US HPV Challenge Program

TEST PLAN FOR N-BUTYL PROPIONATE CAS # 590-01-2

American Chemistry Council Oxo Process Panel

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INTRODUCTION

The American Chemistry Council (ACC) Oxo Process Panel and The Dow Chemical Company have reviewed and summarized the existing environmental and toxicological data for n-butyl propionate and submit for review and public comment a Test Plan under the United States Environmental Protection Agency's (USEPA) High Production Volume (HPV) Chemical Challenge Program.

Robust Summaries (Appendix 1) have been prepared for key studies. The reliability of existing data has been evaluated using Klimisch scores and USEPA guidance. Additional information, other than screening information data set (SIDS) endpoints, is provided in the Robust Summaries and SIDS Dossier for n-butyl propionate. Endpoints addressed in the Robust Summaries and this Test Plan include:

Physical/Chemical Properties

- Melting point
- Boiling point
- Octanol/water partition coefficient

Environmental Fate

- Photodegradation
- Stability in water (hydrolysis)
- Transport and distribution (Fugacity modeling)
- Biodegradation

Ecotoxicity

- Acute toxicity to fish
- Acute toxicity to aquatic invertebrates
- Toxicity to aquatic plants (algae)

Mammalian Toxicity

- Acute toxicity
- Repeated-dose toxicity
- Genetic toxicity
- Reproductive toxicity
- Developmental toxicity

Adequate data are available for all pertinent physical/chemical property endpoints. Published and unpublished data satisfy the requirements for mammalian toxicity and aquatic toxicity endpoints. However, with the exception of biodegradation, environmental fate endpoints for n-butyl propionate are not available. Additional work for n-butyl propionate is recommended for the purposes of the HPV Program, and includes photodegradation, water stability, and fugacity modeling.

CHEMICAL DESCRIPTION

n-Butyl propionate (CAS # 590-01-2) is a colorless liquid with a characteristic odor. It is produced by the esterification of butanol and propionic acid in a high pressure closed system reaction. Water is the by-product of esterification. Butyl propionate is used for high solid coatings in automotive finishes, appliance coatings, enamels, lacquers, and printing inks. It is also used in polymerization reactions for acrylic resins. Butyl propionate is not used in consumer applications.

PHYSICAL - CHEMICAL PROPERTIES

Data are available for all pertinent chemical and physical properties of n-butyl propionate (see Table 1 and Appendix 1). The sources of information to address these endpoints are collections of data or handbooks such as The Merck Index and the CRC Handbook of Chemistry and Physics. n-Butyl propionate is a liquid at ambient temperatures with a melting (freezing) point of –89 ºC, a boiling point of 146.8 ºC, and a density of 0.875 g/cm^3 at 20 ºC. The calculated partition coefficient is 2.025 and it has limited solubility in water. Data are available for all physical-chemical endpoints; no additional work is proposed for the purposes of the HPV Program (see Table 2).

ENVIRONMENTAL FATE PATHWAYS

Information regarding atmospheric photodegradation, stability in water, and distribution within the environment (Level III Fugacity modeling) are lacking and efforts are currently underway to complete the environmental fate pathways information. A biodegradation study demonstrated a BOD_5 of 59% and a BOD_{20} of 92%, indicating that n-butyl propionate is "readily biodegradable".

The environmental fate pathways data are not adequate. Additional work for environmental fate endpoints, to include photodegradation, stability in water, and transport and distribution within the environment (Level III Fugacity modeling), is recommended.

ECOTOXICITY

Aquatic studies have been performed on fish, aquatic invertebrates, aquatic plants (algae) and bacteria (see Table 1 and Appendix 1). The static 96-hour LC_{50} in fathead minnow (*Pimephales promelas*) is 43 mg/l. A 48-hour static study using the pelagic invertebrate *Daphnia magna* demonstrated an LC_{50} of 86 mg/l. The 72- and 96-hour EC_{50} values for algae (*Pseudokirchneriella subcapitata*) were 175 and 239 mg/mL, respectively; the NOEC for both intervals was 82.2 mg/mL. A bacterial toxicity study (non-SIDS endpoint), which demonstrated an IC50 (median concentration that inhibited bacterial growth) of 508 mg/l. There are no studies available which assess the toxicity of n-butyl propionate to algae.

The ecotoxicity data are adequate. No additional work is recommended.

MAMMALIAN TOXICITY

Toxicity studies demonstrate that n-butyl propionate is of low acute toxicity by all routes of exposure (oral LD_{50} = 11,031 – 12,344 mg/kg; inhalation LD_{50} > 4000 ppm; dermal LD_{50} > 14,008 mg/kg). Irritation studies indicate that n-butyl propionate produces slight skin irritation and moderate eye irritation. Results from a guinea pig Maximization Test suggest that n-butyl propionate is not a sensitizer.

Negative *in vitro* bacterial mutagenicity data are available for multiple strains of *Salmonella typhimurium* from a definitive Ames test as well as an *Escherichia coli* mutagenicity assay. A negative *in vitro* chromosomal aberration study using rat lymphocytes is also available.

There are several repeat-dose toxicity studies in rats (11 days, 2 weeks, and 13 weeks) by the inhalation route of exposure, which demonstrated low overall toxicity; however, reversible degeneration of the olfactory epithelium was observed in all studies at concentrations above 500 ppm.

A definitive developmental toxicity study in pregnant female rats produced maternal toxicity but no developmental toxicity in offspring. A 13-week inhalation study in male and female rats demonstrated that repeated exposure to n-butyl propionate had no effect on male or female reproductive organs.

Finally, the neurobehavioral effects (non-SIDS endpoint) of repeated inhalation exposure to n-butyl propionate in rats was assessed using a functional observation battery (FOB) of tests designed to detect alterations in central and peripheral nervous system function. No changes were observed in FOB evaluations in response to repeated exposure to n-butyl propionate.

There are adequate data to address all mammalian toxicity endpoints (see Table 1 and Appendix 1) and no additional work is recommended.

CONCLUSION AND RECOMMENDATIONS

There are sufficient chemical/physical data available for n-butyl propionate. Adequate data indicates that n-butyl propionate is of low priority for further work for mammalian toxicity, skin irritation and sensitization, and eye irritation.

Although ecotoxicity endpoints have been satisfied, the environmental fate data are insufficient to meet HPV Program criteria. Additional recommended work includes photodegradation, stability in water (hydrolysis), and transport and distribution within the environment (Level III Fugacity modeling).

REFERENCES

1.Klimisch, H.J., Andreae, M., and Tillmann, U. 1997. A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. *Regulatory Toxicology and Pharmacology* 25: 1-5.

2.USEPA. 1999. Determining the Adequacy of Existing Data. Available on USEPA website at http://www.epa.gov/chemrtk/datafin.htm.

Table 1. Data Available for n-Butyl Propionate (CAS # 590- 01-2)*

Endpoint	Value	Method or Source
Physical-Chemical		
Melting point	-89 ºC	Handbook data
Boiling point	146.8 ºC	Handbook data
Density	0.875 g/cm^3 at 20 ºC	Handbook data
Partition coefficient	2.025	Handbook data
Water solubility	2000 mg/l at 20ºC	The Dow Chemical Company
Vapor Pressure	3.8 hPa at 20ºC	
Vapor density	4.5 (air = 1)	Handbook data
Environmental Fate		
Photodegradation	no data	
Stability in water	no data	
Fugacity modeling	no data	
Biodegradation	92 % after 20 days	APHA, 1985.
Ecotoxicity		
Acute toxicity to fish	*Pimephales promelas* 96-hr LD_{50} = 43 mg/l	USEPA/600/4-85/013
Acute toxicity to invertebrates	Daphnia magna 48-hr LD_{50} = 86 mg/l	USEPA/600/4-85/013
Toxicity to algae	Pseudokirchneriella subcapitata *96-hr ED_{50} = 239 mg/l* *NOEC = 82.2 mg/l*	OECD 201, EEC 92/69 C.3 USEPA 40CFR797.1500, TSCA revision Fed Reg 50 No.188
Mammalian Toxicity		
Acute toxicity	*LD_{50} = 11,031- 12,344 mg/kg* LC_{50} > 4000 ppm LD_{50} > 14,008 mg/kg	Oral, rat Inhalation, rat Dermal, rabbit
Acute irritation	*Very slight irritation* Moderate irritation	Skin irritation, OECD 404 Eye irritation, OECD 405
Dermal Sensitization	*Negative*	Guinea pig maximization test, OECD Guideline 406
Mutagenicity	*Negative*	Ames test with 5 tester strains and *E.coli* strain WP2*uvr*ApKM101
Chromosomal aberration	*Negative*	USEPA OPPTS 870.5375 rat lymphocytes
Repeated dose toxicity	*NOEL = 250 ppm*	EPA 40CFR 54 798.2450 (1989) 13-week inhalation study in rats
Reproductive toxicity	*NOEL = 1500 ppm*	EPA 40CFR 54 798.2450 (1989) 13-week inhalation study in rats
Developmental toxicity	*NOEL (maternal tox) = 500 ppm* NOEL (develop tox) $\geq$ 2000 ppm	EPA 40CFR 54 798.4900 (1985) inhalation study in pregnant rats
Neurotoxicity	*NOEL = 3200 ppm*	Equivalent to OECD 413 9-exposure inhalation study in rats

*Robust summaries and references can be found in the butyl propionate Dossier (Appendix 1)

Table 2: Test Plan for n-Butyl Propionate (CAS 590-01-2)

Endpoint	Data Available	Testing Recommended
Physical-Chemical Data		
Melting point	Yes	
Boiling point	Yes	
Density	Yes	
Partition coefficient	Yes	
Water solubility	Yes	
Flash point	Yes	
Vapor density	Yes	
Environmental Fate		
Photodegradation	No	Yes
Stability in water	No	Yes
Fugacity Modeling	No	Yes
Biodegradation	Yes	
Ecotoxicity		
Acute toxicity to fish	Yes	
Acute invertebrate toxicity	Yes	
Toxicity to algae	Yes	
Mammalian Toxicity		
Acute toxicity	Yes	
Acute irritation	Yes	
Dermal Sensitization	Yes	
Mutagenicity	Yes	
Chromosomal aberration	Yes	
Repeated dose toxicity	Yes	
Reproductive toxicity	Yes	
Developmental toxicity	Yes	