

21.04.2010

SUBSTANCE	Urea
EC NUMBER	200-315-5
CAS NUMBER	57-13-6
Lead Registrant	Borealis Agrolinz Melamine GmbH

IUCLID headings	Available data	Method	Comments, Description of test material	Klimisch Ranking
4 Physical and chemical properties				
4.1 Appearance/physical state/colour	Lide DR, CRC Handbook of Chemistry and Physics	Visual inspection only	Crystalline solid, Urea	2 (key)
4.2 Melting point/freezing point	Gwerder C et al, Institute of Safety and Security	EU Method A.1	Melting point: 134°C, Urea	1 (key)
4.2 Melting point/freezing point	Lide DR, CRC Handbook of Chemistry and Physics	No data	Melting point: 133.3°C at 1013 hPa, Urea	2 (supporting)
4.3 Boiling point	Lide DR, CRC Handbook of Chemistry and Physics	No data	The substance decomposes before the boiling point is reached, Urea	2 (key)
4.4 Density	Gwerder C et al, Institute of Safety and Security	EU Method A.3	1.33 g/cm ³ at 20°C, Urea	1 (key)
4.4 Density	Lide DR, CRC Handbook of Chemistry and Physics	Similar to OECD 109	1.323 g/cm ³ at 20°C, Urea	2 (supporting)
4.5 Particle size distribution (Granulometry)	Awaiting data			
4.6 Vapour pressure	Hamilton Jones A, J. Chem. Eng. Data	Similar to EU Method A.4	1.2x10 ⁻⁵ mmHg at 25°C	2 (key)
4.7 Partition coefficient	Junghans M, BMG Engineering AG	EU Method A.8	Octanol-water partition coefficient: -1.73, Urea	1 (key)
4.7 Partition coefficient	Hansch C et al, Exploring QSAR	QSAR estimation	logKow: -2.11, Urea	2 (supporting)
4.8 Water solubility	Gwerder C et al, Institute of Safety and Security	EU Method A.6	624 g/L at 20°C, Urea	1 (key)
4.8 Water solubility	Yallowky SH, Database of Aqueous Solubilities	No data	545000 mg/L at 25°C, Urea	2 (supporting)
4.9 Solubility in organic solvents / fat solubility	Not applicable			
4.10 Surface tension	Waiver			
4.11 Flash point	Waiver			
4.12 Auto flammability	Gwerder C et al, Institute of Safety and Security	EU Method A.16	No evidence of autoflammability, Urea	2 (key)
4.13 Flammability	Gwerder C et al, Institute of Safety and Security	EU Method A.10	Not flammable, Urea	1 (key)
4.13 Flammability	Sax NI & Lewis SR, Hawley's Condensed Chemical Dictionary	No data	Non-flammable in air, Urea	2 (supporting)
4.14 Explosiveness	Waiver			
4.15 Oxidising properties	Waiver			
4.16 Oxidation reduction potential	Not applicable			

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4.17 Stability in organic solvents and identity of relevant degradation products	Waiver			
4.18 Storage stability and reactivity towards container material	Not applicable			
4.19 Stability: thermal, sunlight, metals	Not applicable			
4.20 pH	Not applicable			
4.21 Dissociation constant	Gwerder C et al, Institute of Safety and Security	OECD 112	pKb < 0.6, Urea	1 (key)
4.21 Dissociation constant	Perrin DD, Dissociation Constants of Organic Bases in Aqueous Solution	No data	0.10 at 21°C, Urea	2 (supporting)
4.22 Viscosity	Waiver			
4.23 Additional physico-chemical information	Not applicable			
5 Environmental fate and pathways				
5.1 Stability				
5.1.1 Phototransformation in air	Not applicable			
5.1.2 Hydrolysis	Waiver			
5.1.3 Phototransformation in water	Not applicable			
5.1.4 Phototransformation in soil	Not applicable			
5.2 Biodegradation				
5.2.1 Biodegradation in water: screening tests	Verschueren K, Handbook of Environmental Data on Organic Chemicals	Biodegradation by psychrophilic bacteria	Maximum degradation rate: 11.6 mg/L at 20°C, Urea	2 (weight of evidence)
5.2.1 Biodegradation in water: screening tests	BASF AG	OECD 302B	60% degradation at 10 days, Urea	2 (weight of evidence)
5.2.1 Biodegradation in water: screening tests	Schwarz, BASF AG	OECD 301A	DOC removal after 21 days: 90-100%, Dimethyl Urea	1 (weight of evidence)
5.2.2 Biodegradation in water and sediment: simulation tests	Waiver			
5.2.3 Biodegradation in soil	Vlek PLG & Carter MF, Soil Science	Similar to OECD 304A	3% degradation in flood water and 64% in soil after 30 hours, Urea	2 (weight of evidence)
5.2.3 Biodegradation in soil	Gunkel K et al, Acta Hydrochimica et Hydrobiologica	Review article	The main mode of urea degradation is enzymatic mineralisation, Urea	2 (weight of evidence)
5.2.4 Mode of degradation in actual use	Not applicable			
5.3 Bioaccumulation				
5.3.1 Bioaccumulation: aquatic / sediment	Kaushik SJ, Ann. Nutr. Metab	No data	Dietary urea is readily absorbed in the digestive tract of trout, Urea	
5.3.2 Bioaccumulation: terrestrial	Not applicable			

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5.4 Transport and distribution				
5.4.1 Adsorption / desorption	Hongprayoon C, Soil Science Society of America Journal	Diffusion & hydrolysis over 30 days in soil	Adsorption coefficient: 0.037-0.064, Urea-N	2 (key)
5.4.2 Henry's Law constant	Not applicable			
5.4.3 Distribution modelling	Not applicable			
5.4.4 Other distribution data	Not applicable			
5.5 Environmental data				
5.5.1 Monitoring data	Not applicable			
5.5.2 Field studies	Not applicable			
5.6 Additional information on environmental fate and behaviour	Not applicable			
6 Ecotoxicological Information				
6.1 Aquatic toxicity				
6.1.1 Short-term toxicity to fish	Juhnke I & Ludemann D, Zeitschrift fuer Wasser und Abwasser	Acute toxicity to fish	48-h LC50 in <i>Leuciscus idus melanotus</i> : > 10000 mg/L, Urea	2 (weight of evidence)
6.1.1 Short-term toxicity to fish	Palanichamy S, Environment and Ecology	Similar to OECD 203	96-h LC50 in <i>Tilapia mossambica</i> : 22500 mg/L, Urea	2 (weight of evidence)
6.1.1 Short-term toxicity to fish	Dobriyal AK & Bahuguna AK, Himalayan Chemical and Pharmaceutical Bulletin	Acute toxicity to fish	96-h LC50 in <i>Barillus barna</i> : > 9100 mg/L, Urea	2 (weight of evidence)
6.1.1 Short-term toxicity to fish	BASF AG	Acute toxicity to fish	96-h LC50 in <i>Leuciscus idus</i> : > 6810 mg/L, Urea	2 (weight of evidence)
6.1.2 Long-term toxicity to fish	Waiver			
6.1.3 Short-term toxicity to aquatic invertebrates	Bringmann G & Kuhn R, Zeitschrift fuer Wasser und Abwasser Forschung	DIN 38412 Teil 11	24-h EC50 in <i>Daphnia magna</i> : > 10000 mg/L, Urea	2 (key)
6.1.3 Short-term toxicity to aquatic invertebrates	Tchounwou PB et al, Archives of Environmental Contamination and Toxicology	Acute toxicity to snails	24-h LC50 in <i>Helisoma trivolis</i> : 22998 mg/L, Urea	2 (supporting)
6.1.3 Short-term toxicity to aquatic invertebrates	Tchounwou PB et al, Archives of Environmental Contamination and Toxicology	Acute toxicity to snails	24-h LC50 in <i>Biomphalaria havanensis</i> : 26024 mg/L, Urea	2 (supporting)
6.1.3 Short-term toxicity to aquatic invertebrates	Kramer VC et al, Journal of Invertebrate Pathology	Acute toxicity to mosquito larvae	4-h LC50 in <i>Aedes aegypti</i> larvae: 60000 mg/L, Urea	2 (supporting)
6.1.4 Long-term toxicity to aquatic invertebrates	Waiver			
6.1.5 Toxicity to aquatic algae and cyanobacteria	Bringmann G & Kuhn R, Vom Wasser	Cell multiplication inhibition test	192-h toxicity threshold in <i>Scenedesmus quadricauda</i> : > 10000 mg/L, Urea	2 (weight of evidence)
6.1.5 Toxicity to aquatic algae and cyanobacteria	Bringmann G & Kuhn R, Vom Wasser	Cell multiplication inhibition test	192-h toxicity threshold in <i>Microcystis aeruginosa</i> : 47 mg/L, Urea	2 (weight of evidence)
6.1.5 Toxicity to aquatic algae and cyanobacteria	Bringmann G & Kuhn R, Water Research	Cell multiplication inhibition test	7-d toxicity threshold in <i>Scenedesmus quadricauda</i> : > 10000 mg/L, Urea	2 (weight of evidence)

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6.1.6 Toxicity to aquatic plants other than algae	Not applicable			
6.1.7 Toxicity to microorganisms	Bringmann G & Kuhn R, Water Research	Cell multiplication inhibition test	72-h toxicity threshold in <i>Entosiphon sulcatum</i> : 29 mg/L; 16-h toxicity threshold in <i>Pseudomonas putida</i> : > 10000 mg/L, Urea	2 (key)
6.1.8 Toxicity to other aquatic organisms	Not applicable			
6.2 Sediment toxicity	Waiver			
6.3 Terrestrial toxicity				
6.3.1 Toxicity to soil macroorganisms except arthropods	Wei-Chun Ma et al, Agriculture, Ecosystems and Environment	Long term fertiliser exposure, field study	Urea fertiliser reduced earthworm numbers and biomass, Urea	2 (key)
6.3.2 Toxicity to terrestrial arthropods	Waiver			
6.3.3 Toxicity to terrestrial plants	Krogmeier MJ et al, Proceedings of the National Academy of Sciences of the United States of America	Leaf tip necrosis	NOEC in soybean plant: 9 mg/leaf/dy in 0.6 ml water for 7 days, Urea	2 (key)
6.3.4 Toxicity to soil microorganisms	Waiver			
6.3.5 Toxicity to birds	FDA, Health Hazard Determination Report	Determination of lowest lethal dose	LDLo in <i>Columdiae</i> : 16000 mg/kg/bw, Urea	4 (supporting)
6.3.6 Toxicity to other above-ground organisms	Not applicable			
6.4 Biological effects monitoring	Not applicable			
6.5 Biotransformation and kinetics	Not applicable			
6.6 Additional ecotoxicological information	Not applicable			
7 Toxicological information				
7.1 Toxicokinetics, metabolism and distribution				
7.1.1 Basic toxicokinetics	No data			
7.1.2 Dermal absorption	Bronaugh L et al, Toxicology and Applied Pharmacology	In vitro & in vivo dermal absorption study	Low dermal absorption capabilities: 7-8% applied dose absorbed after 5 days, [¹⁴ C]Urea	2 (weight of evidence)
7.1.2 Dermal absorption	CIR Panel, International Journal of Toxicology	Review article	Absorption across normal human skin in vitro: 9.5%, Urea	1 (supporting)
7.2 Acute Toxicity				
7.2.1 Acute toxicity: oral	Sato N et al, Oyo Yakuri Pharmacometrics	Similar to OECD 401	LD50 male rat: 14300 mg/kg bw; female rat: 15000 mg/kg bw, Urea	2 (weight of evidence)

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7.2.1 Acute toxicity: oral	Sato N et al, Oyo Yakuri Pharmacometrics	Similar to OECD 401	LD50 male mouse: 11500 mg/kg bw; female mouse: 13000 mg/kg bw, Urea	2 (weight of evidence)
7.2.1 Acute toxicity: oral	Stiles DA et al, J. Dairy Science	Effects of diet on urea toxicity in cows	LDLo in male/female cows: 600 mg/kg bw, Urea	2 (supporting)
7.2.1 Acute toxicity: oral	Button C, Journal of the South African Veterinary Association	Investigative non-standard study	Ldlo in male pigs: > 16000 mg/kg bw, Urea	4 (supporting)
7.2.2 Acute toxicity: inhalation	Waiver			
7.2.3 Acute toxicity: dermal	Waiver			
7.2.4 Acute toxicity: other routes	Sato N et al, Oyo Yakuri Pharmacometrics	Acute toxicity, single subcutaneous dose	LD50 male rat: 9400 mg/kg bw; female rat: 8200 mg/kg bw, Urea	2 (supporting)
7.2.4 Acute toxicity: other routes	Sato N et al, Oyo Yakuri Pharmacometrics	Acute toxicity, single subcutaneous dose	LD50 male mouse: 9200 mg/kg bw; female mouse: 10700 mg/kg bw, Urea	2 (supporting)
7.2.4 Acute toxicity: other routes	Sato N et al, Oyo Yakuri Pharmacometrics	Acute toxicity, single intravenous dose	LD50 male rat: 5400 mg/kg bw; female rat: 5300 mg/kg bw, Urea	2 (supporting)
7.2.4 Acute toxicity: other routes	Sato N et al, Oyo Yakuri Pharmacometrics	Acute toxicity, single intravenous dose	LD50 male mouse: 4600 mg/kg bw; female mouse: 5200 mg/kg bw, Urea	2 (supporting)
7.3 Irritation / corrosion				
7.3.1 Skin irritation / corrosion	Frosch PJ & Kligman AM, Cutaneous Toxicity	Chamber-scarification test in human volunteers	Not irritating to intact skin at 30%, Urea	2 (supporting)
7.3.1 Skin irritation / corrosion	Lashmar UT et al, Journal of Pharmacy and Pharmacology	Histopathological examination following topical application	No irritation to intact mouse skin, no histopathological changes at 10% dose, Urea	2 (supporting)
7.3.1 Skin irritation / corrosion	Hooiveld MJJ, NOTOX BV	OECD 404, EU B.4	Not irritating to rabbit skin, Urea	1 (key)
7.3.2 Eye irritation	Kirsch P & Kersebohm B, BASF AG	OECD 405	Mildly irritating to rabbit eyes, Urea	2 (key)
7.4 Sensitisation				
7.4.1 Skin sensitisation	Waiver			
7.4.2 Respiratory sensitisation	Waiver			
7.5 Repeated dose toxicity				
7.5.1 Repeated dose toxicity: oral	Fleischman RW et al, Journal of Environmental Pathology and Toxicology	Carcinogenicity study	12-month NOAEL in mice: 45000 ppm, Urea	2 (weight of evidence)
7.5.1 Repeated dose toxicity: oral	Fleischman RW et al, Journal of Environmental Pathology and Toxicology	Carcinogenicity study	12-month NOAEL in rats: 45000 ppm, Urea	2 (weight of evidence)
7.5.2 Repeated dose toxicity: dermal	Sato N et al, Oyo Yakuri Pharmacometrics	28-day dermal exposure	No toxicity was observed following application of 40% urea to rat skin for 28 days, Urea	2 (key)
7.5.2 Repeated dose toxicity: dermal	Sato N et al, Oyo Yakuri Pharmacometrics	25-week dermal exposure	No toxicity was observed following application of 40% urea to rat skin for 25 weeks, Urea	2 (key)
7.5.3 Repeated dose toxicity: inhalation	Waiver			

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7.5.4 Repeated dose toxicity: other routes	Balestri PL et al, Experimentia	Subchronic subcutaneous toxicity	Low toxicity in dogs at 10% solution injected s.c. for 45 days, Urea	4 (key)
7.6 Genetic toxicity				
7.6.1 Genetic toxicity in vitro	Ishidate M et al, Gann Monograph on Cancer Research	Similar to OECD 471	Ames test: negative, Urea	2 (weight of evidence)
7.6.1 Genetic toxicity in vitro	Shimizu H et al, Japanese Journal of Industrial Health	Similar to OECD 471	Ames test: negative, Urea	2 (weight of evidence)
7.6.1 Genetic toxicity in vitro	Mortelmans K et al, Environmental Mutagenesis	Similar to OECD 471	Ames test: negative, Urea	2 (weight of evidence)
7.6.1 Genetic toxicity in vitro	Ishidate M et al, Gann Monograph on Cancer Research	Similar to OECD 473	CHL chromosome aberration test: positive, but DT20 value is well in excess of the limit concentration recommended by OECD 473, low clastogenic potential, Urea	2 (weight of evidence)
7.6.1 Genetic toxicity in vitro	Ishidate M & Odashima S, Mutation Research	Chromosome aberration screening assay, chinese hamster cells	Chromosome aberration: negative, Urea	2 (weight of evidence)
7.6.1 Genetic toxicity in vitro	Wangenheim J & Bolcsfoldi G, Mutagenesis	Similar to OECD 476	Mouse lymphoma assay: negative, Urea	2 (weight of evidence)
7.6.1 Genetic toxicity in vitro	Garberg M et al, Mutation Research	DNA damage in mouse lymphoma cells	Positive results were only achieved with very high concentrations, Urea	2 (supporting)
7.6.1 Genetic toxicity in vitro	Sina JF et al, Mutation Research	DNA damage, rat hepatocyte assay	No evidence of single strand breaks, Urea	2 (supporting)
7.6.2 Genetic toxicity in vivo	Chaurasia OP & Sinha SP, Cytologia	Bone marrow chromosome assay in mice	Ambiguous, however the study only employed a single extremely high dose, Urea	3 (supporting)
7.7 Carcinogenicity				
7.7 Carcinogenicity	Fleischman RW et al, Journal of Environmental Pathology and Toxicology	12-month carcinogenicity screening study	NOAEL in rats: 45000 ppm, Urea	2 (weight of evidence)
7.7 Carcinogenicity	Fleischman RW et al, Journal of Environmental Pathology and Toxicology	12-month carcinogenicity screening study	NOAEL in mice: 45000 ppm, Urea	2 (weight of evidence)
7.8 Toxicity to reproduction				
7.8.1 Toxicity to reproduction	Waiver			
7.8.2 Developmental toxicity / teratogenicity	Mora S et al, Acta Veterinaria Scandinavica	Injection into egg air sac during incubation	Mortality: 838-38.9%, dose-dependent, Urea	3 (supporting)
7.8.2 Developmental toxicity / teratogenicity	Seipelt H et al, Zeitschrift fur Urologie und Nephrologie	Administration to pregnant rats, examination of pup kidneys	No hypertrophy/kidney changes detected in pups, no teratogenic effects noted, Urea	2 (weight of evidence)

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7.8.3 Toxicity to reproduction: other studies	Not applicable			
7.9 Specific investigations				
7.9.1 Neurotoxicity	Not applicable			
7.9.2 Immunotoxicity	Not applicable			
7.9.3 Specific investigations: other studies	Tabachnick J & LaBadie JH, The Journal of Investigative Dermatology	In vivo study on urea content of epidermis	Total urea content in guinea pig epidermis: 37.7 µmoles/gm wet wt, Urea	2 (supporting)
7.9.3 Specific investigations: other studies	Wellner K & Wohlrab W, Arch. Dermatol. Res	In vivo study of urea in stratum corneum	Total urea content in a 2.5 cm ² sample human skin was 23 µg, Urea	2 (key)
7.10 Exposure related observations in humans				
7.10.1 Health surveillance data	Not applicable			
7.10.2 Epidemiological data	Not applicable			
7.10.3 Direct observations: clinical cases, poisoning incidents and other	Not applicable			
7.10.4 Sensitisation data (humans)	Stuttgen G, Der Hautarzt	Review article	Long term medical use of urea for the treatment of dermatitis is not associated with irritant/sensitisation effects	2 (supporting)
7.10.4 Sensitisation data (humans)	Alchangian LV et al, Vestnik Dermatologii Venerologii	Sensitisation responses in human volunteers	No evidence of skin sensitisation at 10% concentration, Urea	2 (supporting)
7.10.4 Sensitisation data (humans)	Loden M, Acta Derm Venereol	Assessment of skin reactions in patients	No evidence of sensitisation reactions at 4% concentration, Urea	2 (supporting)
7.10.5 Exposure related observations in humans: other data	Not applicable			
7.11 Toxic effects on livestock and pets	Not applicable			
7.12 Additional toxicological information	Not applicable			

