Substance Profile for The Challenge 2',4',5',7'-tetrabromo-3',6'-dihyroxyspiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one (D & C Red No. 21) CAS No. 15086-94-9

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. Substances found to meet the criteria under section 64 are subject to risk management measures.

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, or of commercial interest, 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

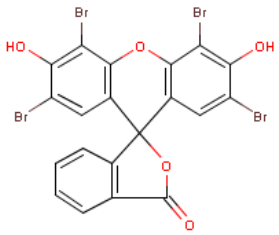
to apply a weight of evidence approach and the precautionary principle when conducting and interpreting the results of an assessment, sufficient data are currently available to conclude whether these substances meet the criteria under section 64 of CEPA 1999.

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 document, specific information that may be used to inform risk assessment and to develop and benchmark best practices for risk management and product stewardship.

The substance 2',4',5',7'-tetrabromo-3',6'-dihyroxyspiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one was identified as a high priority for action as it was found to be persistent, bioaccumulative and inherently toxic to aquatic organisms and is believed to be in commerce in Canada. 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, this substance will be referred to as D & C Red No. 21.

CAS Registry Number	15086-94-9
Inventory names	2',4',5',7'-tetrabromo-3',6'-dihyroxyspiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one; 2-(3,6-dihydroxy-2,4,5,7-tetrabromoxanten-9-y); 2,4,5,7-Tetrabromo-3,6-fluorandiol; 2,4,5,7-Tetrabromofluorescein
Other names	CI Solvent Red 43; Eosin Acid; D & C Red No. 21; Eosin Y, spirit soluble; Japan Red 223; or Bromeosin
Chemical group	Discrete organic
Chemical sub-group	Xanthene Dye
Chemical formula	$C_{20}H_8Br_4O_5$
Chemical structure	
SMILES	O=C(OC(c(c(Oc1c(c(O)c(c2)Br)Br)c(c(O)c3Br)Br)c3)(c12)c4cccc5)c45
Molecular mass	647.9 g/mol

No reports of manufacture in or import into Canada of this substance at or above the reporting threshold of 100 kg in the 2000 calendar year were received in response to a Notice published under section 71 of CEPA 1999. Data collected pursuant to this Notice indicated that for D & C Red No. 21, one foreign company voluntarily reported export of this substance to Canada. Further information was not provided (Environment Canada, 2001). It has been used in the pigment/dye/printing ink industry sectors, and in cosmetics, soap and cleaning products.

THE CHALLENGE

Respecting direction under section 76.1 of CEPA 1999, and in the absence of additional relevant information as a result of this Challenge, the Ministers are predisposed to conclude, based on a screening assessment, that this substance satisfies the definition of toxic under section 64 of CEPA 1999. As such, the Ministers are prepared to then 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.

If it is determined that the substance meets the virtual elimination criteria in subsection 77(4) of CEPA 1999, then subsequent risk management activities will be based on the objective of eliminating the release of any measurable quantity of the substance to the environment. In the absence of further information on existing management practices for a substance, actions would be proposed based on the assumption of worst-case practices. The management actions being considered for such substances at this time include prohibition through regulations, of the manufacture, use, sale, offer for sale and import of this substance, except for those activities controlled under the *Pest Control Products Act* and/or the *Food and Drugs Act.*

Exceptionally, should no information be identified to indicate that this substance is in commerce in Canada, the Ministers will conclude, based on a screening assessment, that this substance does not satisfy the definition of toxic under section 64 of CEPA 1999. However, given the properties of this substance, there is concern that new activities for the substance that have not been identified or assessed under CEPA 1999 could lead to the substance meeting the criteria set out in section 64 of the Act. Therefore it would be recommended that this substance be subject to the Significant New Activity provisions specified under subsection 81(3) of the Act, to ensure that any new manufacture, import or use of this substance in quantities greater than 100 kg/year is notified, and that ecological and human health risk assessments are conducted as specified in section 83 of the Act prior to the substance being introduced into Canada.

Section 71 Notice

Under the Challenge, information deemed necessary for improved decision making may be gathered by the Minister of Environment using section 71 of CEPA 1999. This information may be used for the purpose of assessing whether a substance is toxic or is capable of becoming toxic as defined under section 64 of CEPA 1999, or for the purpose of assessing whether to control, or the manner in which to control a substance.

The information mandated through the notices may relate to, among other things; quantity of the substance imported, manufactured, used, or released, concentrations, suppliers, customers, as well as types of uses of the substance.

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.

Opportunity to Submit Additional Information to Inform Screening Assessment

The Ministers of Health and Environment are inviting the submission of additional information for consideration during screening assessment of this substance. Data of the types described in the following paragraphs are considered most relevant, although other submitted information will be considered.

Data on the persistence, bioaccumulation, and potential for toxicity of the substance to organisms in different environmental media – Through the categorization exercise, available experimental data were collected up to December 2005. Where acceptable experimental data were not available, Quantitative Structure Activity Relationships (QSARs) or read across data were used to fill the data gaps. Since experimental data are preferred, interested parties have an opportunity to provide new or additional relevant experimental study information on the persistence, bioaccumulation, and potential for toxicity of this substance to organisms in different environmental media (air, water, sediment, soil). Efforts should focus on providing data for the endpoints for which quality experimental data does not already exist, as demonstrated by the information summarized in Appendix II of this document. As submitted data will be evaluated for completeness and robustness, it is recommended that stakeholders follow the guidance for test protocols and alternative approaches for test data, as described in Section 8 of the "Guidelines for the Notification and Testing of New Substances: Chemicals & Polymers".[1]

Data on the toxicity of the substance to human health - Through the categorization exercise, the high health priorities for action were those substances identified by various agencies as representing a high health hazard on the basis of potential to induce cancer, and/or adversely affect reproduction and development, two critical determinants of the health of Canadians of all ages. The hazard classifications used were those developed by national or international agencies in which large numbers of substances have been classified for endpoint-specific hazard based on original review and critical evaluation of data, assessments of weight of evidence and extensive peer review. Interested parties have an opportunity to provide new or additional relevant experimental study information on the toxicity of the substance to human health which could inform the screening assessment.

Responses to this part of the challenge for this substance should be received at the address provided below by November 13, 2007.

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[1] "Guidelines for the Notification and Testing of New Substances: Chemicals & Polymers (version 2005)", Government of Canada, Available from http://www.ec.gc.ca/substances/nsb/eng/cp_guidance_e.shtml

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 this part of the challenge for this substance should be received at the address provided below by November 13, 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
2',4',5',7'-tetrabromo-3',6'-dihyroxyspiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one (D & C Red No. 21)
CAS No. 15086-94-9

Introduction

Under the *Canadian Environmental Protection Act, 1999* (CEPA, 1999), Health Canada undertook to categorize 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 persistant (P) and/or bioaccumulative (B) 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 low hazard.

D & C Red No. 21 is considered to meet the criteria for LPE under SimET and does not meet the criteria for high hazard under SimHaz. This document summarizes the currently available information on which the SimET and SimHaz results are based.

Exposure Information from Health Related Components of DSL Categorization

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

D & C Red No. 21 has been determined to be LPE based on a consideration of the DSL nomination information listed below.

Nomination Information for DSL

Quantity in Commerce

The quantity reported to be manufactured, imported or in commerce in Canada during the calendar year 1986 was 2,000 kg

Number of Notifiers

The number of notifiers for the calendar years 1984-1986 was fewer than 4.

Use Codes and Description

The following DSL use codes have been identified for the substance:

13 Colourant - pigment/stain/dye/ink
51 Function other than that listed in codes 02-50
60 Cosmetics
93 Soap and Cleaning Products

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

D& C Red No. 21 has not been classified for hazard by any of the agencies considered under the SimHaz tool and therefore does not meet the criteria for high hazard under SimHaz.

Uncertainties

SimET and SimHaz have been developed as robust tools for effectively identifying substances from the DSL considered to be human health 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.

References

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

Appendix II
Ecological Information
to Support The Challenge for
2',4',5',7'-tetrabromo-3',6'-dihyroxyspiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one
(D & C Red No. 21)
CAS No. 15086-94-9

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. In addition, an industry survey was conducted for the year 2000 through a Canada Gazette Notice issued pursuant to section 71 of CEPA 1999 (Environment Canada, 2001). This Notice requested data on the Canadian manufacture, import, uses and releases of the substance.

Physical and Chemical Properties

Table 1 contains modelled physical-chemical properties of D & C Red No. 21 which are relevant to its environmental fate. Experimental data were not available.

Table 1. Physical and chemical properties for D & C Red No. 21.

Property	Type	Value	Temperature (°C)	Reference
Boiling Point (°C)	Modelled	653.18		MPBPWIN v1.41
Melting Point (°C)	Modelled	284.15		MPBPWIN v1.41
Log Kow (Octanol-water partition coefficient) (dimensionless)	Modelled	6.91	25	Kowwin v.1.67
Log Koc (Organic carbon-water partition coefficient) (dimensionless)	Modelled	6.635		PCKOCWIN v1.66
Vapour Pressure (Pa)	Modelled	2.586×10^{-15}	25	MPBPWIN v1.41
Henry's Law Constant (Pa-m^3/mol)	Modelled	2.28×10^{-13} (2.246×10^{-18} atm-m^3/mol)	25	HenryWin v3.10
Water Solubility (mg/L)	Modelled	2.878×10^{-5}	25	WSKOWWIN v1.41

Manufacture, Importation and Uses

Manufacture and Importation

Environment Canada conducted an industry survey pursuant to section 71 of the Canadian Environmental Protection Act, 1999 requesting industrial information on manufactured and/or imported quantities, uses and releases of 123 substances. Any person who manufactured or imported a total quantity greater than 100 kg of a substance listed in the Notice (whether alone, in a mixture or in a product), was obligated to report. Data collected pursuant to this Notice indicated that for D & C Red No. 21, one foreign company voluntarily reported export of this substance to Canada. Further information was not provided (Environment Canada, 2001).

Elsewhere, it has been identified as a European Union (EU) Low Production Volume Chemical, indicating that production within the EU has been estimated to be in the order of 10 tonnes per year. In 2002, it was reported to the U.S. Environmental Protection Agency (EPA) under the Inventory Update Rule as having a use of 4.5 to 225 tonnes.

Uses

For information on use codes reported to the DSL in 1986, refer to Appendix I.

The use information voluntarily reported by the foreign company in response to the S. 71 survey (Environment Canada, 2001) has been claimed as confidential business information.

It is a red solvent dye that may be used for paper, inks and drugs and is useful for staining difficult tissues (Encyclopedia Britannica and StainsFile, 2007). It is a permitted colouring agent in drugs for internal and external use in Canada (Food and Drug Act, 1985). It is also permitted as a colourant in drugs and cosmetics in the U.S. and is allowed in all cosmetic products in the European Union.

Releases, Fate and Presence in the Environment

Releases

D & C Red No. 21 is not naturally produced in the environment. Releases from anthropogenic sources have not been quantified.

Since there were no reports of import or manufacture at or above the reporting threshold of 100 kg in 2000, releases of this substance to the Canadian environment are presumed to be very low.

Fate

The high log Kow and Koc values indicate that this substance will likely partition to soil and sediments. Indeed, the results of the Level III Fugacity modelling indicates that if the chemical is released equally into the three major environmental compartments (air, water and soil), it will mainly partition into soil and sediments (Table 2) where the chemical has been indicated to persist (Table 3a).

Table 2. Results of the Level III fugacity modelling (EPIWIN V3.12)

	Fraction of Substance Partitioning to Each Medium (%)			
Substance Released to:	**Air**	**Water**	**Soil**	**Sediment**
Air (100%)	0.0009	0.208	85.7	14.1
Water (100%)	0	1.46	0	98.5
Soil (100%)	0	0.003	99.8	0.187
Air, Water, Soil (33.3% each)	0.0003	0.676	53.8	45.6

A vapour pressure of 2.6×10^{-15} Pa and Henry's Law Constant of 2.28×10^{-13} Pa-m^3/mol indicate that D & C Red No. 21 is not volatile. Therefore, even if released to air, it will quickly sorb to particulate matter and partition to soil and sediment as indicated by the results of the Level III fugacity modelling (Table 2) (99%).

Similarly, the low water solubility of 2.88×10^{-5}mg/L indicates that if released to water, D & C Red No. 21 will not remain in the aqueous phase. Again, it will sorb to particulate matter and settle out to sediment (98.5%).

D & C Red No. 21 is expected to have extremely high adsorptivity to soil (i.e. expected to be immobile) based on an estimated log Koc of ~6.6. D & C Red No. 21 is also expected to persist in soil (Table 3a). The extremely low vapour pressure and Henry's Law Constant indicate that volatilization will not occur from soil surfaces and the low water solubility indicates that D & C Red No. 21 will not be mobilized from the soil phase. Therefore, if released to soil, D & C Red No. 21 will remain in this compartment, which is illustrated by the results of the Level III fugacity modelling (Table 2).

Therefore, if D & C Red No. 21 is released to the environment, soil and sediment are expected to be the major media of concern, as illustrated by the results of fugacity modelling (Table 2).

Presence in the Environment

No monitoring data relating to the presence of this substance in environmental media (air, water, soil, sediment) have yet been identified.

Evaluation of P, B and iT Properties

Environmental Persistence

Once released into the environment, D & C Red No. 21 appears to be relatively persistent, mainly in water, soil and sediments as shown in Table 3a. As dyes are generally designed to persist, this result is not unexpected.

No experimental persistence data for air are available for D & C Red No. 21. QSAR predictions show that once released to air, this chemical would be oxidized in this environmental compartment, as indicated by an atmospheric oxidation half life value of 1.87 days.

Table 3a. Modelled data for persistence

Medium	Fate Process	Endpoint	Value	Reference
Air	Atm-oxidation	Half life (days)	1.87	AOPWIN v1.91
Water/Soil	Biodegradation	Half life (days)	182	BIOWIN v4.02 (Ultimate Survey Model)
Water/Soil	Biodegradation	Probability	0.0133	BIOWIN v4.02 (MITI Non-linear)

No experimental data on biological degradation of D & C Red No. 21 have yet been identified.

For estimating degradation in water and soil, a QSAR weight-of-evidence approach (ESD, 2006a) was applied using the models shown in Table 3a. Based on these results, the estimated measures for biodegradation indicate that D & C Red No. 21 can be considered persistent in water and soil. The modelled data indicate that the half-life in water and soil is expected to be longer than 182 days.

To extrapolate to a half-life in soils and sediments, an approach has been developed using Boethling's extrapolation factors (BIOWIN v4.01), which involves extrapolating the half life in sediment from that estimated for water ($t_{1/2\ water} : t_{1/2\ sediment} = 1:4$). Therefore, in sediments the half-life is expected to exceed 728 days.

The long-range transport potential (LRTP) of D & C Red No. 21 from its point of release into air is estimated to be low according to the model prediction presented in Table 3b. The TaPL3 model was used to estimate Characteristic Travel Distance (CTD), defined as the maximum distance traveled by 63% of the substance; or in other words, the distance that 37% of the substance may travel beyond. Beyer et al (2000) have proposed CTD's of >2000 km as representing high LRTP, 700-2000 km as moderate, and <700 km as low. Based on the result shown in Table 3b, this substance is expected to remain primarily in the areas close to its emission sources.

Table 3b – Model Predicted Characteristic Travel Distance (CTD) for D & C Red No. 21

Characteristic Travel Distance	Model (Reference)
479 km	TaPL3 (CEMC, 2003)

The modelled data (Table 3a) demonstrate that the substance meets the persistence criteria (half-lives in water and soil ≥ 182 days; in sediments ≥ 365 days) as set out in the Persistence and Bioaccumulation Regulations (Government of Canada 2000).

Potential for Bioaccumulation

There is no empirical bioaccumulation data available for D & C Red No. 21.

The modelled log Kow value of D & C Red No. 21 indicates that this chemical has the potential to bioaccumulate in the environment (Table 1).

The Modified GOBAS BAF middle trophic level model produced a BAF of 2,884,032 L/kg (Table 4). The three other BCF models provide a weight-of evidence to support the bioconcentration potential of this substance. Metabolism information for this substance was not available, nor was it considered in the BAF models.

Table 4. Modelled data for bioaccumulation

Test Organism	Endpoint	Value wet wt	Reference
Fish	BAF	2,884,032 L/kg	Gobas BAF T2MTL (Arnot and Gobas, 2003)
Fish	BCF	36,308 L/kg	Gobas BCF T2LTL (Arnot and Gobas, 2003)
Fish	BCF	56,234 L/kg	OASIS v1.20
Fish	BCF	16,634 L/kg	BCFWIN v2.15

The weight of evidence indicates that the substance meets the bioaccumulation criteria (BCF, BAF ≥5000) as set out in the Persistence and Bioaccumulation Regulations (Government of Canada 2000).

Ecological Effects

A - In the Aquatic Compartment

There is no empirical acute fish toxicity data available for this substance.

There is modelled evidence that the substance causes harm to aquatic organisms at relatively low concentrations (e.g. acute LC50≤1mg/L) [Table 5]. A range of aquatic toxicity values were obtained from the various QSAR models considered, however none provided reliable toxicity estimates for D & C Red No. 21, as the predictions indicated that acute effects would be expected beyond the range of water solubility. Therefore, following the weight of evidence approach for combining QSARs to determine the pivotal inherent toxicity value, the ECOSAR Neutral Organic fish 14 day LC50 equation

was used (ESD, 2006a). A safety factor of 100 was applied to the non-polar narcosis based estimate of aquatic toxicity for D & C Red No. 21 as it was predicted, by ASTER, to have a mode of action other than narcosis (U.S. EPA, 1999). Verhaar et al. (1992) originally developed this method whereby application factors could be used to extrapolate estimated toxicity from baseline narcosis to polar narcosis and reactive modes of action. The results indicate that the substance is highly hazardous to aquatic organisms (i.e. acute LC/EC50≤1.0mg/L).

Table 5 Modelled data for aquatic toxicity

Test Organism	Type of Test	Endpoint	Value (mg/L)	Reference
Fish	Acute	LC50	0.00046	ECOSAR Neutral Organic SAR

B - In Other Media

Table 6. Empirical data for Other Toxicity

Organism	Test Type	Route	Dose	Reference
Frog	LDL_0	Subcutaneous	1000mg/kg	Abdernalden's Handbuch der Biologischen Arbeitsmethoden, 1935
Mouse	LDL_0	Subcutaneous	450 mg/kg	Abdernalden's Handbuch der Biologischen Arbeitsmethoden, 1935

The toxicity studies listed in Table 6 have not been evaluated for robustness.

Potential to Cause Ecological Harm

Evidence that a substance is highly persistent and bioaccumulative as defined in the Persistence and Bioaccumulation Regulations of CEPA 1999 (Government of Canada, 2000) together with evidence of commercial activity provides a significant indication of its potential to be entering the environment under conditions that may have harmful long term ecological effects (ESD, 2006b). Substances that are persistent remain in the environment for a long time after being released, increasing the potential magnitude and duration of exposure. Substances that have long half-lives in mobile media (air and water) and partition into these media in significant proportions, have the potential to cause widespread contamination. Releases of small amounts of bioaccumulative substances may lead to high internal concentrations in exposed organisms. Highly bioaccumulative and persistent substances are of special concern, since they may biomagnify in food webs, resulting in very high internal exposures, especially for top predators. Evidence that a substance is both highly persistent and bioaccumulative, when taken together with other information (such as evidence of toxicity at relatively low concentrations, and evidence of uses and releases) may therefore be sufficient to indicate that the substance has the potential to cause ecological harm.

The information collected to date suggests that D & C Red No. 21 has the potential to cause ecological harm if it were to be released in the Canadian environment. Once released into the environment, because of its resistance to degradation, it could remain in water, sediment, and/or soil for a long time. As it persists in the environment, and because of its lipophyllic character, it could bioaccumulate and possibly be biomagnified in trophic food chains. It has also demonstrated relatively high toxicity to aquatic organisms. However, the lack of importation or manufacture of D & C Red No. 21 in Canada at significant volumes suggests very low releases of this chemical into the Canadian environment.

Uncertainties

Information and data on concentrations in the Canadian environment are currently lacking. However, the lack of importation or manufacture of D & C Red No. 21 in Canada at significant volumes suggests very low releases of this chemical into the Canadian environment.

Dyes are generally not considered to be model-difficult because of lack of inclusion in ecotoxicity model training sets. Rather, the water solubility of these substances is difficult to ascertain, and the uncertainty, therefore, resides in determining their bioavailability. Since the predictions of inherent toxicity of D & C Red No. 21 derived from QSAR models indicated that acute effects would be expected beyond the range of bioavailability, additional uncertainty is recognized with predicting the inherent toxicity using a generic narcotic equation with an application factor (ESD, 2006a).

The effects data do not address toxicity in soil and sediments, which have been identified as the primary media of concern based on partitioning estimates. The only effects data identified apply to pelagic aquatic exposures, although the water column is not the medium of primary concern.

There is also uncertainty associated with basing the overall conclusion that D & C Red No. 21 may be causing ecological harm, solely on information relating to its persistence, bioaccumulation, relative toxicity and use pattern. Typically quantitative risk estimates (i.e., risk quotients or probabilistic analyses) are important lines of evidence when evaluating a substances potential to cause environmental harm. However when risks for persistent and bioaccumulative substances such as D & C Red No. 21 are estimated using such quantitative methods, they are highly uncertain and are likely to be underestimated (ESD, 2006b). Given that long term risks associated with persistent and bioaccumulative substances cannot at present be reliably predicted, quantitative risk estimates have limited relevance. Furthermore since accumulations of such substances may be widespread and are difficult to reverse, a conservative response to uncertainty (that avoids underestimation of risks) is justified.

References

AOPWIN. 2000. Version 1.91. U.S. Environmental Protection Agency. http://www.epa.gov/oppt/exposure/pubs/episuite.htm

Abdernalden's Handbuch der Biologischen Arbeitsmethoden. Vol. 4, Pg. 1289, 1935 as cited in ChemIDplus Lite. National Library of Medicine, Specialized Information Services. Last modified in 2004. http://chem2.sis.nlm.nih.gov/chemidplus/chemidlite.jsp (Accessed in 2005)

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