

Substance Profiles for The Challenge

Toluene Diisocyanates

CAS RN	91-08-7	2,6-diisocyanato-1-methyl-benzene (2,6 toluene diisocyanate)
CAS RN	584-84-9	2,4-diisocyanato-1-methyl-benzene (2,4-toluene diisocyanate)
CAS RN	26471-62-5	1,3-diisocyanatomethyl-benzene (mixed isomers of toluene diisocyanate)

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) required the Minister of Health and Minister of the Environment to categorize the approximately 23 000 substances on the Domestic Substances List (DSL). Categorization involved identifying those substances on the DSL that are a) considered to be persistent (P) and/or bioaccumulative (B), based on criteria set out in the *Persistence and Bioaccumulation Regulations* (Government of Canada, 2000), and “inherently toxic” (iT) to humans or other organisms, or b) that present, to individuals in Canada, the greatest potential for exposure (GPE).

Further to this activity, the Act requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that meet the categorization criteria. A screening assessment involves a scientific evaluation of available information for a substance to determine whether the substance meets the criteria set out in section 64 of CEPA 1999. Based on the results of a screening assessment, the Ministers can propose taking no further action with respect to the substance, adding the substance to the Priority Substances List (PSL) for further assessment or recommending the addition of the substance to the List of Toxic Substances in Schedule 1 of CEPA 1999 and, where applicable, the implementation of virtual elimination of releases to the environment.

A number of substances have been identified by the Ministers as high priorities for action based on the information obtained through the categorization process. This includes substances:

- that were found to meet all of the ecological categorization criteria, including persistence, bioaccumulation potential and inherent toxicity to aquatic organisms (PBiT), and that are known to be in commerce in Canada, and/or
- that were found either to meet the categorization criteria for GPE or to present an intermediate potential for exposure (IPE), and were identified as posing a high hazard to human health based on available evidence on carcinogenicity, mutagenicity, developmental toxicity or reproductive toxicity.

Based on a consideration of the ecological and/or human health concerns associated with these substances, and the requirement under section 76.1 of CEPA 1999 for the Ministers to apply a weight of evidence approach and the precautionary principle when conducting

and interpreting the results of an assessment, sufficient data are currently available to consider these substances as meeting the criteria under Section 64 of CEPA 1999.

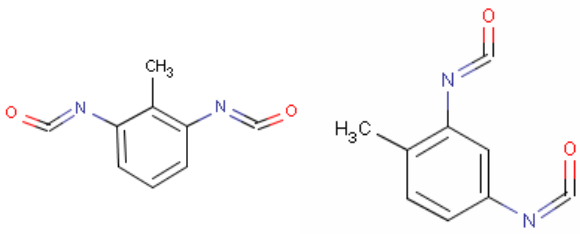
As such, the Ministers have issued a Challenge to industry and other interested stakeholders through publication in Canada Gazette Part I December 9, 2006 to submit, within the timelines stated in the Challenge section of this publication of this document below, specific information that may be used to develop and benchmark best practices for risk management and product stewardship.

The Toluene diisocyanate substances were identified as high priorities for action as they were determined to have a high potential for exposure to individuals in Canada (GPE or IPE), and are considered to present a high hazard to human health. The technical human health and ecological information that formed the basis for concern associated with this substance is contained in Appendices I and II, respectively.

Substance Identity

For the purposes of this document, the term Toluene diisocyanate (TDI) is used to refer to all three substances in this document.

CAS Registry Number	<p><i>Substance 1:</i> 91-08-7;</p> <p><i>Substance 2:</i> 584-84-9;</p> <p><i>Substance 3:</i> 26471-62-5</p>
Inventory names	<p><i>Substance 1:</i> benzene, 2,6-diisocyanato-1-methyl-; 2,6 toluene diisocyanate</p> <p><i>Substance 2:</i> benzene, 2,4-diisocyanato-1-methyl-; 2,4 toluene diisocyanate</p> <p><i>Substance 3:</i> benzene, 1,3-diisocyanatomethyl-; mixed isomers of toluene diisocyanate</p>
Other names	<p><i>Substance 1:</i> Benzene, 1,3-diisocyanato-2-methyl-; 2-methyl-m-phenylene diisocyanate; 1,3-Diisocyanato-2-methylbenzene; 2,6-Isomer of Toluene Diisocyanate; 2,6 Diisocyanatotoluene; 2,6-TDI; Toluene-2,6-diisocyanate; 2-Methyl-m-phenylene isocyanate; Isocyanic acid, 2-methyl-m-phenylene ester</p> <p><i>Substance 2:</i> 1,3-Diisocyanato-4-methylbenzene; 2,4-Diisocyanato-1-methylbenzene; 2,4-TDI; 2,4-Toluene diisocyanate (2,4-TDI); 4-Methyl-1,3-phenylene diisocyanate; 4-Methyl-m-phenylene isocyanate; 4-Methyl-meta-phenylene diisocyanate; Isocyanic acid, 4-methyl-m-phenylene ester</p> <p><i>Substance 3:</i></p>

	<i>m</i> -tolylidene diisocyanate; Benzene, 1,3-diisocyanatomethyl-; <i>m</i> -tolylidene diisocyanate; Crude tolylene diisocyanate; 1,3-Diisocyanatomethylbenzene ; TDI (mixed isomers); Toluenediisocyanate mixed isomer; Benzene, 1,3-Diisocyanatomethyl; Toluene diisocyanate (mixed isomers); Diisocyanatotoluene; Isocyanic acid, methyl- <i>m</i> -phenylene ester; Methyl- <i>m</i> -phenylene isocyanate; Methylphenylene isocyanate; TDI; TDI 80; TDI 80/20; Toluene diisocyanate; Toluene diisocyanate (80% 2,4-TDI; 20% 2,6-TDI); Toluenediisocyanate (mixed isomers); Tolylene diisocyanate; Tolylene isocyanate;
Chemical group	Discrete organics
Chemical sub-group	Aromatic Diisocyanates
Chemical formula	C ₉ H ₆ N ₂ O ₂
Chemical structure	 <p style="text-align: center;"><i>2,6 toluene diisocyanate</i> <i>2,4 toluene diisocyanate</i></p>
SMILES	<chem>O=C=Nc(c(ccc1N=C(=O))C)c1</chem>
Molecular mass	175.17 g/mol

All three Chemical Abstract System numbers representing the two isomers of Toluene diisocyanate (TDI) and mixtures of the two isomers were notified to the DSL. Depending on the TDI compound, between 6 to 9 companies notified these substances to the Domestic Substances List, reporting from 12,000 to 30,200 tonnes in commerce in 1986. These compounds were notified for a variety of uses including; adhesives, binders, sealants, formulation components for polymers, paint and coating additives and in a variety of industrial sectors including; automotive, aircraft, and watercraft, electrical and electronic products, paint and coating and the plastic and synthetic coatings sectors. Recent information on TDI indicates that it is used primarily in the production of polyurethane foams. The flexible and semi-rigid polyurethane foams have a variety of industrial applications including use in furniture, carpet underlay, bedding, and by the transportation sector (e.g. panels, padding and bumpers). The rigid polyurethane foams also have applications reported for thermal insulation in housing, refrigerated trucks, rail cars and containers, refrigerators and freezers, and in pipe insulation.

THE CHALLENGE

Respecting direction under section 76.1 of CEPA 1999, information obtained during conduct of categorization is sufficient to conclude that criteria under Section 64 of CEPA 1999 are met for this substance in that it “may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health”. As such, the Ministers are prepared to recommend to the Governor in Council that this substance be added to the List of Toxic Substances in Schedule 1 of CEPA 1999 with the intent of initiating the development of risk management measures taking into account socio-economic considerations. The measures will be subject to review in light of new scientific information, including monitoring and ongoing assessment activities.

Section 71 Notice

Information needed for improved decision-making with regard to risk assessment and management of this substance is being gathered using section 71 of CEPA 1999. This notice applies to any person who, during the 2006 calendar year, manufactured or imported a total quantity greater than 100 kilograms of the substance, whether alone, in a mixture, in a product or in a manufactured item.

The 2006 information mandated through the notice relates to, among other things, quantity of the substance imported, manufactured or used, types of uses of the substance, and releases of the substance to the environment.

Copies of the section 71 notice and guidance on how to comply with it are available from the Government of Canada Chemicals Portal (www.chemicalsubstanceschimiques.gc.ca), or from the contact provided below.

Responses to the section 71 notice must be received at the address provided below by June 5, 2007.

Opportunity to Submit Additional Information on Current Uses and Existing Control Measures to Inform the Risk Management Approach for this Substance

The Ministers of Health and Environment are inviting the submission of additional information that is deemed beneficial by interested stakeholders, relating to the extent and nature of the management/stewardship of substances listed under the Challenge.

Organizations that may be interested in submitting additional information in response to this invitation include those that manufacture, import, export or use this substance whether alone, in a mixture, in a product or in a manufactured item.

Additional information is being invited in the following areas:

- Import, manufacture and use quantities
- Substance and product use details
- Releases to the environment and spill management
- Current and potential risk management and product stewardship actions
- Existing legislative or regulatory programs controlling/managing the substance
- Information to support the development of a regulatory impact assessment.

A questionnaire is available which provides a detailed template as an example for the submission of this information. Guidance on how to respond to the challenge questionnaire is also available. Interested stakeholders are invited to provide available additional information, recognizing that not all questions in the questionnaire may be relevant to a particular substance, use, or industrial sector.

Copies of the questionnaire and associated guidance are available from the Government of Canada Chemicals Portal (www.chemicalsubstanceschimiques.gc.ca), or from the contact provided below.

Responses to the questionnaire should be received at the address provided below by June 5, 2007.

Request for Documents and Submission of Information

Documents and instructions may be requested from the following contact. Information in response to the above Challenge must be submitted to this address.

DSL Surveys Coordinator
Place Vincent Massey, 20th Floor
351 Saint Joseph Boulevard
Gatineau QC K1A 0H3
Tel: 1-888-228-0530 / 819-956-9313
Fax: 1-800-410-4314 / 819-953-4936
Email: DSL.surveyco@ec.gc.ca

Appendix I
Human Health Information
to Support The Challenge for
Toluene Diisocyanates

CAS RN	91-08-7	2,6-diisocyanato-1-methyl-benzene (2,6 toluene diisocyanate)
CAS RN	584-84-9	2,4-diisocyanato-1-methyl-benzene (2,4-toluene diisocyanate)
CAS RN	26471-62-5	1,3-diisocyanatomethyl-benzene (mixed isomers of toluene diisocyanate)

Introduction

Under the *Canadian Environmental Protection Act, 1999* (CEPA, 1999), Health Canada undertook to categorize all substances on the Domestic Substances List (DSL) to identify those representing the greatest potential for human exposure (GPE) and those among a subset of substances considered persistent (P) and/or bioaccumulative (B) by Environment Canada that are also considered to be “inherently toxic” to humans.

In order to efficiently identify substances that represent the highest priorities for screening assessment from a human health perspective, Health Canada developed and applied a Simple Exposure Tool (SimET) to the DSL to identify those substances that meet the criteria for GPE, Intermediate Potential for Exposure (IPE) or Low Potential for Exposure (LPE), and a Simple Hazard Tool (SimHaz) to identify those substances that pose a high or a low hazard.

Mixed isomers of toluene diisocyanate, CAS No. 26471-62-5, are considered to meet the criteria for GPE under SimET and for high hazard under SimHaz. The 2,4- and 2,6-isomers of toluene diisocyanate, when considered separately were each deemed to meet the criteria for IPE under SimET and high hazard under SimHaz. This document summarizes the currently available information used to support the inclusion of these substances in the Challenge.

Exposure Information from Health Related Components of DSL **Categorization**

As mentioned above, SimET was developed and used to identify substances on the DSL considered to represent GPE. This approach was based on three lines of evidence: 1) the quantity in commerce in Canada, 2) the number of companies involved in commercial activities in Canada (i.e., number of notifiers), and 3) the consideration by experts of the potential for human exposure based on various use codes. The proposed approach was released for public comment in November 2003 and also enabled designation of

substances as presenting an Intermediate (IPE) or Lowest Potential for Exposure (LPE), based on criteria for quantity and nature of use (Health Canada, 2003)

Results of the Application of SimET

Mixed isomers of toluene diisocyanate have been determined to be GPE and the 2,4- and 2,6- isomers of toluene diisocyanate, when considered separately were each deemed to meet the criteria for IPE under SimET based on a consideration of the DSL nomination information listed below.

Nomination Information for DSL

Quantity in Commerce

The quantity of 26471-62-5 reported to be manufactured, imported or in commerce in Canada during the calendar year 1986 was 24 000 000 kg

The quantity of 91-08-7 reported to be manufactured, imported or in commerce in Canada during the calendar year 1986 was 12 000 000 kg

The quantity of 584-84-9 reported to be manufactured, imported or in commerce in Canada during the calendar year 1986 was 30 200 000 kg

Number of Notifiers

The number of notifiers for the calendar years 1984-86 for 91-08-7 was six.

The number of notifiers for the calendar years 1984-86 for 584-84-9 was six.

The number of notifiers for the calendar years 1984-86 for 26471-62-5 was nine.

Use Codes and Description

The following DSL use codes have been identified for the substances represented by the three CAS numbers:

CAS No. 26471-62-5

- 4 Adhesive/binder/sealant/filler
- 21 Formulation component
- 28 Monomer
- 30 Paint/coating additives
- 36 Polymer, component of a formulation
- 51 Function other than that listed in codes 02-50
- 56 Automotive, Aircraft and Watercraft
- 61 Electrical or Electronic Products
- 80 Paint and Coating
- 86 Plastics
- 87 Plastics and Synthetic Resins

CAS No. 584-84-9

- 4 Adhesive/binder/sealant/filler
- 10 Chemical intermediate - organic
- 21 Formulation component
- 51 Function other than that listed in codes 02-50
- 52 Adhesive and Sealant Production
- 56 Automotive, Aircraft and Watercraft
- 77 Organic Chemicals, Specialty
- 80 Paint and Coating
- 86 Plastics
- 87 Plastics and Synthetic Resins
- 98 Used in industry other than those specified in codes 51-97

CAS No. 91-08-7 (Note: pure 2,6-toluene diisocyanate is not commercially available)

- 4 Adhesive/binder/sealant/filler
- 10 Chemical intermediate - organic
- 21 Formulation component
- 36 Polymer, component of a formulation
- 51 Function other than that listed in codes 02-50
- 52 Adhesive and Sealant Production
- 56 Automotive, Aircraft and Watercraft
- 86 Plastics
- 98 Used in industry other than those specified in codes 51-97

Potential Uses in Canada

Mixtures of 2,4- and 2,6-toluene diisocyanate (TDI) isomers dominate industrial use of TDI.

Pure 2,4- isomer is used in some specialty elastomers applications.

Pure 2,6- isomer has no industrial use (Allport et al., 2003)

TDI is reacted with a polyol in the presence of surfactant, catalyst and blowing agent to form polyurethane foam (PUF). Production of PUF accounts for about 90% of TDI supply, the majority of which is used in flexible foam. The distribution of use of flexible PUF is as follows, furniture 32%, transportation 30%, carpet underlay 20%, bedding 10%, packaging 8%, other 10% (Chemexpo, 1999). Rigid PUF panels are used for thermal insulation in housing, refrigerated trucks, rail cars and containers, refrigerators and freezers, and in pipe insulation. Semi-flexible and semi-rigid PUF are used in automotive panels, padding and bumpers. TDI may be used as part of the isocyanate component, together with other isocyanates in semi-rigid and semi-flexible foams. (NLM 2006, Allport et al., 2003)

TDI is used for producing material other than PUF in approximately these proportions: polyurethane coatings 4%, cast elastomers 2%, sealants 2%, miscellaneous including fibres 2%. (Chemexpo, 1999)

TDI or a TDI adduct is used in polyurethane-modified alkyd paints and coatings including automotive and marine paint, wood varnish, floor treatment, wire and powder coating. Castable urethane elastomers are used in adhesives, sealants, automotive parts, shoe soles, wheels, pond liners, blood bags, and other products. Sealants and adhesives may be produced from TDI or a TDI adduct.

TDI is used in the production of coatings for textiles for durability and waterproofing and in the production of polyurethane used to make the fabric Spandex. TDI may be used as a cross-linking agent in nylon 6 production. (NLM 2006, NTP 2005)

Methylene diisocyanate has replaced TDI in some applications. The extent of the substitution is not known.

Hazard Information from Health Related Components of DSL Categorization

Simple Hazard Tool (SimHaz)

SimHaz is a tool that has been used to identify, among all of the approximately 23 000 substances on the DSL, those considered to present either high or low hazard to human health based on formalized weight of evidence criteria and/or peer review/consensus of experts. This tool has been developed through extensive compilation of hazard classifications of Health Canada and other agencies and consideration of their robustness based on availability of transparent documentation of both process and criteria (Health Canada, 2005).

Results of the Application of SimHaz

The 2,4- and 2,6- isomers and mixed isomers of toluene diisocyanates are considered to be potentially high hazard substances based on the following classifications for carcinogenicity.

The International Agency for Research on Cancer (IARC) has classified toluene diisocyanate as Carcinogenicity Group 2B (possibly carcinogenic to humans). IARC noted that there is inadequate evidence for the carcinogenicity of toluene diisocyanates in humans, but there is sufficient evidence for the carcinogenicity of toluene diisocyanates in experimental animals (IARC, 1999).

The European Commission (EC) has classified toluene diisocyanate as Category 3 for carcinogenicity (Causes concerns for humans owing to possible carcinogenic effects) (European Commission, 1997; European Commission 2004; ESIS, 2006).

The United States National Toxicology Program (NTP) has classified toluene diisocyanate as reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity in experimental animals (NTP, 2005).

Uncertainties

SimET and SimHaz have been developed as robust tools for effectively identifying substances from the DSL considered to be human health related priorities for further consideration. It is recognized that they do not include a number of elements normally considered in a human health risk assessment such as a comprehensive characterization of exposure and hazard, a comparison of exposure metrics to hazard metrics and a detailed analysis of uncertainties. However, as a result of the combination of the severe hazard properties of these substances and their high potential for exposure to humans, evaluation of whether there is a need for preventative and protective actions is required.

References

Allport, D.C., Gilbert, D. and Outterside, S. eds. 2003. MDI and TDI: Safety, Health and the Environment: A Source Book and Practical Guide. Chichester, England, Wiley.

Chemexpo. 1999. Chemical Profile on Toluene diisocyanate. Cited in NLM, NIH Hazardous Substances Data Bank 2006. Toluene Diisocyanate. National Library of Medicine, National Institutes of Health.
<http://toxnet.nlm.nih.gov/>

European Commission 1997. Toluene di-isocyanates. Summary Record. Commission Working Group on the Classification and Labelling of Dangerous Substances. Meeting at ECB Ispra, 15-21 October 1997. ECBI/51/97 - Rev. 3
http://ecb.jrc.it/classlab/SummaryRecord/5197r3_sr_CM1097.doc

European Commission 2004. 2-methyl-m-phenylene diisocyanate. 4-methyl-m-phenylene diisocyanate. M-tolylidene diisocyanate. Commission Directive 2004/73/EC of 29 April 2004. Annex 1A. Official Journal of the European Communities 16.6.2004. L 216/49.
http://ecb.jrc.it/DOCUMENTS/Classification-Labelling/ATPS_OF_DIRECTIVE_67-548-EEC/29th_ATP.pdf

ESIS 2006. CAS No. 91-08-7. 2-methyl-m-phenylene diisocyanate. CAS No. 584-84-9. 4-methyl-m-phenylene diisocyanate. CAS No. 26471-62-5. M-tolylidene diisocyanate. ESIS Version 4.50. European Chemical Substances Information System.
<http://ecb.jrc.it/esis/>

Health Canada 2003. Proposal for Priority Setting for Existing Substances on the Domestic Substances List under the Canadian Environmental Protection Act, 1999: Greatest Potential for Human Exposure.

http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/contaminants/existsub/exposure/greatest_potential_human_exposure-risque_exposition_humaine_e.pdf

Health Canada 2005. Proposed Integrated Framework for the Health-Related Components of Categorization of the Domestic Substances List under CEPA 1999

http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/contaminants/existsub/framework-int-cadre_e.pdf

IARC 1999. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 71. Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide (part two). World Health Organization. International Agency for Research on Cancer. Lyon, France. Toluene Diisocyanates. p.865-879.

<http://www.inchem.org/documents/iarc/vol71/031-toldiisocyan.html>

NLM, NIH Hazardous Substances Data Bank 2006. Toluene Diisocyanate. National Library of Medicine, National Institutes of Health.

<http://toxnet.nlm.nih.gov/>

NTP 2005. 11th Report on Carcinogens. US National Toxicology Program. Department of Health and Human Services. Substance Profile: Toluene Diisocyanate.

<http://ntp.niehs.nih.gov/ntp/roc/eleventh/profiles/s177tdi.pdf>

Ontario Ministry of the Environment, 2005. Ontario Air Standards for Toluene Diisocyanate (TDI)

**Appendix II
Ecological Information
to Support The Challenge for
Toluene Diisocyanates**

CAS RN	91-08-7	2,6-diisocyanato-1-methyl-benzene (2,6 toluene diisocyanate)
CAS RN	584-84-9	2,4-diisocyanato-1-methyl-benzene (2,4-toluene diisocyanate)
CAS RN	26471-62-5	1,3-diisocyanatomethyl-benzene (mixed isomers of toluene diisocyanate)

Introduction

The information in this document will form the basis of a screening assessment under section 74 of CEPA, 1999. Data relevant to an ecological screening assessment were identified in original literature, review documents, commercial and government databases prior to December 2005. Properties and characteristics may also have been estimated using Quantitative Structure Activity Relationship (QSAR) models. Model predictions for all 3 TDI substances were identical, and therefore differences between TDI isomers were not observed in the output from these models.

Physical and Chemical Properties

Table 1 contains experimental and modelled physical-chemical properties of Mixed Isomers of toluene diisocyanate which are relevant to the environmental fate of all 3 TDI compounds.

Table 1. Phys-chem properties for commercial mixture of 2,4 TDI and 2,6-TDI (80/20).

Property	Type	Value	Temperature (C°)	Reference
log Kow	Modeled	3.74	25	Kowwin v.1.67
log Kow	Experimental	3.4		Yakabe et al, 2000
Melting point	Experimental	11-14 °C		HSDB (2003)
Boiling point	Experimental	251 °C		HSDB (2003)
log Koc	Modeled	0.35-3.96		PCKOCWIN v.1.66; ASTER
Vapour Pressure	Experimental	0.0015 kPa/ 0.000661 mm Hg 0.023 mm Hg	20 25	Fisk and Langer, 1995 HSDB, 2003
Henry's Law Constant	Modeled	1.11 e-5 atm- m ³ /mole	25	EPIWINv3.12
Water solubility	Experimental	insoluble in water		Pemberton, D. and Tury, B (2004)

TDI is insoluble in water (hydrophobic) and is miscible in a number of common organic solvents including; alcohol, monoethyl ether, ether, acetone, carbon tetrachloride, benzene, chlorobenzene, kerosene and olive oil. TDI is highly volatile (IPCS PIM 1997). TDI has a characteristic odour which allows it to be detected readily (odour recognition at 2.10 ppm), however, at the maximum recommended concentration (0.02 ppm) TDI is not detectable by its smell (HSDB 2003).

Manufacture, Importation, and Uses

Manufacture and Importation

Refer to Appendix I

Uses

Refer to Appendix 1

Releases, Fate and Presence in the Environment

Releases

Toluene diisocyanates are synthetic organic compounds and are not known to naturally occur in the environment (IPCS PIM 1997). Based on information collected from the National Pollutant Release Inventory (NPRI; see Table 2) most releases reported are to air, with no releases reported directly to water or land (excluding data collected by NPRI on disposal and recycling). The number of facilities reporting to NPRI has remained fairly constant from 1994-2002, with 27 to 38 facilities reporting in a given year.

Table 2. Summary of Releases to Air Reported for TDI to NPRI 1999-2002

CAS	Year	Releases To Air
26471-62-5	1999	1.418
26471-62-5	2000	0.749
26471-62-5	2001	92.561
26471-62-5	2002	0.932
584-84-9	1999	0.005
584-84-9	2000	0.004
584-84-9	2001	0.016
584-84-9	2002	0.061
91-08-7	1998	
91-08-7	2000	
91-08-7	2001	
91-08-7	2002	

(Source NPRI)

Fate

Environmental fate modelling requires knowledge of the physical-chemical properties of the TDI isomers. Table 3 reports the values relevant to assess the fate of TDI in a unit world environment. The extent to which modelling of the environmental distribution and partitioning between the various media is useful for this group of chemicals is questionable, by virtue of the reactivity of diisocyanates in water, soil (particularly moist soil) and sediment.

Table 3: Results of the Level III fugacity modelling (EPIWIN V3.04)

Receiving media	% in Air	% in Water	% in Soil	% in Sediment
Air (100%)	52.5	14	31.7	1.79
Water (100%)	0.32	88.2	0.193	11.3
Soil (100%)	0.00672	0.249	99.7	0.0319
Water, Soil (50% each)	0.0662	16.9	80.8	2.17
Air, Water (50% each)	5.35	81.1	3.23	10.4
Air, Soil (50% each)	1.28	0.583	98.1	0.0746
Air, water, soil (33.3% each)	1.11	16.9	79.9	2.16

Multimedia modelling of the partitioning of TDI indicates that, depending on the medium to which they are released, these compounds can partition to an appreciable extent into air, water and soil. When released to air the principle medium of initial released (based on NPRI data), it is expected that some TDI will partition to water and soil. Given that hydrolysis was not considered when generating the Level III fugacity results, the extent to which these results reflect the partitioning behaviour of these substances in the environment is questionable.

In water, soil and sediment, and under conditions typical to the environment, it is expected that TDI's affinity to react with amines more strongly than with water, combined with its relative insolubility in water, would result in reactions that lead to the formation of a solid crust of polyureas, encasing unreacted TDI. Hydrolysis in the presence of water in these three media, which acts as a catalyst for further reactions between the diisocyanates and amines, is expected to be the primary driver in the fate of TDI in the environment. The role hydrolysis plays in the environmental fate of these chemicals is described in further detail in the Rationale for P, B and iT Status section.

Presence in the Environment

As a result of its low aqueous solubility and inherent reactivity with water it is not expected that significant concentrations of TDI would be found in the water (or moist soil and sediment), and this has been seen to be the case. In fact, TDI has not been detected in any aquatic studies (Pemberton and Tury 2004).

Evaluation of P, B and iT Properties

Environmental Persistence

The fate and behaviour of TDI in the atmosphere is an important factor influencing the persistence of these compounds in the environment. TDI is volatile, although emissions are generally regarded as low from industrial processes (IPCS PIM 1987, Tury et al 2003). Indirect photolytic degradation as a result of photogenerated hydroxyl radicals has been demonstrated to be a significant degradation pathway for these compounds (Pemberton and Tury 2004). Surprisingly, despite the reactivity of TDI with water, Tury et al (2003) observed that reaction (i.e. hydrolysis) with atmospheric water was not significant. There is good agreement between the modelled and experimental atmospheric half life data for these compounds with AOPWIN v1.91 predicting a half-life of 1.7 days using the default global average concentrations for hydroxyl radicals 1.5×10^6 OH radicals/cm³ (12h day). Experimentally Tury et al (2003) reported a half life of 1.4 days for TDI based on experimental reaction rates and also noted that photooxidation did not appear to lead to the formation of toluene diamines (TDA) (<0.05%) (Tury et al 2003). Atkinson (1989) also calculated a half life in air for the three TDI compounds of 1.5 days based on experimental reaction rates with hydroxyl radicals (Atkinson, 1989). Based on the evidence available, it is believed that TDI should not be considered persistent in the atmosphere based on reactions with photogenerated hydroxyl radicals.

The TDI compounds also do not appear to persist in water, soil, or sediment, and in fact, their residence time in these media may be quite short, relatively speaking. However, given the reactive nature of these compounds the degradation products from these reactions in the environment, namely polyureas and toluene diamines (TDA) were also examined. TDI compounds are considered transient in media where water is present (e.g. water, moist soils, sediment) with half-lives of under a minute noted (Yakabe et al, 1999). However, the reaction of an amine with isocyanate is faster than the hydrolysis reaction of water with isocyanate, which, in the case of a diisocyanate like TDI, leads primarily to reactions forming polyureas (Yakabe et al 1999, Pemberton and Tury 2004). Polyureas are generally considered to be inert, insoluble solids; albeit persistent for millennia.

As previously described, under conditions typical to the environment it is expected that TDI's affinity to react with amines more strongly than with water, and its relative insolubility in water, would result in reactions that lead to the formation of a solid crust of polyureas encasing the unreacted material (TDI). This crust serves to limit the contact of the unreacted TDI with the surrounding water, while simultaneously limiting the egress of amine, thereby enhancing the reactions with amines within this encrusted region, which then leads to an even higher yield of polyureas (Pemberton and Tury 2004). This phenomenon has been observed in a number of studies including those by Yakabe et al (1999) and Tury et al (2003).

It is well documented in numerous studies that the aromatic diisocyanates will hydrolyze and react rapidly in both water and soil (Pemberton and Tury 2004, Heimbach et al 1996, Yakabe et al 1999, Tury et al 2003). In addition, hydrolysis predictions generated using

the HYDROWIN model (part of the EPIWIN suite) are in agreement with the conclusions of the experimental data. Although the model does not predict a hydrolysis half-life, it does state that substance contains an isocyanate group and that the $t_{1/2}$ is expected to be < 10 minutes (Hydrowin v1.67 results).

As noted, the major transformation product of TDI is inert polyureas, which are both insoluble and anticipated to persist in the environment for millennia. Polyureas have been identified as polymers of low ecological concern, both because of their inert characteristics, and based on the expectation that they are not bioavailable, and thus unlikely to accumulate in organisms and food chains, and subsequently exert effects, in the environment. Besides polyureas, however, there is also the potential for TDA to form as a by-product of the hydrolysis of TDI, although the formation of TDA is generally considered negligible relative to the formation of polyureas in aqueous media. Yakabe et al (1999) conducted a series of experiments to determine under which scenarios it can be anticipated that TDA may form to a significant extent. Overall, Yakabe et al (1999) observed that TDA production is markedly less under static, unstirred conditions, and that only with good agitation and low loadings of TDI is TDA a major reaction product. In all other cases, the major reaction product was a solid material, found to be polyurea under further analysis (Yakabe et al 1999). I should also be noted that the scenarios which resulted in a significant, albeit low, concentration of TDA in the water column would occur under what would normally be considered unnaturally high dispersion/agitation, and therefore, are not likely to occur in nature.

Nonetheless, appreciable TDA yields were noted with loadings less than 10 mg/L, therefore TDI under certain release scenarios could be viewed as a significant source of TDA to aquatic environments. As a result, it was deemed necessary to consider the persistence of TDA in its evaluation of TDI compounds. Studies provided showed extensive biodegradation under various OECD test protocols. Data provided from the panel showed that for both TDA and MDA (a close analog of TDA) > 70% DOC removal was observed in OECD 302B and 302C inherent biodegradability tests performed by BASF and reported in the European Union Risk Assessment for 4, 4-MDA. Substances such as 2,4-TDA were observed to have 93-100% DOC removal rate in 6 days, and >70% DOC removal in 3 days for 4,4-MDA (BASF AG, 1988, BASF AG, 1993 and ECB 2001).

Based on the weight of evidence approach developed for categorization, these TDA substances would not meet the persistence criteria. As a result, it is believed that these TDA chemicals are not persistent based on experimental and modeled data.

Table 3a. Modeled Data for Persistence of TDI

Medium	Fate Process	Endpoint	Value (Range if applicable)	Model
Air	atm-oxidation	half-life (days)	0.6685	EPIWIN v3.12
Water/Soil/ Sediment	Hydrolysis	half-life (days)	< 10 minutes	Hydrowin v1.67
Water/Soil/ Sediment	Biodegradation	half-life (days)	15 – 60	BIOWIN v4.02
Water/Soil/ Sediment	Biodegradation	Probability of rapid biodegradation	0.002 – 0.2186	BIOWIN v4.02 TOPKAT Aerobic Biodegradability (v6.2)
Water/Soil/ Sediment	BOD	half-life (days)	> 15	ASTER

The empirical and modelled data (Table 3a) demonstrate that these TDI substances do not meet the persistence criteria (half-lives in soil and water ≥ 182 days/ air ≥ 2 days) as set out in the Persistence and Bioaccumulation Regulations (Government of Canada 2000).

Potential for bioaccumulation

It is expected that these TDI substances do not bioaccumulate because their tendency to hydrolyze rapidly makes their uptake and accumulation virtually impossible. The 3 Toluene diisocyanates were not categorized as bioaccumulative, and this decision was reaffirmed by the additional information provided by industry as well as additional literature searches performed. While the models employed for categorization are likely not appropriate for highly reactive chemicals such as TDI in aqueous media, it is useful to summarize them to further the weight of evidence. Table 4a and b presents the bioaccumulation data for both TDI and TDA

Table 4a. Empirical Data for Bioaccumulation of TDA

Test Organism	Substance	Type	Endpoint	Value wet wt (L/Kg) (range if applicable)	Reference
Fish (Carp)	TDA	Experimental	BCF	<5 to <50	MITI 1992

Table 4b. Modeled Data for Bioaccumulation of TDI

Test Organism	Substance	Type	Endpoint	Value wet wt (L/Kg) (range if applicable)	Model
Fish	TDI	Modeled	BAF	380	GOBAS BAF T2MTL (Arnot & Gobas 2003)
Fish	TDI	Modeled	BCF	151-1183	Gobas BCF T2LTL (Arnot & Gobas 2003); OASIS; BCFWIN v2.15

The BCF models predicted a BCF in the range of BCF 151-1183 and a BAF of BAF 380. All of which indicate that these substances have a low potential for bioaccumulation in aquatic organisms. The predicted log Kow for these substances is approximately 3.74. However, it is worth noting that both the log Kow predictions, and the BCF models

which depend them, likely overestimate the lipophilicity of these compounds because of the rapid reactivity and hydrolysis in water. The Kow model KOWWIN v1.67 while providing a prediction also notes in its output that that isocyanates hydrolyze and therefore the estimates are questionable. This rapid hydrolysis with water also limits the determination of log Kow experimentally, and as a result reliable experimental log Kow's are not readily available in the literature. A log Kow of 3.4 was determined experimentally using OECD methods, however, it was of uncertain significance in terms of TDI's environmental fate and behaviour, again, because of TDI's reactivity in the aquatic environment (Yakabe et al 1999, Pemberton and Tury 2004).

TDI is expected to not only hydrolyze rapidly into its transformation products, making TDI generally unavailable to aquatic organisms, but that given the highly reactive properties of diisocyanates, the parent compounds are likely metabolized/degraded at rates significant enough to counter any potential for bioaccumulation or biomagnification. In addition, they are also likely hydrolyzed in the gastrointestinal tract, thereby reducing the potential for uptake of the parent chemical from the gut. TDI substances have been found to be highly reactive in body fluids, with a half life of less than 30 seconds in serum and less than 20 minutes in stomach contents (IPCS EHC 1987). TDI's react easily with moist mucous membranes, forming primary amines, ultimately reacting further with TDI to form Urea compounds (Yakabe et al 1999, Pemberton and Tury 2004, IPCS PIM 1997). The IPCS (1997) reports that some studies on 2,6-TDI in rats showed that in the gastrointestinal tract primarily polymers were formed, and furthermore that most TDI derived material was eliminated by the organism (IPCS PIM 1997). It is believed that TDI reacts with the tissues they contact rather than being absorbed and distributed in the body (IPCS EHC 1987).

The transient existence of TDI in water also makes estimating bioaccumulation experimentally equally difficult. As discussed previously, due to the rapid transformation of TDI into primarily inert polyureas, and in some cases TDA, bioaccumulation of TDI is not expected in organisms. However, there was concern with the potential accumulation of some of products of hydrolysis. It was determined during categorization that the polyureas are a group of low concern polymers with no, or negligible, potential for bioaccumulation in organisms and food chains. There was, however, a concern over the formation of toluene diamines (TDA) as a result of the hydrolysis of TDI in certain situations, primarily rapid dispersion at low release concentrations; other scenarios tended to lead overwhelmingly towards the formation of inert polyureas as opposed to TDA (Pemberton and Tury 2004, Yakabe et al 1999). Regardless of the extent of TDA formation from the reaction of TDI in water, experiments investigating the bioaccumulation of 2,4-TDA (CAS 95-80-7) found a BCF of <5 to <50. While these BCF are based on nominal concentrations, and therefore likely underestimating the true BCF, it still provides strong evidence that TDA compounds themselves are not bioaccumulative (MITI 1992). In addition, Log Kow predictions for these compounds are predicted to be very low (log Kow 0.16) which indicates these substances are not likely to accumulate in organisms in the environment.

In light of this information, it is believed that given the highly reactive properties of diisocyanates, that the parent compounds (TDI) are likely metabolized/degraded at rates significant enough to counter any potential for bioaccumulation or biomagnification. In addition, they are likely hydrolyzed in the gastrointestinal tract, thereby reducing the potential for uptake of the parent chemical from the gut.

The weight of evidence indicates that these substances do not meet the bioaccumulation criterion (BCF, BAF \geq 5000) as set out in the Persistence and Bioaccumulation Regulations (Government of Canada, 2000).

Ecological Effects of TDI compounds

In the Aquatic Compartment

Due to the anticipated transient existence of TDI in aqueous media, including moist soils, it is unlikely that ecological effects will be elicited by the parent TDI compounds. It is likely that test results for TDI in aquatic environments are actually testing the toxicity of the degradation products of TDI. Data on the ecological effects of TDI to sediment dwelling organisms is limited, but reactivity in this medium is expected to be similar to that observed in both the aquatic and moist soil environments. It is anticipated that TDI released to water will primarily form inert polyureas which have the potential to be deposited to sediment, forming an inert component of the sediment strata. While persistent, laboratory and field studies on these inert polyureas have indicated that in small quantities they pose virtually no potential for adverse impacts on the aquatic environment (Heimbach et al 1996).

A submission by the Aromatic diisocyanates panel of the American Chemistry Council (ACC) during DSL categorization addressed the issue of ecotoxicity of the aromatic Diisocyanate compounds, which include TDI. The panel's proposal argued that because of the rapid hydrolysis of these substances any potential toxicity would be mitigated, and that this mitigation would be unlikely to be predicted by any of the QSARs employed for categorization (Tury et al 2003, Heimbach 1996, Yakabe et al 1999). Environment Canada agrees with this assessment by the panel. However, because of the expected rapid degradation of the parent in the aquatic environment, it was felt necessary to examine the hydrolysis degradation products for potential aquatic toxicity. Tables 5a and b presents the ecotoxicity data, both modeled and experimental for TDI and its degradation products to aquatic organisms.

Table 5a. Empirical Data for TDI and its degradation products

Compound	Test Organism	Type of Test	Endpoint	Value (mg/L)	Reference
TDI (mixed isomers)	Fish (Oncorhynchus mykiss)	Acute (96h)	LC50	133	Tadokoro et al 1997
2,4-TDI	Fish (Pimephales promelas)	Acute (96h)	LC50	164	Curtis et al, 1979
TDI (mixed isomers)	Shrimp (Mysidopsis bahia)	Acute (48h)	EC50	18.3	Tadokoro et al , 1997
TDI (mixed isomers)	Daphnia	Acute (48h)	EC50	12.5	Tadokoro et al , 1997
TDI (mixed isomers)	Algae (Chorella vulgaris)	Acute (96h)	EC50	4300	Tadokoro et al , 1997
2,4-TDI	Grass Shrimp (palaemonetes pugio)	Acute (96h)	EC50	508.3	Curtis et al, 1979
2,4-TDA	Daphnia magna	Acute (48h)	EC50	1.6	Pederson et al ,1998
2,4-TDA	Fish (Orange-red killifish)	Acute 48(h)	LC50	850 mg/L	MITI 1992

Table 5b. Modeled Data for TDI and its degradation products

Compound	Test Organism	Type of Test	Endpoint	Value (mg/L)	Reference
2,4 TDA and 2,6-TDA	Daphnia Magna	Acute (48h)	EC50	3.5-3.7	TOPKAT, ECOSAR
2,4 TDA and 2,6-TDA	Fish	Acute (96h)	LC50	219-2800	ECOSAR; TOPKAT, A.I. Expert System; OASIS Forecast, ASTER
TDI (all)	Daphnia magna/water flea	Acute (48h)	EC50	1.5	Topkat v6.2 Daphnia EC50 (v3.1)
TDI (all)	Pimephales promelas/Fathead Minnow	Acute(96h)	LC50	2.97	OASIS Forecast
TDI (all)	Fish	Acute(14d)	LC50	7.13	ECOSAR v.0.99h
TDI (all)	Pimephales promelas/Fathead Minnow	Acute (96h)	LC50	49.1	Topkat v6.2 Fathead Minnow LC50 (v3.2)
TDI (all)	Pimephales promelas/Fathead Minnow	Acute(96)	LC50	276.78	Artificial Intelligence Expert System Basic PNN with Gaussian Kernel (Corrections included)
TDI (all)	Daphnia magna/water flea	Acute (48h)	EC50	1.5	Topkat v6.2 Daphnia EC50 (v3.1)
TDI (all)	Pimephales promelas/Fathead Minnow	Acute (96h)	LC50	2.97	OASIS Forecast

Results from the short term studies of TDI were considered reliable, although it is noted repeatedly in many of the studies that it is in fact the degradation products (hydrolysis) whose toxicity is being measured in the bioassays. In toxicity studies where TDA was measured, to establish how much had formed, levels of only 4-16 mg/l were measured, which is considerably lower than the LC50 values reported for these compounds to fish (Pemberton and Tury 2004). These levels of TDA are in the range of concentrations where effects to *Daphnia magna* have been observed in at least one study, and model predictions (Pederson et al 1998, Environment Canada QSAR predictions). While TDA appears to be toxic at quite low levels to *Daphnia magna*, the EC50 observed still falls outside the criteria for acute toxicity developed for inherent toxicity as part of categorization of ≤ 1 mg/L. As expected, there was an increased toxicity to fish when TDI was dispersed into the test medium via high speed shearing, which enhances the

formation of TDA. However, these conditions do not reflect those expected in the natural environment and are, in that sense, of limited relevance (Pemberton and Tury 2004). Unfortunately, reliable long term studies on the toxicity of TDI to aquatic organisms are currently lacking; although it is expected that the rapid disappearance of TDI in the aqueous media would have a negligible impact on the overall ecotoxicity of the compounds. In the tests which are available studying the long term toxicity of TDI, it was observed that at a value of 10 mg/l, damage to the skin occurred, this was attributed to irritation to the fish's skin caused by direct contact with TDI (Pemberton and Tury 2004)

Based on the available information TDI and its degradation products are expected to exhibit low to moderate acute toxicity to aquatic organisms.

In Other Media

Ecotoxicity data available for TDI in the terrestrial environment are limited. However, generally these compounds were found to have no acute effects to earthworms and the plants which were tested. NOEC's, EC50 and LC50 results were all observed to be >1000 mg/kg dw soil by Van der Hoeven et al (1992a,b). Here as well, it is anticipated that any ecotoxicity noted is due to soluble reaction products such as TDA. Studies described in the GIL Report (2004) indicate that ecotoxicity of TDA to the plants *Avena sativa* and *Lactuca sativa* was higher, with EC50's of 320 and 1000 mg/kg dw soil reported, respectively (GIL Report, 2004). The European Union's IUCLID (2000) dataset cites a number of oral LC50 test results for birds (*Agelaius phoeniceus*) to 2,4-TDI and 2,6-TDI at ≥ 100 mg/kg body weight.

Toxic effects from inhalation and dermal contact are better understood endpoints for TDI, however, these data have generally been produced to address human health concerns, occupational exposure in particular, and do not necessarily reflect exposure pathways anticipated for terrestrial non-human organisms in the environment.

Potential to Cause Ecological Harm

Based on the available information, the three TDI substances do not persist in the environment and are not bioaccumulative. Information on concentrations of toluene diisocyanate in the environment has not been identified at this time. The experimental and modeled ecotoxicological data does indicate that while toluene diisocyanate could cause low to moderate harm to aquatic organisms, at relatively low concentration in the water. Information on potential impacts in other environmental compartments has not been identified.

6. References

Arnot, J.A. and Gobas, F.A.P.C. 2003. A Generic QSAR for Assessing the Bioaccumulation Potential of Organic Chemicals in Aquatic Food Webs. *QSAR Comb. Sci.* 22(3): 337-345.

ASTER. Assessment Tools for the Evaluation of Risk. U.S. Environmental Protection Agency. Environmental Research Laboratory, Duluth, MN. 1993
http://www.epa.gov/med/Prods_Pubs/aster.htm

BCFWIN 2000. Version 2.15. U.S. Environmental Protection Agency.
<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

BIOWIN 2000. Version 4.02. U.S. Environmental Protection Agency.
<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

CEMC (Canadian Environmental Modelling Centre). 2002. Level III v. 2.70 model. Version dated September 2003. Trent University, Peterborough, Ontario. <http://www.trentu.ca/cemc/models/EQC2.html> (downloaded March, 2004).

Curtis, M.W., Copeland, T.L. and C.H. Ward. 1978. Aquatic toxicity of substances proposed for spill prevention regulation. In: Proc. Natl. Conf. Control of Hazardous Material Spills, Miami Beach, FL: 99-103.

ECOSAR 2004. Version 0.99h. U.S. Environmental Protection Agency.
<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

EPIWIN 2000. Version 3.12 U.S. Environmental Protection Agency.
<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

Heimbach, F. et al. 1996. Fate and Biological Effects of Polymeric MDI (4,4-diphenylmethane diisocyanate and homologues) in small artificial ponds. *Ecotox. Environ. Safety* 33: 143-153

HENRYWIN. 2000. Version 1.90. U.S. Environmental Protection Agency.
<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

HSDB 2003. CAS 26471-62-5. Hazardous Substances Data Bank. Generated on October 19, 2006.
<http://toxnet.nlm.nih.gov>

HYDROWIN v.1.67 model (part of the US EPA's EPIWIN suite of QSAR models)

IUCLID 2000. CAS RN. 26471-62-5. m-tolylidene diisocyanate. European Commission. European Chemicals Bureau. Creation date. 18 February 2000.

KOWWIN. 2000. Version 1.67. U.S. Environmental Protection Agency.
<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

MITI. Ministry of International Trade & Industry. 1992. Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan. Chemical Products Safety Division Basic Industries Bureau, Ministry of International Trade & Industry, Edited by Chemicals Inspection & Testing Institute, Japan.

MPBPWIN 2000. Version 1.41. U.S. Environmental Protection Agency.
Information available to <http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

NPRI. National Pollutant Release Inventory. Environment Canada
http://www.ec.gc.ca/pdb/npri/npri_home_e.cfm

Oasis Forecast 2005. Version 1.20. Laboratory of Mathematical Chemistry. Bourgas, Bulgaria.
www.oasis-lmc.org

PCKOCWIN. 2000. Version 1.66. U.S. Environmental Protection Agency.

<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

Pedersen, F., et al., 1998. Immobilisation test of aniline compounds with the crustacean *Daphnia magna*.

Pemberton, D. and Tury, B. 2004. TDI Industry Risk Assessment: Sections on physico-chemical properties, environmental exposures, and environmental effects. GIL Report 2004/E.

Tadokora H, et al. 1997. Ecotoxicities of TDI and TDA to fish, algae and aquatic invertebrates. IN: Chemicals Inspection and Research Institute, Japan. III Report No. 11217

Topkat 2004. Version 6.2. Accelrys, Inc.

<http://www.accelrys.com/products/topkat/index.html>

Tury, B et al. 2003. Fate and Potential Environmental Effects of methylenediphenyl diisocyanate and toluene diisocyanate released into the atmosphere. J. Air & Waste Manage.Assoc. 53:61-66

Yakabe, Y. et al 1999. Fate of methylenediphenyl diisocyanate and toluene diisocyanate in the aquatic environment. Environ.Sci.Technol. 33 (15) 2579-2583

WSKOWWIN. 2000. Version 1.41. U.S. Environmental Protection Agency.

<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>