

TEST PLAN FOR SEC-BUTYL UREA

Sec-butyl urea CAS No. 689-11-2	Data Available	Data Acceptable	Testing Required
Study	Y/N	Y/N	Y/N
PHYSICAL/CHEMICAL CHARACTERISTICS			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
ENVIRONMENTAL FATE			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Transport (Fugacity)	Y	Y	N
Biodegradation	Y	Y	N
ECOTOXICITY			
Acute Toxicity to Fish	Y*	Y	N
Acute Toxicity to Invertebrates	Y*	Y	N
Acute Toxicity to Aquatic Plants	Y*	Y	N
MAMMALIAN TOXICITY			
Acute Toxicity	Y	Y	N
Repeated Dose Toxicity	N/A	N/A	N/A
Developmental Toxicity	Y*	Y	N
Reproductive Toxicity	N/A	N/A	N/A
Genetic Toxicity Gene Mutations	N	N	Y
Genetic Toxicity Chromosomal Aberrations	N	N	Y
*Data for a related material, isobutylidene diurea, is available.			

13 January 2003

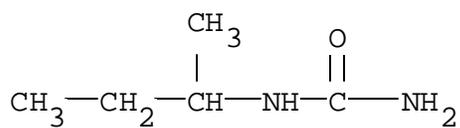
Existing published and unpublished data were collected and scientifically evaluated to determine the best possible study or studies to be summarized for each required endpoint. In the spirit of this voluntary program, other data of equal or lesser quality are not summarized, but are listed as related references at the end of each appropriate section, with a statement to reflect the reason why these studies were not summarized.

1.0 Substance Information

CAS Number: 689-11-2

Chemical Name: Urea, (1-methylpropyl)-

Structural Formula:



Other Names: Urea, sec-butyl-
N-sec-butylurea
Sec-butylurea
Secondary butylurea
Urea, 1-sec-butyl-

Exposure Limits: No Data.

2.0 Physical/Chemical Properties

2.1 Melting Point

Value: No Data
Decomposition: No Data
Sublimation: 171°C
Pressure: No Data
Method: No Data
GLP: Unknown
Reference: DuPont Co. (1992). Material Safety Data Sheet No. B0000007 (November 17).
Reliability: Not assignable because limited study information was available.

Additional References for Melting Point: None Found.

2.2 Boiling Point

Value: 224.95°C
Decomposition: No Data
Pressure: 760 mm Hg
Method: Modeled. MPBPWIN, v. 1.4 module of EPIWIN 3.05 (Syracuse Research Corporation). MPBPWIN estimates the normal boiling point using an adaptation of the Stein and Brown (1994) method, which is an extension and refinement of the Joback method (Joback, 1982; Reid et al., 1987).
GLP: Not Applicable
Reference: Stein, S. E. and R. L. Brown (1994). J. Chem. Inf. Comput. Sci., 34:581-587.

Joback, K. G. (1982). A Unified Approach to Physical Property Estimation Using Multivariate Statistical Techniques. Stevens Institute of Technology, submitted to the Dept. of Chem. Eng. for M.S. Degree at the Massachusetts Institute of Technology in June 1984 (see also: Reid et al., 1987).

Reid, R. C. et al. (1987). The Properties of Gases and Liquids. 4th edition, Chapter 2, McGraw-Hill, Inc., NY.
Reliability: Estimated value based on accepted model.

Additional References for Boiling Point: None Found.

2.3 Density

Value: Specific gravity = 0.25-0.28
Temperature: No Data
Method: No Data
GLP: Unknown
Results: No additional data.
Reference: DuPont Co. (1992). Material Safety Data Sheet No. B0000007 (November 17).
Reliability: Not assignable because limited study information was available.

Additional References for Density: None Found.

2.4 Vapor Pressure

Value: 0.00294 mm Hg
Temperature: 25°C
Decomposition: No Data
Method: Modeled. MPBPWIN, v. 1.4, module of EPIWIN 3.05 (Syracuse Research Corporation). MPBPWIN estimates vapor pressure (VP) by three separate methods: (1) the Antoine method, (2) the modified Grain method, and (3) the Mackay method. All three use the normal boiling point to estimate VP.
GLP: Not Applicable
Reference: Lyman, W. J. et al. (1990). Handbook of Chemical Property Estimation Methods, Chapter 14, American Chemical Society, Washington, DC.

Lyman, W. J. (1985). In: Environmental Exposure From Chemicals, Volume I, Chapter 2, Neely, W. B. and G. E. Blau (eds.), CRC Press, Inc., Boca Raton, FL.
Reliability: Estimated value based on accepted model.

Additional References for Vapor Pressure: None Found.

2.5 Partition Coefficient (log Kow)

Value: 0.31
Temperature: 25°C
Method: Modeled. KOWWIN, v. 1.66, module of EPIWIN 3.05 (Syracuse Research Corporation). KOWWIN uses “fragment constant” methodologies to predict log P. In a “fragment constant” method, a structure is divided into fragments (atom or larger functional groups) and coefficient values of each fragment or group are summed together to yield the log P estimate.
GLP: Not Applicable
Reference: Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.
Reliability: Estimated value based on accepted model.

Additional References for Partition Coefficient (log Kow): None Found.

2.6 Water Solubility

Value: 4 WT%
Temperature: 20°C
pH/pKa: No Data
Method: No Data
GLP: Unknown
Reference: DuPont Co. (1992). Material Safety Data Sheet No. B0000007 (November 17).
Reliability: Not assignable because limited study information was available.

Value: 10 WT%
Temperature: 60°C
pH/pKa: No Data
Method: No Data
GLP: Unknown
Reference: DuPont Co. (1992). Material Safety Data Sheet No. B0000007 (November 17).
Reliability: Not assignable because limited study information was available.

Additional References for Water Solubility: None Found.

2.7 Flash Point: No Data.

2.8 Flammability

Value: Lower Explosive Limit: 0.023 g/L
Limiting Oxygen Concentration: >12%
Minimum Ignition Energy: 20-50 mJ
Method: A Hartmann Dust Tube was used to determine the lower explosive limit (LEL), limiting oxygen concentration (LOC), and minimum ignition energy (MIE). A weighed sample was placed into a cup at the base of a sealed stainless steel tube. A continuous AC arc was energized between 2 tungsten electrodes in the tube as a pulse of air dispersed the sample into a cloud. If the sample concentration was above the LEL, defined as the lowest dust concentration sufficient for sustained flame propagation, the arc would cause the material to deflagrate and the resulting pressure increase would be detected by a pressure transducer in the top of the tube. Pressure/time and rate/time measurements were recorded. LEL was reported as the highest dust concentration resulting in a "NO GO" (pressure increase <1 psig over initial dispersion pressure).

<1 psig over initial dispersion pressure).

The LOC, defined as the highest oxygen concentration permissible to prevent combustion for any dust concentration, was determined with a modified version of the above procedure. Ignition was attempted on dust samples of various concentrations that were dispersed by oxygen/nitrogen mixtures of known compositions. The sample was tested at decreasing oxygen levels until a point was reached where no combustion events were observed (pressure increase <1 psig over initial dispersion pressure) for any of the concentrations tested. This level was reported as the LOC.

The test method for MIE involved subjecting dust clouds of varying concentrations to electrical sparks of different energy levels. The test sample was placed in a sample cup at the base of an acrylic tube and was dispersed into a cloud by a blast of low pressure air. After a preset time delay to allow cloud formation, a low energy triggering spark was discharged between 2 electrodes to initiate discharge of a higher energy DC spark stored in a capacitor. A combustion event (“GO”) was evidenced by observation of a flame accompanied by bursting of a full diameter paper rupture disc at the top of the tube. For a given energy level, tests were conducted at varying dust concentrations; if a “GO” event was obtained in 10 trials for any of the concentrations tested, the energy level was reduced and the tests repeated. This procedure was continued until an energy level was reached where no combustion events were observed in 10 trials for any of the concentrations tested. The MIE was then reported as being located between this energy level and the next highest energy level tested.

The LEL, LOC, and MIE values determined by these procedures are valid for atmospheric pressure and ambient temperature only.

GLP: Unknown
Reference: DuPont Co. (1995). Unpublished Data, “Dust Explosivity Characteristics of Sec-butyl Urea” (July 18).
Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Flammability:

DuPont Co. (1992). Material Safety Data Sheet No. B0000007 (November 17).

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	No Data, but inspection of the chemical structure indicates that sec-butyl urea does not contain structural fragments typically subject to aqueous photolysis.
Indirect Photolysis:	No Data
Breakdown Products:	No Data
Method:	Inspection of chemical structure.
GLP:	Not Applicable
Reference:	Harris, J. C. (1990). Rate of Aqueous Photolysis, Chapter 8, In: Lyman, W. J. et al. (eds.). <u>Handbook of Chemical Property Estimation Methods</u> , American Chemical Society, Washington, DC.
Reliability:	Estimate based on known qualitative structure-activity relationships.

Additional References for Photodegradation: None Found.

3.2 Stability in Water

Concentration:	No Data
Half-life:	No value. The estimated rate of hydrolysis is extremely slow, beyond the typical range for quantitative model estimates.
% Hydrolyzed:	No Data
Method:	Modeled. HYDROWIN, v. 1.67 module of EPIWIN v3.05 (Syracuse Research Corporation). HYDROWIN estimates aqueous hydrolysis rate constants for the following chemical classes: esters, carbamates, epoxides, halomethanes and selected alkyl halides. HYDROWIN estimates acid- and base-catalyzed rate constants; it does NOT estimate neutral hydrolysis rate constants. The prediction methodology was developed for the U.S. Environmental Protection Agency and is outlined in Mill et al., 1987.
GLP:	Not Applicable
Reference:	Mill, T. et al. (1987). "Environmental Fate and Exposure Studies Development of a PC-SAR for Hydrolysis: Esters, Alkyl Halides and Epoxides," EPA Contract No. 68-02-4254, SRI International, Menlo Park, CA.
Reliability:	Estimated value based on accepted model.

Additional References for Stability in Water: None Found.

3.3 Transport (Fugacity)

Media: Air, Water, Soil, and Sediments
Distributions: Air: 0.0594%
Water: 44.6%
Soil: 55.2%
Sediment: 0.0757%
Half-life: Air: 29 hours
Water: 360 hours
Soil: 360 hours
Sediment: 1.44x10³ hours

Adsorption

Coefficient: Estimated log Koc = 0.84

Desorption: Not Applicable

Volatility: Not Applicable

Method: Modeled.

Henry's Law Constant - HENRYWIN v. 3.10 module of EPIWIN v3.05 (Syracuse Research Corporation). Henry's Law Constant (HLC) is estimated by two separate methods that yield two separate estimates. The first method is the bond contribution method and the second is the group contribution method. The bond contribution method is able to estimate many more types of structures; however, the group method estimate is usually preferred (but not always) when all fragment values are available.

Log Koc – Calculated from log Kow by the Mackay Level III fugacity model incorporated into EPIWIN v3.05 (Syracuse Research Corporation).

Environmental Distribution - Mackay Level III fugacity model, in EPIWIN v3.05 (Syracuse Research Corporation). Emissions (1000 kg/hr) to air, water, and soil compartments and the following input values:

Molecular Weight: 116.16

Henry's Law Constant: 1.87x10⁻⁹ atm·m³/mole (HENRYWIN program)

Vapor Pressure: 0.00294 mm Hg (MPBPWIN program)

Melting Point : 171°C (user-entered)

Log Kow: 0.31 (KOWWIN program)

Soil Koc: 0.837 (calculated by Level III model)

GLP: Not Applicable

References: HENRYWIN

Hine, J. and P. K. Mookerjee (1975). J. Org. Chem., 40(3):292-298.

40(3):292-298.

Meylan, W. and P. H. Howard (1991). Environ. Toxicol. Chem., 10:1283-1293.

Fugacity - The methodology and programming for the Level III fugacity model incorporated into EPIWIN v3.05 (Syracuse Research Corporation) were developed by Dr. Donald MacKay and coworkers and are detailed in:

Mackay, D. (1991). Multimedia Environmental Models: The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated value based on accepted model.

Additional Reference for Transport (Fugacity):

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

SRC (Syracuse Research Corporation) (1988). Syracuse Research Corporation Calculated Values (NISC/EF-0007592).

3.4 Biodegradation

Value: Ultimate Biodegradation Timeframe: Weeks. This indicates that sec-butyl urea is expected to be readily biodegradable. The equivalent half-life for the Weeks timeframe is 15 days. Using a first order model, 70% of theoretical oxygen demand would occur in about 26 days.

Breakdown Products: No Data

Method: Modeled. BIOWIN, v. 4.0 module of EPINWINN v3.05 (Syracuse Research Corporation). BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental microorganisms. Estimates are based upon fragment constants that were developed using multiple linear and non-linear regression analyses.

GLP: Not Applicable

Reference: Boethling, R. S. et al. (1994). Environ. Sci. Technol., 28:459-65.

Howard, P. H. et al. (1987). Environ. Toxicol. Chem., 6:1-10.

Howard, P. H. et al. (1992). Environ. Toxicol. Chem., 11:593-603.

Tunkel, J. et al. (2000). Predicting Ready Biodegradability in the MITI Test. Environ. Toxicol. Chem., accepted for publication.

Reliability: Estimated value based on accepted model.

Additional References for Biodegradation: None Found.

3.5 Bioconcentration

Value: BCF = 3.162 (log BCF = 0.500). This BCF value suggests that bioconcentration potential in aquatic organisms is low.

Method: Modeled. BCFWIN v. 2.4 module of EPINWINN v3.05 (Syracuse Research Corporation). BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (Kow) with correction factors based on molecular fragments.

GLP: Not Applicable

Reference: "Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient," SRC TR-97-006 (2nd Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC, Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil Gouchie, Syracuse Research Corp.

Reliability: Estimated value based on accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type: 96-hour LC₅₀
Species: Fish
Value: 3339 mg/L (using log₁₀ Kow of 0.31)
Method: Modeled
GLP: Not Applicable
Test Substance: Sec-butyl urea
Results: No additional data.
Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).
Reliability: Estimated value based on accepted model.

Type: 96-hour LC₅₀
Species: *Salmo gairdneri* (rainbow trout)
Value: >1000 mg/L
Method: OECD Guideline 203, "Fish, Acute Toxicity Test" (1984). No additional information was reported.
GLP: No
Test Substance: Isobutylidene diurea, purity 88%
Results: The LC₅₀ was calculated based on nominal test concentrations. The NOEC, LC₀, and LC₁₀₀ were 1000, 1000, and >1000 mg/L, respectively. No additional information was reported.
Reference: BASF AG (1986). Department of Toxicology, Unpublished investigation (86/173), 19.12.1986 (cited in IUCLID (2000). IUCLID Dataset, "N,N"-(isobutylidene)diurea" (February 18, 2000)).
Reliability: Medium because a suboptimal study design for testing (nominal test concentrations) was used.

Type: 96-hour LC₅₀
Species: Fish
Value: 3.72x10⁵ mg/L (using log₁₀ Kow of -1.68)
Method: Modeled
GLP: Not Applicable
Test Substance: Isobutylidene diurea
Results: No additional data.
Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99),

the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).

Reliability: Estimated value based on accepted model.

Additional References for Acute Toxicity to Fish: None Found.

4.2 Acute Toxicity to Invertebrates

Type: 48-hour EC₅₀
Species: *Daphnia*
Value: 3184 mg/L (log₁₀ Kow of 0.31)
Method: Modeled
GLP: Not Applicable
Test Substance: Sec-butyl urea
Results: No additional data.
Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).
Reliability: Estimated value based on accepted model.

Type: 48-hour EC₅₀
Species: *Daphnia magna*
Value: >1000 mg/L
Method: Directive 84/449/EEC, C.2 "Acute toxicity for *Daphnia*."
No additional information was reported.
GLP: Unknown
Test Substance: Isobutylidene diurea, purity not reported
Results: The EC₅₀ was calculated based on nominal test concentrations. The 48-hour EC₀ and EC₁₀₀ were 250 and >500 mg/L, respectively. The 24-hour EC₀, EC₅₀, and EC₁₀₀ were 500, >500, and >500 mg/L, respectively. No additional information was reported.
Reference: BASF AG (1987). Ecology Laboratory, Unpublished investigation (1108/87) (cited in IUCLID (2000). IUCLID Dataset, "N,N²-(isobutylidene)diurea" (February 18)).
Reliability: Medium because a suboptimal study design for testing (nominal test concentrations) was used.

Type: 48-hour EC₅₀
Species: *Daphnia*
Value: 3.09x10⁵ mg/L (log₁₀ Kow of -1.68)
Method: Modeled
GLP: Not Applicable
Test Substance: Isobutylidene diurea
Results: No additional data.
Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).
Reliability: Estimated value based on accepted model.

Additional References for Acute Toxicity to Invertebrates: None Found.

4.3 Acute Toxicity to Aquatic Plants

Type: 96-hour EC₅₀
Species: Algae
Value: 1806 mg/L (log₁₀ Kow of 0.31)
Method: Modeled
GLP: Not Applicable
Test Substance: Sec-butyl urea
Results: No additional data.
Reference: Meylan, W. M. and P. H. Howard (1999). User's Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).
Reliability: Estimated value based on accepted model.

Type: 96-hour EC₅₀
Species: *Scenedesmus subspicatus* (algae)
Value: >500 mg/L
Method: DIN 38412 Part 9, "Scenedesmus-cell multiplication inhibition test, regulation of the inhibition effect of substances contained in water on green algae." No additional information was reported.
GLP: Unknown
Test Substance: Isobutylidene diurea, purity not reported
Results: The EC₅₀ was calculated based on nominal test concentrations. The 96-hour EC was >500 mg/L. The

concentrations. The 96-hour EC₂₀ was >500 mg/L. The 72-hour EC₂₀ and EC₅₀ were 500 and >500 mg/L, respectively. No additional information was reported.

Reference: BASF AG (1987). Ecology Laboratory, Unpublished investigation (1108/87) (cited in IUCLID (2000). IUCLID Dataset, “N,N”-(isobutylidene)diurea” (February 18)).

Reliability: Medium because a suboptimal study design for testing (nominal test concentrations) was used.

Type: **96-hour EC₅₀**
Species: Algae
Value: 1.56x10⁵ mg/L (log₁₀ Kow of -1.68)
Method: Modeled
GLP: Not Applicable
Test Substance: Isobutylidene diurea
Results: No additional data.
Reference: Meylan, W. M. and P. H. Howard (1999). User’s Guide for the ECOSAR Class Program, Version 0.993 (Mar 99), prepared for J. Vincent Nabholz and Gordon Cas, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC, prepared by Syracuse Research Corp., Environmental Science Center, Syracuse, NY 13210 (submitted for publication).
Reliability: Estimated value based on accepted model.

Additional References for Acute Toxicity to Aquatic Plants: None Found.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type: **Oral ALD**
Species/Strain: Male rats/ChR-CD
Value: 7500 mg/kg
Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

The test substance was administered by intragastric intubation as a suspension in peanut oil in single doses of 670, 2250, 3400, 5000, 7500, 11,000, and 17,000 mg/kg to young adult male rats. Survivors were sacrificed 14 days later. Pathological examination was performed on the survivors.

GLP: No
Test Substance: sec-Butyl urea, purity 90%
Results: Mortality was 0/1, 0/1, 0/1, 0/2, 2/3, 0/2, and 1/2 at 670, 2250, 3400, 5000, 7500, 11,000, and 17,000 mg/kg,

2250, 3400, 5000, 7500, 11,000, and 17,000 mg/kg, respectively. Mortality occurred within 2-3 days after dosing. Toxic signs observed at lethal doses included weight loss, red extremities, incoordination, lacrimation, prostration, and white precipitate from urine. Toxic signs at non-lethal doses were observed up to 2 days after dosing and included slight weight loss initially at =2250 mg/kg; red extremities, unresponsiveness, and incoordination at =3400 mg/kg; and white precipitate from the urine in 1 of 2 rats receiving 5000 mg/kg. At non-lethal doses, no pathologic changes that could be attributed to the test substance were observed in the tissues of rats that were sacrificed 14 days after treatment.

Reference: DuPont Co. (1964). Unpublished Data, Haskell Laboratory Report No. 25-64, "Acute Oral Test" (March 3) (also cited in TSCA Fiche OTS0571269).

Reliability: High because a scientifically defensible or guideline method was used.

Additional Reference for Acute Oral Toxicity:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1963). Unpublished Data, Haskell Laboratory Report No. 99-63, "Acute Oral Test" (September 26) (also cited in TSCA Fiche OTS0571577).

Type: **Acute Inhalation Toxicity:** No Data.

Type: **Acute Dermal Toxicity:** No Data.

Type: **Dermal Irritation:** No Data.

Type: **Dermal Sensitization:** No Data.

Type: **Eye Irritation**

Species/Strain: Rabbits/Strain not reported

Method: No specific test guideline was reported; however, a scientifically defensible approach was used to conduct the study.

Ten mg of the test substance, as powder, was sprinkled into the conjunctival sacs of 2 rabbit eyes. In addition, 0.1 mL of a 10% solution of the test substance in propylene glycol was instilled into the conjunctival sacs of another 2 rabbit eyes. One eye of each pair was irrigated with tap water 20 seconds after contact for a 1-minute interval. The other eye of each

after contact for a 1-minute interval. The other eye of each pair was not washed.

GLP: No
Test Substance: sec-Butyl urea, purity 100%
Results: In the eye that was treated with the powder and washed after treatment, mild corneal injury through 1 day, mild congestion in the iris on the day of treatment, moderate swelling of the conjunctiva at 4 hours, and mild conjunctival irritation through 1 day were observed. In the eye not washed after treatment, moderate localized corneal injury for 2 days, marked congestion of the iris through 1 day, marked conjunctival swelling at 4 hours, and moderate conjunctival irritation at 1 day were observed. The conjunctival irritation diminished through 4 days, and the eye was normal by 7 days.

In the eye that was treated with 0.1 mL 10% solution, no corneal injury, mild congestion through 1 day, and moderate conjunctival irritation on the day of treatment were observed in both treated eyes. The conjunctival irritation was mild through 1 day.

Applying the current EPA eye scoring criteria, sec-butyl urea would be classified as Toxicity Category III, moderate eye irritant, based on corneal involvement clearing in 7 days or less.

Reference: DuPont Co. (1963). Unpublished Data, Haskell Laboratory Report No. 99-63 "Eye Irritation Test" (September 26) (also cited in TSCA Fiche OTS0571577).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Eye Irritation: None Found.

5.2 Repeated Dose Toxicity: Closed System Intermediate; Not a Required Endpoint.

5.3 Developmental Toxicity

Species/Strain: Rats/Wistar
Sex/Number: Female/25 per group
Route of Administration: Gavage
Exposure Period: Days 6-15 post-coitum; Cesarean section on Day 20 post-coitum
Frequency of Treatment: Daily

Exposure Levels: 0, 100, 400, 1000 mg/kg
Method: The procedure used in the test was based on the recommendations of the following guidelines:

Commission Directive 87/302/EEC of 18 November 1987 adapting to technical progress for the 9th time Council Directive 67/548/EEC;

OECD Guideline No. 414;

EPA/FIFRA Pesticide Assessment Guidelines, Subdivision F, NTIS, §83-3, November 1984; and

Testing Guidelines for Toxicology Studies, Japan/MAFF, 1985.

A re-analysis of the stability of the test substance was performed on completion of the study. Analytical verifications of the stability of the IBDU suspensions in 0.5% aqueous carboxymethyl cellulose solution for up to 3 hours after preparation were performed. For verification of the concentrations, samples of the suspensions were twice analyzed by HPLC during the study period. At the beginning of the dosing period, samples were also used to verify the homogeneity of the 100 and 1000 mg/kg/day concentrations.

One to 4 female rats (65-74 days old; mean body weight of approximately 225 g) were mated with 1 male. The day on which sperm was detected in the vaginal smear was defined as Day 0, and the following day as day 1 post-coitum (p.c.). Suspensions of IBDU in 0.5% aqueous carboxymethyl cellulose solution were freshly prepared before oral administration at a volume of 10 mL/kg body weight. All dams were weighed on days 0, 1, 3, 6, 8, 10, 13, 15, 17, and 20 p.c. With the exception of day 0, food consumption was recorded on the same days as body weight. On day 20 p.c. the dams were killed and given a gross autopsy. Body weight changes were determined and the corrected body weight gains were calculated. Intact uterine weight, number of corpora lutea, and number of implants (differentiated into live fetuses, dead implants, early and late resorptions, and dead fetuses) were recorded. The conception rate and pre- and post-implantation losses were calculated.

Fetuses were weighed and examined for external alterations, and sex was determined. Soft tissue examinations were

and sex was determined. Soft tissue examinations were performed on approximately 50% of fetuses after fixation in Bouin's solution, according to the method of Barrow and Taylor, 1969. Fetuses that did not receive a soft tissue examination were fixed in ethyl alcohol, stained, and examined for skeletal alterations.

Dunnett's test was used for statistically evaluating food consumption, body weight, body weight changes, corrected body weight gain, intact uterine weight, fetal and placental weights, the number of corpora lutea, implants, resorptions, live fetuses, and pre- or post-implantation losses. Fisher's exact test was used to evaluate the conception rate, maternal mortality, and all fetal findings.

GLP:

Yes

Test Substance:

Isobutylidenediurea, purity 90%

Results:

The content of active ingredient was 90% prior to the beginning of the study. The re-analysis on its completion confirmed the tentative conclusion the suspensions were stable over a period of 3 hours at room temperature. It was also concluded that the prepared concentrations and the homogenous distribution of the test substance in the carrier were correct.

Pregnancy ratios were 23/25, 22/25, 22/25, and 24/25 at 0, 100, 400, and 1000 mg/kg/day, respectively. There were no mortalities or early deliveries observed at any dose level. No test substance-related effects on body weight, body weight gain, corrected body weight gain, food consumption, clinical signs, mean uterine weights, or gross pathological findings were observed. No test substance-related differences in conception rate, mean number of corpora lutea, implantation sites, values calculated for pre- and post implantation loss, number of resorptions, or viable fetuses were observed. There was no effect on sex ratio, mean placental weight, or mean fetal weight. A summary of other reproductive outcomes (means/litter) are provided in the table below:

<u>Concentration (ppm)</u>	<u>0</u>	<u>100</u>	<u>400</u>	<u>1000</u>
Corpora Lutea:	16.8	15.5	15.8	15.7
Implantations:	15.7	14.5	14.3	14.4
% Pre-implantation loss:	6.7	6.3	10.0	9.8
Dead implants	0.8	1.0	1.1	0.9
% Post-implantation loss:	5.2	7.3	8.6	6.1

Total No. of Live Fetuses:	14.9	13.6	13.2	13.5
Mean Fetal Weight (g):	3.8	3.9	4.0	3.9
Sex Ratio (male:female):	52.8:47.2	53.2:46.8	53.3:46.7	48.3:51.7

Increased incidences of 2 skeletal malformations were unrelated to treatment. The overall malformation rate of the fetal skeletons was statistically significantly increased only in the 100 and 400 mg/kg/day dose groups. The differences observed between these treatment groups and the control fetuses were judged incidental since the frequency of dumbbell-shaped thoracic vertebral body/bodies (asymmetrical) and/or bipartite sternebra(e) with dislocated ossification centers was unusually low in the concurrent control group. Moreover, the slightly, albeit statistically significantly increased number of fetuses at 100 mg/kg/day with skeletal variations was interpreted as being spontaneous due to the lack of a dose-response relationship. Concerning fetal external, soft tissue, and skeletal findings, all differences observed between the control and the treated groups appeared without a clear dose-response relationship and were therefore judged as being without biological relevance. All the relevant findings occurred at incidences that were all within the range of historical control data.

A summary of statistically significant fetal anomalies are provided in the table below. Data are presented as number of fetuses (litters) affected.

<u>Concentration (ppm)</u>	<u>0</u>	<u>100</u>	<u>400</u>	<u>1000</u>
Skeletal, Number examined	177(23)	156(22)	151(22)	168(24)
Thoracic vertebral body/bodies dumbbell shaped (asymmetrical)	0(0)	5(4)	10(7)	5(4)
Sternebra(e) bipartite, ossification centers dislocated	0(0)	1(1)	4(3)	2(2)
Total fetal skeletal malformations	2(2)	9(7)	15(10)	7(5)

Thus there was no indication of IBDU-induced embryo/fetotoxicity or teratogenicity in Wistar rats, even at the highest dose. The NOAEL for the maternal and developing organism was 1000 mg/kg/day.

13 January 2003

Reference: Hellwig, H. et al. (1997). Food Chem. Toxicol., 35:677-681.
Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Developmental Toxicity: None Found.

5.4 Reproductive Toxicity: Closed System Intermediate; Not a Required Endpoint.

5.5 Genetic Toxicity

Type: *In vitro* **Bacterial Reverse Mutation Assay:** No Data.

Type: *In vitro* **Clastogenicity Studies:** No Data.