Biodegradation studies on 3,4-DCA indicate that this potential degradant is expected to undergo limited biodegradation (European Chemicals Bureau 2006).

In estuary waters of the Brisbane River, a degradation half life of 66 days was determined for diuron after monitoring its residues over a 37 week period (Álvarez-Ruiz et al. 2021). This half life considered all combined degradation that occurred through hydrolysis, photolysis and biodegradation pathways in the natural environment (Álvarez-Ruiz et al. 2021).

In simulated water sediment systems using natural river and pond sediments, mineralisation of diuron was only 2–30% of applied radioactivity after 120 days (European Food Safety Authority 2005), indicating limited ultimate degradation.

Diuron is stable to hydrolysis in the pH range 4 to 9, with less than 10% degraded under these pH conditions at 50°C after 5 days in the dark, according to a study conducted according to OECD TG 111 (REACH n.d.). No degradation in pure water in the 5 to 8 pH range was observed in another hydrolysis study (Salvestrini et al. 2002).

Available information on the photolysis of diuron is mixed. An aqueous solution of diuron exposed to natural light for five months followed first order degradation with a half life of 231 days (Jirkovský et al. 1997). Studies under laboratory conditions with simulated light suggest shorter photolytic half lives. An aqueous photolysis half-life of 43 days under laboratory conditions using continuous irradiation by a xenon lamp for 15 days was determined in a photodegradation study that followed US EPA guidelines (REACH n.d.).

## Bioaccumulation

Based on a log $K_{OW}$ value of < 4.2 and measured and calculated bioconcentration factors below the Australian categorisation threshold value (BCF ≥ 2000) (EPHC 2009), diuron has low bioaccumulation potential.

A study according to OECD TG 305 C, modified for use with the mussel Mytilus edulis, determined a whole body bioconcentration factor (BCF) of 5.2 L/kg (REACH n.d.). Another study determined BCFs ranging ≤ 2.9 to 14 L/kg in the common carp (Cyprinus carpio) (Bengtson Nash et al. 2006; NITE n.d.).

Based on the log $K_{OW}$ of 2.89, calculated BCF values for diuron are below 50 L/kg (US EPA 2017). This is consistent with the experimental values in mussels and fish.

A study measuring concentrations of diuron in biota in a food web in the Vaccarès lagoon in France reported biomagnification factors (BMF) greater than 1 between multiple trophic levels (Roche et al. 2009). However, due to uncertainties such as lack of measured environmental concentrations and the unknown impact of seasonal pesticide exposures, this result has not been considered as strong evidence for bioaccumulation.

### Environmental transport

Diuron is not volatile and is not expected to be transported through the atmosphere.

Diuron is persistent in the aquatic environment and has low to medium mobility in soils. This indicates that diuron could have the potential for long range transport in water, as the chemical will be resistant to degradation and potential for only limited proportions of the chemical to settle out to sediments and particulates. However, no information has been identified that suggests that diuron has been detected in remote regions of the world far from sources of release.

## Predicted environmental concentration (PEC)

The predicted environmental concentrations of diuron in this evaluation are based on the levels of the chemical measured in stormwaters, STP effluents, and estuaries of Australian cities. All PECs are considered conservative as they are derived from data expected to capture releases of diuron from both industrial and non-industrial uses.

Based on the available domestic monitoring data, a PEC of 0.61 µg/L is used for stormwaters, 0.34 µg/L for STP effluents and 0.096 µg/L for estuaries.

A PEC of 0.33 µg/kg dry weight was derived for soils amended with diuron containing biosolids, based domestic STP sludge monitoring data.

***Australian monitoring data***

Concentrations of diuron in the Australian environment are expected to result both from industrial and non-industrial uses of diuron (see environment exposure section).

Diuron in the urban environment may originate from industrial use of paints, coatings, renders, and adhesives, or non-industrial uses as an algaecide or an herbicide in urban areas.

Non-industrial herbicide use of diuron is widespread in agricultural areas in Australia. Therefore, the dominant source of diuron in agricultural areas will be non-industrial.

Monitoring studies from urban areas have the highest chance of detecting diuron contributions from industrial uses. However, these studies regularly measure total diuron concentrations and do not differentiate between industrial and non-industrial sources of diuron.

### *Australian urban stormwater*

Diuron measurements in Australian urban stormwaters are reported in 4 studies. The results are tabled below. All concentrations are in micrograms per litre (µg/L):

| Location | Years | Sampling | Range | Reference |
|---|---|---|---|---|
| NSW, QLD, VIC, WA | 2011-2014 | 62 samples, 10 sites | < 0.01–1.67 | Rippy et al. 2017 |
| Melbourne | 2011-2012 | 30 samples, 5 sites | < 0.01–0.087 | Allinson et al. 2017 |
| Adelaide | 2011-2012 | 4 samples, 2 sites | 0.033–0.063* | Page et al. 2014 |
| Darwin | 2010-2011 | 6 samples, 2 sites | < 0.0–0.09 | French et al. 2015 |

*this range is a range of 2 averages.

Aggregating the measurements of diuron across these studies, the median concentration is approximately 0.053 µg/L, with a 95$^{th}$ percentile concentration of approximately 0.61 µg/L. The 95$^{th}$ percentile value is taken as the PEC for diuron in urban stormwater. This value represents a comparatively high concentration of diuron. This value is also protective when considering the uncertainty in industrial and non-industrial contributions to residues in the urban environment.

### *Australian STPs*

Measurements of diuron in effluents of Australian STPs are reported in 6 studies. The results are tabled below; all concentrations are in micrograms per litre (µg/L):

| Location | Years | Sampling | Range | Reference |
|---|---|---|---|---|
| Victoria | 2024 | 4 samples, 4 sites | 0.01–0.11 | Lewis et al. 2025 |
| Australia (all states) | 2019 | 22 pooled samples, 22 sites | < 0.04–0.25 | Knight et al. 2023 |
| Queensland | 2015 | 1 sample, 1 site | 0.34* | Leusch et al. 2018 |
| Perth | 2012 | 1 sample, 1 site | 0.13* | Tang et al. 2014 |
| Darwin | 2010-2011 | 9 samples, 3 sites | < 0.01–0.27 | French et al. 2015 |

*Only value available

Results from Lewis et al. (2025), Knight et al. (2023), and Tang et al. (2014) indicate that diuron concentrations in STP effluent may be similar or higher than influent concentrations. The reasons for this are not clear and were not investigated further.

An additional monitoring study reported higher concentrations of diuron in STP effluent (Clokey et al. 2023). 24 hour composite effluent samples were collected from 10 STPs across Queensland, Victoria, New South Wales, and Tasmania. The reported concentrations ranged from 0.11–3.97 µg/L and were consistently higher than concentrations observed in all other studies. The reasons for this are unclear; however, it is noted that the analytical method had a low recovery (51%) and a relatively high limit of detection (0.19 µg/L). The results of this study are not consistent with other studies. Therefore, the results have not been considered in PEC calculation.

The diuron concentration of 0.34 µg/L from Leusch et al. (2018) is taken as the PEC for diuron in STP effluents. This value is considered to be conservative, as it is higher than most measured concentrations of diuron across multiple studies.

Information on diuron in Australian STP sludge is available from 2 studies:

- Diuron was measured in sludge taken from a STP in NSW as part of a simulation study. The concentration of diuron in the sludge was reported as 50 µg/kg dw (Li et al. 2022).
- Samples of diuron in primary sludge were taken from a STP in NSW over a 12 week period. The reported average concentrations were 0.22 µg/L in the liquid phase, and 21 µg/kg dw in the solid phase (Yang et al. 2016).

***Australian surface waters***

Extensive monitoring data of diuron in Australian rivers, estuaries and coastal waters is available. However, much of the available data are strongly linked to non-industrial uses of diuron.

As this evaluation is focussed on the industrial use of diuron, measurements limited to locations in areas of low agricultural value according to the 2020-21 Australian Agricultural Census (ABARES n.d.) have been considered.

Diuron was detected in 86.5% of urban wetland water samples during a study of 111 urban wetlands in Melbourne, Victoria, over the October 2020 to January 2021 period, but was not detected in sediments (Pettigrove et al. 2023). Diuron was also detected in 100% of water samples from 3 urban streams in Sydney, NSW over the October 2017 to March 2018 period (Allinson M. et al. 2023). These studies did not quantify the concentration of diuron in the samples.

Diuron was measured in surface water upstream and downstream of 5 Victorian STPs (Lewis et al 2025). The concentration of diuron ranged from < 0.01–0.02 µg/L upstream of the STPs and ranged from < 0.01–0.04 µg/L in the mixing zone 2–15 km downstream of the STPs.

A diuron concentration of 0.02 µg/L was measured in a small creek in the Gold Coast urban area (Leusch et al. 2018). The grab sample was taken in November 2015.

Quantitative sampling has been regularly performed across many Queensland waterways through the work of the Water Quality and Investigations team in the Queensland Department of the Environment, Tourism, Science and Innovation (Queensland Government n.d.). However, many of the sampling locations are either within or downstream of areas with significant agricultural (non-industrial) activity. Other sampling locations are upstream of urban areas where contributions from industrial uses are expected to be minimal.

In the dataset, data for diuron in surface waters from an urban area are available for the Ross River in Townsville. Diuron concentrations were 0.02 µg/L or below in 277 out of 285 measurements taken over the years 2017–2024. The remaining 8 measurements were at or below 0.05 µg/L diuron.

Studies monitoring diuron concentrations were found in the literature, for the Sydney, Brisbane, and Melbourne estuaries. Diuron was detected in 100% of samples in these post-2012 studies (Álvarez-Ruiz et al. 2021; Anim et al. 2020). The highest concentration of diuron, 0.096 µg/L, was found in the Sydney estuaries discharging into the harbour. This

concentration is taken as the PEC for diuron in surface waters and is considered conservative due to expected contributions from anti-fouling and other non-industrial uses.

***Australian soil and sediments***

No Australian monitoring information of diuron in non-agricultural soils, including urban soils receiving urban run-off, were identified.

Biosolids obtained from STPs may be applied to agricultural soils. A PEC for diuron in soil resulting from biosolid application was calculated considering the highest observed concentration of diuron in Australian sludge (50 µg/kg dw), typical biosolid application rates, and a soil bulk density of 1,500 kg/m$^3$. The PEC of diuron in Australian soils amended with biosolids is calculated as 0.33 µg/kg dw (EPHC 2009). This calculation does not consider contributions from non-industrial uses of diuron, which are expected to result in higher concentrations.

No Australian monitoring information of diuron in relevant sediments was identified.

A range of PECs for sediment were calculated using the equilibrium partitioning method, the reported $K_{OC}$ values for diuron and the PECs of diuron in STP effluent and surface waters. The estimated PECs of diuron in urban sediment range from 0.73–23.8 µg/kg dw.

***International monitoring studies***

Monitoring studies in many countries have shown that diuron is a major contaminant of rivers, groundwaters, estuaries and ports due to the combined inputs from agricultural and industrial uses of this chemical (Blanchoud et al. 2007).

Average concentrations in the range 0.007–0.1 µg/L and highest of 0.27 µg/L are reported for stormwaters in several European countries (Nickel et al. 2021; Paijens et al. 2021; Pitarch et al. 2016). Higher concentrations are reported for North America, with an average of 0.54 µg/L and highest of 1.79 µg/L in stormwaters from 17 States (Ensminger et al. 2013; Masoner et al. 2019).

Similar levels (average range 0.026–0.32 µg/L and highest 2.39 µg/L) were reported for effluents from water treatment plants in various European (Kõrgmaa et al. 2020; Launay et al. 2016; Masiá et al. 2013; Munz et al. 2017) and Asian countries: average range 0.019–0.2 µg/L and highest 4.02 µg/L (Kim and Kim 2024; Qiang et al. 2024).

Diuron concentrations in groundwater have been reported in the range 0.002 to 0.076 µg/L in America (Elliott et al. 2024; Stefano et al. 2022) and 0.01 to 11.6 µg/L in Europe (Hensen et al. 2018; Hermosin et al. 2013). Most residues in marinas and commercial ports (ranging 0.002–2.19 µg/L), and are mostly attributed to emissions from antifouling paints (Ansanelli et al. 2017; Martínez et al. 2001; Montes et al. 2023; Okamura et al. 2003).

# Environmental effects

Diuron is an inhibitor of the photosystem II protein complex in the chloroplasts of cells. Diuron is generally highly toxic to all organisms reliant on photosynthesis, including algae, cyanobacteria and higher plants.

Emerging evidence indicates that diuron is also toxic to fish at low concentrations and chronic exposures, particularly when exposed during early life stages.

## Effects on aquatic Life

### Acute toxicity

The following measured median lethal concentration (LC50) and median effective concentration (EC50) values were retrieved from the scientific literature (Magnusson et al. 2008), the ECOTOX Knowledgebase (US EPA n.d.), and the APVMA review of diuron (APVMA 2011b):

| Taxon | Endpoint | Method |
|---|---|---|
| **Fish** | 96 h LC50 = 4.19 mg/L | *Oncorhynchus clarkii* (Cutthroat trout)<br>Static, nominal |
| **Invertebrate** | 48 h LC50 = 1.4 mg/L | *Daphnia magna* (waterflea)<br>OECD TG 202<br>Static, nominal |
| **Algae** | 72 h EC50 = 0.0077 mg/L | *Navicula sp.* (diatom algae)<br>Static, nominal<br>Growth rate |

Diuron is toxic to algae in acute exposures. It also causes effects to some marine organisms, with an endpoint of 24-hour LC50 of 4.8 mg/L for larvae of the coral *Acropora tumida* (Bao VWW et al. 2011).

### Chronic toxicity

The following measured No Observed Effect Concentrations (NOEC) were retrieved from the ECOTOX Knowledgebase (US EPA n.d.), and the APVMA review of diuron (APVMA 2011b):

| Taxon | Endpoint | Method |
|---|---|---|
| **Fish** | 60 d NOEC = 26 µg/L | *Pimephales promelas* (Fathead minnow)<br>Static, nominal<br>Mortality |
| **Invertebrates** | 8 d NOEC = 10 µg/L | *Cerodaphnia dubia* (waterflea)<br>Semi-static, nominal<br>Mortality |
| **Algae** | 96 h NOEL = 0.44 µg/L | *Pseudokirchneriella subcapitata* (Green algae)<br>OPP 123-2<br>Static |

Diuron is toxic to fish, daphnia, and algae in long-term exposures.

A study on the corals *Acropora millepora* and *Pocillopora damicornis* indicated a 96 h NOEC (survival) of 0.1 mg/L for both species (Negri et al. 2005). However, bleaching occurred in *P.damicornis* at concentrations as low as 0.001 mg/L.

A study performed according to OECD TG 234 indicated a 35 day NOEC of 1 µg/L for post-hatch survival of zebrafish (*Danio rerio*) embryos to diuron (ECHA 2024).

Other related non-guideline chronic studies have indicated toxic effects to vertebrates exposed to low concentrations of diuron as embryos. Impacts on reproduction endpoints have been observed in studies on marine medaka (*Oryzias melastigma*). Hatching success was significantly reduced for marine medaka reared for 6 months in seawater containing approximately 0.5 µg/L diuron (Bao Y et al. 2022; Zhou et al. 2022). In another study, Japanese medaka (*Oryzias latipes*) embryos exposed to 0.2 µg/L diuron had significantly reduced survivability (Li et al. 2021).

### Species sensitivity distributions (SSDs)

Diuron has a specific toxic mode of action to plants and algae that inhibits photosynthesis. As a result, the established approaches to calculating species sensitivity distributions (SSDs) for diuron generally only consider endpoints for phototrophic species.

#### *Australian and New Zealand Guidelines for Fresh and Marine Water Quality*

The Australian and New Zealand Guidelines for Fresh and Marine Water Quality provide default guideline values for diuron in freshwater and in marine waters. Endpoints for fish and other aquatic organisms were not included in the derivation of the guideline values.

Very high reliability freshwater values were derived using chronic data from 16 freshwater phototrophic species from 4 phyla (ANZG 2025). The guidelines include a value of 0.52 µg/L for 95% species protection and a value of 0.88 µg/L for 90% species protection.

High reliability marine guideline values were derived using chronic data from 12 marine phototrophic species from 7 phyla and 7 classes (ANZG 2024). The guidelines include a value of 0.59 µg/L for 95% species protection.

## Effects on terrestrial Life

Ecotoxicity information is available for terrestrial organisms. Selected information has been summarised.

Acute 72 hour LC50 values of 1.17 mg/kg dry soil and LC10 of 0.37 mg/kg dry soil have been determined for the earthworm *Eisenia andrei* (Lackmann et al. 2018). Springtails (*Folsomia candida*) had 28 day LC50 of 703 mg/kg dry soil and NOEC of 10 mg/kg dry soil, respectively (Campiche et al. 2006).

Average observed 21 day NOEL endpoints for growth of edible crop plants and cotton range from 0.067 mg/kg soil for tomatoes to 1.4 mg/kg soil for corn (US EPA 1992). For gardening plants, growth NOELs are in the range 6.0 mg/kg soil for daffodils, tulips and iris (Al-Khatib 1996) to 25 mg/kg soil for common morning-glory (Cole and Coats 1973). Broad leaved trees, including fruit trees, have NOELs in the range 2.7 mg/kg soil for cherry trees and 5.3 mg/kg for various forest trees (Lawrie and Clay 1989) to 21.3 mg/kg soil for apple trees (Mukula 1962).

## Effects on sediment dwelling life

Some ecotoxicity information is available for sediment dwelling organisms.

An acute 96 hour LC50 value of 1.2 mg/L was observed for the freshwater stonefly (*Pteronarcys californica*) (Mayer and Ellersieck 1986). A chronic 10 day survival NOEC of 1.9 mg/L was observed for larvae of the midge *Chironomus tentans* (Nebeker and Schuytema 1998).

## Endocrine effects

Diuron causes chronic effects in fish at low exposure concentrations, including causing impacts on reproductive success. Mechanistic studies demonstrate that there may be multiple modes of action involved. While diuron appears to have endocrine activity, currently, a clear causal pathway between observed effects and a defined endocrine mode of action cannot be drawn.

The WHO/IPCS framework for assessing endocrine disruptors requires a causal link between observed effects and an endocrine mode of action (WHO/IPCS 2002). Many of the observed effects of diuron are not unique to alterations in endocrine function.

The majority of studies considered in this evaluation have not been performed to OECD guidelines, but they are considered reliable for weight of evidence consideration in line with the OECD conceptual framework for evaluating chemicals for endocrine disruption (OECD 2018). The studies considered in this evaluation have been assigned levels in line with the framework:

- Level 5 – *in vivo* assays providing comprehensive data on adverse effects on endocrine relevant endpoints over extensive parts of the life cycle of the organism.
- Level 4 – *in vivo* assays providing data on adverse effects on endocrine relevant endpoints.
- Level 3 – *in vivo* assays providing data about selected endocrine mechanisms or pathways.
- Level 2 – *in vitro* assays providing data about selected endocrine mechanisms or pathways.

The study design, including exposure concentrations, was also considered when determining the reliability and relevance of studies below.

***Endocrine activity***

While *in vitro* evidence suggests potential endocrine modes of action of diuron, *in vivo* results in fish demonstrate a variety of hormonal changes.

Several *in vitro* assays demonstrate that diuron has anti-androgenic activity (Bauer et al. 1998; Kojima et al. 2004; Orton et al. 2009; Vinggaard et al. 1999) and potential to be an agonist of the aryl hydrocarbon receptor (AhR) (Noguerol et al. 2006; Zhao et al. 2006; further discussion in ECHA 2024).

However, *in vivo* assays at similar exposure concentrations suggest a range of hormonal effects. These include anti-androgenicity (Boscolo Pereira et al. 2015; Nam et al. 2023), estrogen agonistic effects (Felício et al. 2016; Zhou et al. 2022), and anti-estrogenic behaviour (Nam et al. 2023).

*In vivo* evidence for some metabolites of diuron, such as 3,4-DCA, also suggest anti-androgenic effects on hormone levels in fish (Boscolo Pereira et al. 2015; Pereira Boscolo et al. 2018).

***Adverse effects in whole organisms***

Evidence from multiple *in vivo* studies shows that diuron exposure at low concentrations causes effects in fish. Some of these effects may be linked to endocrine activity. However, consistent effects that align with modes of action suggested by the *in vitro* data are not observed. Additionally, many endpoints are also influenced by general toxicity and the relative contribution of endocrine and non-endocrine effects cannot be determined.

A multigenerational level 5 study on marine medaka (*Oryzias melastigma*) observed that diuron reduced hatching success of F1 embryos from F0 pairs reared in 0.5 µg/L or 5 µg/L diuron (Bao Y et al. 2022). No reason for this effect was suggested and no sex hormone analysis or histopathology was performed on F0 fish. The F1 generation were then reared in clean seawater. Analysis of the unexposed F1 females showed significantly reduced female gonadosomatic index (GSI), reduced sex hormones, and reduced expression of vitellogenin genes. These effects were attributed to an epigenetic effect, and not a previously known mode of action. Analysis of F1 male fish showed no significant changes to sex hormones and that testis development was unaffected.

A related level 4 study reared marine medaka (*Oryzias melastigma*) in diuron concentrations ranging from 0.005 µg/L to 5 µg/L for 6 months (Zhou et al. 2022). Reduced fertilisation rate and hatching success was observed for F1 embryos from F0 pairs reared in 0.5 µg/L or 5 µg/L diuron. Analysis was performed on the F0 males. Significant reductions in GSI were observed across all concentrations. Significantly increased 17β-oestradiol levels were only observed in the 0.5 µg/L treatment, while reductions in sperm production were observed only in the 0.05 µg/L and 5 µg/L exposure groups. No significant reduction in testosterone was observed in any exposure group. The authors attributed to these impacts to potential AhR agonist activity.

Significant mortality was observed in a level 3 study that exposed Japanese medaka (*Oryzias latipes*) embryos to diuron (Li et al. 2021). The non-guideline study observed that the survival rate reduced from 87% to 63% in the 0.2 µg/L exposure group. The reported exposure conditions are unclear whether exposure was limited to 10 day exposure of embryos or constant exposure until sexual maturity. Analysis of secondary sex characteristics indicated that feminisation of male fish had also occurred. The responsible mode of action for this is unknown. The authors suggested that the observed increased *cyp19a* gene expression was reflective of increased 17β-oestradiol (E2) production in male fish. However, no sex hormone analysis was performed to confirm this, and no gonadal histopathology was performed. Additionally, no link was made between the decrease in survivability and the feminisation effect.

Limited evidence is available that shows co-incidence of impacts on hormones and changes in reproductive organs.

One level 4 study significantly reduced 11-ketotestosterone levels alongside reductions in GSI in juvenile seabream (*Pagrus major*) and black rockfish (*Sebastes schlegelli*) exposed to 10 µg/L diuron for 60 days were observed (Nam et al. 2023).

Exposure to 0.2 µg/L of the metabolites of diuron (DCPMU, DCMU, 3,4-DCA) significantly reduced testosterone and 11-ketotestosterone levels in adult male Nile tilapia (*Oreochromis niloticus*). Significant histopathological changes in testes and reductions in GSI were also observed in this level 3 study.

Many other studies, with similar or greater diuron concentrations, show no effect on sexual development.

A level 4 OECD TG 234 fish sexual development test performed on zebrafish (*Danio rerio*) was reported in the evaluation from Finnish Safety and Chemicals Agency (Tukes) (ECHA 2024). No significant endocrine relevant effects were observed up to 100 µg/L diuron. A generic ecotoxicity endpoint of reduction in post-hatch survival was observed with a NOEC of 1 µg/L. Other level 3 studies on Nile tilapia (*Oreochromis niloticus*) at 0.1–0.2 µg/L diuron for 25 days show no impacts on GSI or gonad morphology (Boscolo Pereira et al. 2015; 2016).

Overall, the available studies demonstrate that diuron does have adverse effects on whole fish at low and environmentally relevant exposure concentrations. However, a consistent causal mode of action that explains the breadth of observed effects occurring at similar exposure concentrations is not evident. While endpoints such as changes in GSI, reduced hatching success, reduced survivability, and reduced fecundity, may be influenced by endocrine active substances, they may also be impacted by non-endocrine mode of actions (ECHA & EFSA 2018; OECD 2018).

***Endocrine assessments from international agencies***

Recently, the Finnish Safety and Chemicals Agency (Tukes), on behalf of the European Chemicals Agency (ECHA) (ECHA 2024), evaluated the available endocrine relevant information for diuron. They concluded, under the ECHA/EFSA framework (ECHA & EFSA 2018), that the observed effects of diuron were 'both adverse and highly likely to be endocrine active substance mediated', and that a 'conclusion on biologically plausible link can be reached without detailed [mode of action] analysis based on existing knowledge and the lack of [non-endocrine mode of action]'.

This determination is still subject to review by the ECHA Committee for Risk Assessment.

## Predicted no-effect concentration (PNEC)

The following PNECs for diuron have been considered, based on the Australia and New Zealand Guidelines (ANZG) default guideline values:

- 0.88 µg/L for diuron in stormwater, in line with the 90% freshwater species protection value and the highly disturbed nature of stormwater-affected waters. This value is expected to be protective as the guideline values are derived from chronic data and stormwaters are generally expected to be short-term exposures (ANZG n.d.).
- 0.52 µg/L for diuron in STP effluents, in line with the 95% freshwater species protection value
- 0.59 µg/L for diuron in urban estuaries, in line with the 95% marine species protection value.

The ANZG default guideline values were derived only using phototrophic species. The recent chronic fish studies showing that diuron impact hatching success in fish were not considered in the calculation. However, the chosen levels of protection are in line with the observed effect concentrations for fish in these studies and they are expected to be sufficiently protective.

For assessment of soils amended with biosolids from STPs, a PNEC of 6.7 µg/kg dw was derived from the lowest measured chronic endpoint for tomatoes (21 d NOEL = 67 µg/kg soil). An assessment factor of 10 was used, as reliable chronic ecotoxicity data are available for at least 2 trophic levels in soil biota, including multiple data for plants which are the

trophic level most sensitive to diuron (EPHC 2009).

# Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed chemical according to domestic environmental hazard thresholds (DCCEEW n.d.) is presented below:

## Persistence

Persistent (P). Based on poor degradation results and measured half lives exceeding 60 days in water and 180 days in soil, diuron is categorised as Persistent.

## Bioaccumulation

Not Bioaccumulative (Not B). Based on measured bioconcentration factors (BCF) of 5.2 in mussels and log $K_{OW}$ value less than 4.2, diuron is categorised as Not Bioaccumulative.

## Toxicity

Toxic (T). Based on acute ecotoxicity endpoints below 1 mg/L and chronic ecotoxicity endpoints below 0.1 mg/L, diuron is categorised as Toxic.

# Environmental risk characterisation

Based on the PEC and PNEC values determined above for stormwaters, STP effluents, estuaries and soil amendments, the following Risk Quotients (RQ = PEC ÷ PNEC) have been calculated for release of diuron into the aquatic and soil environments:

| Compartment | PEC | PNEC | RQ |
|---|---|---|---|
| **Urban stormwaters** | 0.61 µg/L | 0.88 µg/L | 0.68 |
| **STP effluents** | 0.34 µg/L | 0.52 µg/L | 0.65 |
| **Urban estuaries** | 0.096 µg/L | 0.59 µg/L | 0.16 |
| **Soil (via biosolids application)** | 0.33 µg/kg | 6.7 µg/kg | 0.05 |

The calculated RQ values for diuron in various surface waters and in biosolid amended soil are less than 1. Environmental levels of diuron are expected to be below levels of concern.

The RQ calculations rely on concentrations from Australian monitoring data which may include contributions from both industrial and non-industrial uses. Additionally, the surface water PECs have been selected from maximum or high percentile values. Typical concentrations are expected to be lower than the chosen PEC values. As such, the RQ calculations are expected to be conservative for the industrial uses of diuron.

Emerging evidence indicates that diuron can cause chronic toxic effects in fish at concentrations as low as 0.5 µg/L. It is unclear whether these effects are due to endocrine

activity or another mode of action. Based on the weight of evidence, the above risk calculation is considered to be sufficiently protective of any currently observed population relevant fish endpoints.

### Uncertainty – Environmental Evaluation

This environmental evaluation was conducted based on a set of information that may be incomplete or limited in scope. Some relatively common data limitations can be addressed through use of conservative assumptions (OECD 2019) or quantitative adjustments such as assessment factors (OECD 1995). Others must be addressed qualitatively, or on a case-by-case basis (OECD 2019).

The most consequential areas of uncertainty for this environmental evaluation are:

- The available Australian monitoring data may overestimate the risks from industrial uses of diuron to the environment. The current monitoring data may contain residues from both non-industrial and industrial uses of diuron. The environmental risks of the industrial use alone cannot be determined without targeted monitoring from areas dominated by the industrial use of diuron.
- There are potential but unclear additional risks to aquatic life based on emerging evidence of chronic toxicity to fish. The PNECs considered in the risk calculation are currently expected to be protective of population relevant effects at relevant environmental exposure concentrations. However, reconsideration of the PNEC may be required if new information becomes available on the long-term effects of diuron on aquatic vertebrates.
- The evaluation of the endocrine activity of diuron indicated a variety of modes of action, and inconsistency between effects observed *in vitro* and *in vivo* in aquatic life. Re-evaluation of the endocrine effects of this chemical may be required if new information becomes available to demonstrates a convincing link between the endocrine activity of diuron and adverse effects on exposed wildlife.

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