# Screening Assessment

# Aromatic Azo and Benzidine-based Substance Grouping

# Certain Diarylide Yellow Pigments

**Environment Canada**
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# Synopsis

Pursuant to sections 68 or 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment onfive structurally related diarylide yellow pigments. These substances constitute a subgroup of the Aromatic Azo and Benzidine-based Substance Grouping being assessed as part of the Substance Groupings Initiative of the Government of Canada's Chemicals Management Plan (CMP) based on structural similarity and applications. Substances in this Grouping were identified as priorities for assessment as they met the categorization criteria under subsection 73(1) of CEPA 1999 and/or were considered as a priority based on other human health concerns.

The Chemical Abstracts Service Registry Number (CAS RN)[1], *Domestic Substances List* (DSL) name, Colour Index (C.I) generic name, and chemical acronym of the five substances are presented in the following table.

**Identity of five diarylide yellow pigments in the Aromatic Azo and Benzidine-based Substance Grouping**

| CAS RN | DSL name | C.I. generic name | Chemical acronym |
|---|---|---|---|
| 5102-83-0 | Butanamide, 2,2′-[(3,3′-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxo- | Pigment Yellow 13 | PY13 |
| 5567-15-7[a] | Butanamide, 2,2′-[(3,3′-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(4-chloro-2,5-dimethoxyphenyl)-3-oxo- | Pigment Yellow 83 | PY83 |
| 6358-85-6 | Butanamide, 2,2′-[(3,3′-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[3-oxo-N-phenyl- | Pigment Yellow 12 | PY12 |
| 78952-70-2 | Butanamide, 2-[[3,3′-dichloro-4′-[[1-[[(2-chlorophenyl)amino]carbonyl]-2-oxopropyl]azo][1,1′-biphenyl]-4-yl]azo]-N-(2,4-dimethylphenyl)-3-oxo- | N/A | CPAOBP |
| 90268-24-9[a] | Pigment Yellow 176 | Pigment Yellow 176 | PY176 |

Abbreviations: N/A, not available.

[1] The Chemical Abstracts Service Registry Number (CAS RN) is the property of the American Chemical Society and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the government when the information and the reports are required by law or administrative policy, is not permitted without the prior written permission of the American Chemical Society.

[a] These substances were not identified under subsection 73(1) of CEPA 1999 but were included in this assessment as they were considered as priorities based on other human health concerns.

These five diarylide yellow pigments do not occur naturally in the environment. Four of the five substances have been reported to be manufactured in Canada and/or imported for use in industrial activities. Some of the substances are also present in consumer products and cosmetics. No data on measured concentrations in the Canadian environment (or in other countries) have been identified for any of these substances.

## Environment

Diarylide yellow pigments exist principally as particles in the nanometer or low micrometer size range, and the pigment powder is typically composed of primary particles (i.e., the crystal lattice of a pigment), aggregates and agglomerates. These pigments have very low solubility in both water (generally, in the low micrograms per litre range) and in octanol (below 1 mg/L); because of this, it was proposed that a quotient of the molar solute concentrations in octanol and in water ($S_{oct}/S_w$) would reasonably represent the octanol–water partition coefficients ($K_{ow}$) for these pigments. The physical and chemical properties and the particulate nature of these substances suggest that soil and sediments would be the two major environmental media to which diarylide yellow pigments partition.

Experimental data indicate that under aerobic conditions, diarylide yellow pigments are expected to degrade slowly in water, soil and sediments.

Diarylide yellow pigments are not expected to bioaccumulate given their physical and chemical properties (i.e., based on the particulate character of these substances, their very low solubility in both water and octanol, and the high weight and large size of molecules of these substances).

Due to the limited bioavailability of diarylide yellow pigments, no effects were found at the concentration of 1 000 mg/kg soil or sediment (dry weight) in chronic soil and sediment toxicity studies. These pigments also showed no effect at saturation in acute and chronic aquatic ecotoxicity studies in which solvents were not used. Based on these studies, diarylide yellow pigments are not expected to be harmful to aquatic, soil-dwelling or sediment-dwelling organisms at low concentrations.

To evaluate potential exposures to diarylide yellow pigments in the environment, predicted environmental concentrations (PEC) were estimated; an industrial release scenario was chosen to evaluate the potential exposure to these substances. Predicted no-effect concentration (PNEC) values for each relevant environmental compartment (soil, sediment and water) were calculated based on the experimental critical toxicity values (CTVs). Calculated risk quotient (PEC/PNEC) values were much lower than 1 for each environmental compartment (soil, sediment and water), indicating that harm to organisms in these media is not expected.

Considering all available lines of evidence presented in this Screening Assessment, there is low risk of harm to organisms and the broader integrity of the environment from the diarylide yellow pigmentsevaluated in this assessment. It is concluded that these diarylide yellow pigments do not meet the criteria under paragraphs 64(*a*) or 64(*b*) of CEPA 1999, as they are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

## Human Health

For the human health assessment, exposure of the general population of Canada to these diarylide yellow pigments is not expected to be significant from environmental media while potential exposure by dermal, oral, and inhalation routes may occur from the use of these substances in consumer products and cosmetics. These substances are expected to exhibit low to negligible absorption and low toxicity. The margins between the estimates of exposure from the use of consumer products and cosmetics, and conservative effect levels are considered adequate to address uncertainties in the exposure and health effects databases.

Based on the information presented in this Screening Assessment, it is concluded that the diarylide yellow pigments evaluated in this assessment do not meet the criteria under paragraph 64(*c*) of CEPA 1999 as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

## Overall Conclusion

It is concluded that the five diarylide yellow pigments evaluated in this assessment do not meet any of the criteria set out in section 64 of CEPA 1999.

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# 1. Introduction

Pursuant to sections 68 or 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999), the Minister of the Environment and the Minister of Health conduct screening assessments of substances to determine whether these substances present or may present a risk to the environment or to human health.

The Substance Groupings Initiative is a key element of the Government of Canada's Chemicals Management Plan (CMP). The Aromatic Azo and Benzidine-based Substance Grouping consists of 358 substances that were identified as priorities for assessment, as they met the categorization criteria under section 73 of CEPA 1999 and/or were considered as a priority based on human health concerns (Environment Canada and Health Canada 2007). Some substances within this Substance Grouping have been identified by other jurisdictions as a concern due to the potential cleavage of the azo bonds, which can lead to the release of aromatic amines that are known or likely to be genotoxic and/or carcinogenic.

While many of these substances have common structural features and similar functional uses as dyes or pigments in multiple sectors, diversity within the substance group has been taken into account through the establishment of subgroups. Subgrouping based on structural similarities, physical and chemical properties, and common functional uses and applications accounts for variability within this substance grouping and allows for subgroup-specific approaches in the conduct of screening assessments. This Screening Assessment considers substances that belong to the Diarylide Yellow Pigments subgroup. Consideration of azo bond cleavage products (aromatic amines) is a key element of human health assessment in each subgroup. Some aromatic amines, commonly referred to as EU22 aromatic amines,[2] as well as associated azo dyes are restricted in other countries (EU 2006). Information on the subgrouping approach for the Aromatic Azo and Benzidine-based Substance Grouping under Canada's CMP, as well as additional background information and regulatory context, is provided in a separate document prepared by the government of Canada (Environment Canada and Health Canada 2013.

Seven diarylide yellow pigments (Chemical Abstracts Service Registry Numbers [CAS RNs] 5102-83-0, 5567-15-7, 6358-85-6, 78952-70-2, 90268-24-9, 7147-42-4 and 29398-96-7) originally constituted a subgroup of the Aromatic Azo and Benzidine-based Substance Grouping. Two substances in this subgroup, BPAOPB (CAS RN 7147-42-4)

[2] Twenty-two aromatic amines listed in Appendix 8 of Regulation (EC) No. 1907/2006.

and Pigment Brown 22 (PB22; CAS RN 29398-96-7), have been previously assessed by the Government of Canada under the Challenge Initiative of the CMP (Environment Canada and Health Canada 2010, 2011). PB22 is not included in this Screening Assessment as no significant new information was identified since its assessment in 2010, and because this non-azo pigment does not inform the other azo-based diarylide yellow pigments in this subgroup. Similarly, no significant new information was identified for BPAOPB since its Challenge assessment and therefore this substance is not included in the current Screening Assessment. However, BPAOPB is used in this report for read-across purposes due to its structural similarity to the other diarylide yellow pigments in this subgroup. Therefore, only the remaining five substances (CAS RN 5102-83-0, 5567-15-7, 6358-85-6, 78952-70-2 and 90268-24-9) are considered in this Screening Assessment.

Screening assessments focus on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA 1999, by examining scientific information to develop conclusions by incorporating a weight of evidence approach and precaution.[3]

This Screening Assessment includes consideration of information on chemical properties, environmental fate, hazards, uses and exposure, including additional information submitted by stakeholders. Relevant data were identified up to December 2013. Empirical data from key studies as well as some results from models were used to reach conclusions. When available and relevant, information presented in assessments from other jurisdictions was considered.

The Screening Assessment does not represent an exhaustive or critical review of all available data. Rather, it presents the most critical studies and lines of evidence pertinent to the conclusion.

[3] A determination of whether one or more of the criteria of section 64 are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA 1999 on the substances in the Chemicals Management Plan (CMP) is not relevant to, nor does it preclude, an assessment against the hazard criteria for WHMIS (Workplace Hazardous Materials Information Systems) that are specified in the Controlled Products Regulations, which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA 1999 does not preclude actions being taken under other sections of CEPA or other Acts.

The Screening Assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. The ecological and human health portions of this assessment have undergone external written peer review and consultation. Comments on the technical portions relevant to the environment were received from Dr. Harold Freeman (North Carolina State University, USA) and Dr. Gisela Umbuzeiro (University of Campinas, Brazil). Comments on the technical portions relevant to human health were received from Dr. Harold Freeman (North Carolina State University, USA), Dr. David Josephy (University of Guelph, Canada), Dr. Michael Bird (University of Ottawa, Canada) and Dr. Kannan Krishnan (University of Montreal, Canada). Additionally, the draft of this Screening Assessment was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the Screening Assessment remain the responsibility of Health Canada and Environment Canada.

The critical information and considerations upon which the Screening Assessment is based are given below.

# 2. Identity of Substances

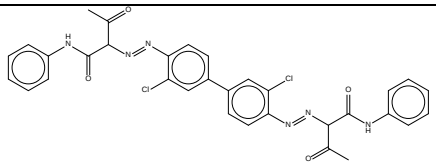
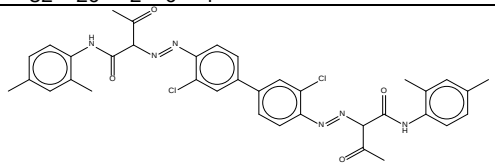
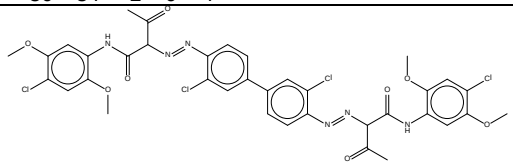
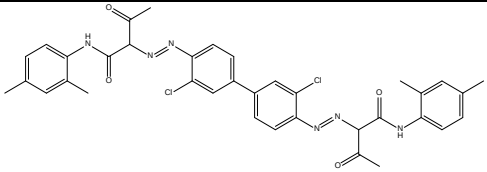
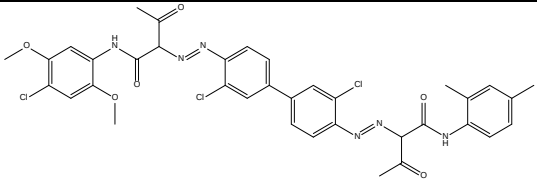
This Screening Assessment focuses on five substances that belong to the subgroup of Diarylide Yellow Pigments that is part of the Aromatic Azo and Benzidine-based Substance Grouping. The identities of the individual substances in this Screening Assessment are presented in Table 2-1. The CAS RNs, *Domestic Substances List* (DSL) names, Colour Index (C.I.) generic names, C.I. constitution numbers and chemical acronyms of these substances are presented in Table 2-1. Chemical acronyms are derived from the C.I. generic names when available; otherwise, they are based on the DSL names. A list of additional chemical names (e.g., trade names) is available from the National Chemical Inventories (NCI 2007).

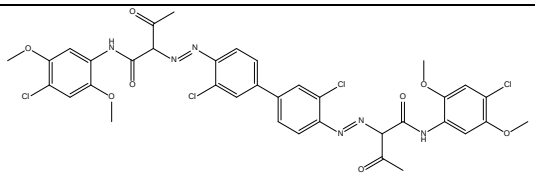
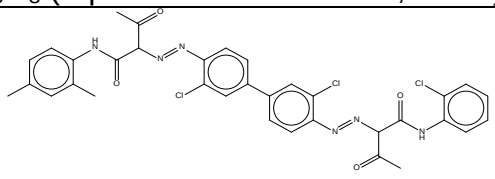
**Table 2-1. Identity of the five diarylide yellow pigments**

| CAS RN | DSL name | C.I. generic name (C.I. constitution number) | Chemical acronym |
|---|---|---|---|
| 6358-85-6 | Butanamide, 2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[3-oxo-N-phenyl- | Pigment Yellow 12 (C.I. 21090) | PY12 |
| 5102-83-0 | Butanamide, 2,2′-[(3,3′-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxo- | Pigment Yellow 13 (C.I. 21100) | PY13 |
| 5567-15-7 | Butanamide, 2,2′-[(3,3'-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(4-chloro-2,5-dimethoxyphenyl)-3-oxo- | Pigment Yellow 83 (C.I. 21108) | PY83 |
| 90268-24-9 | C.I. Pigment Yellow 176 | Pigment Yellow 176 (C.I. 21103) | PY176 |
| 78952-70-2 | Butanamide, 2-[[3,3'-dichloro-4'-[[1-[[(2-chlorophenyl)amino]carbonyl]-2-oxopropyl]azo][1,1'-biphenyl]-4-yl]azo]-N-(2,4-dimethylphenyl)-3-oxo- | C.I. name and number not available | CPAOBP |

The chemical structures, molecular formulas and molecular weights of all five diarylide yellow pigments are presented in Table 2-2. As presented in Table 2-2, all substances in this subgroup are disazo diarylide pigments containing a 3,3′-dichlorobenzidine (3,3′-DCB) fragment in their structures.

**Table 2-2. Chemical structures, molecular formula and molecular masses for the five diarylide yellow pigments**

| Substance | Chemical structure and molecular formula[1] | Molecular weight (g/mol) |
|---|---|---|
| PY12 |  $C_{32}H_{26}Cl_2N_6O_4$ | 630 |
| PY13 |  $C_{36}H_{34}Cl_2N_6O_4$ | 686 |
| PY83 |  $C_{36}H_{32}Cl_4N_6O_8$ | 819 |
| PY176 | Three structures suggested in the REACH registration dossier for this UVCB substance are presented below to more comprehensively characterize the substance. | |
| PY176 |  $C_{36}H_{34}Cl_2N_6O_4$ (representative structure, PY13) | 686 |
| PY176 |  $C_{36}H_{33}Cl_3N_6O_6$ (representative structure, CAS RN 124236-34-6) | 752 |

| Substance | Chemical structure and molecular formula[1] | Molecular weight (g/mol) |
|---|---|---|
| PY176 |  $C_{36}H_{32}Cl_4N_6O_8$ (representative structure, PY83) | 819 |
| CPAOBP |  $C_{34}H_{29}Cl_3N_6O_4$ | 692 |

Abbreviations: REACH, Registration, Evaluation, Authorisation and Restriction of Chemicals; UVCB, unknown or variable composition, complex reactions products, or biological materials

The diarylide yellow pigment PY176 is a UVCB (unknown or variable composition, complex reaction products, or biological materials) substance—i.e. it is not a discrete chemical, and thus it may be characterized by a mixture of structures. Structural information for PY176 has been reported in the European Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) registration dossier for this substance and is available in a database maintained by the European Chemicals Agency (ECHA 2012). Therefore, three structures reported for PY176 (two of which are PY13 and PY83) are presented in Table 2-2 to more comprehensively characterize the substance. Although Schmidt et al. (2007) indicated that PY176 is a mixture of only the two different pigments (PY13 and PY83), for the purposes of this assessment, all three structures that were reported in the REACH registration dossier are considered for this substance.

## 2.1 Selection of Analogues and Use of (Q)SAR Models

Guidance on the use of read-across approaches has been prepared by various organizations such as the Organisation for Economic Co-operation and Development (OECD). It has been applied in various regulatory programs including the European Union's (EU) Existing Substances Programme. The general method for analogue selection and the use of (quantitative) structure–activity relationship ((Q)SAR) models is provided in Environment Canada and Health Canada (2013). For characterization of human health effects, the basis for the use of analogues and/or (Q)SAR modelling data is documented in the Health Effects Assessment section of this report.

Analogues used to inform the ecological assessment were selected based on structural similarity and the availability of relevant empirical data pertaining to physical-chemical

properties, persistence, bioaccumulation and ecotoxicity. Such data were used as read-across data for those Diarylide Yellow Pigments that lacked empirical data, where appropriate, or to support the weight of evidence of existing empirical information. Although analogue data are used preferentially to fill data gaps for the substances in this assessment, the applicability of (Q)SAR models to the Diarylide Yellow Pigments is determined on a case-by-case basis.

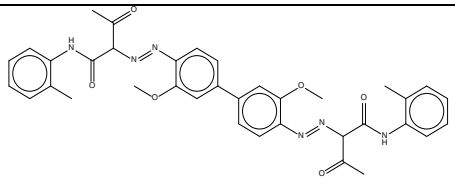
The five identified analogues are presented in Table 2-3.

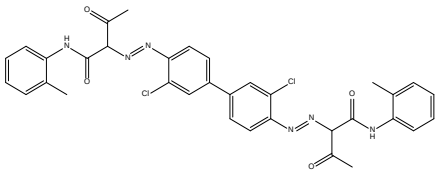
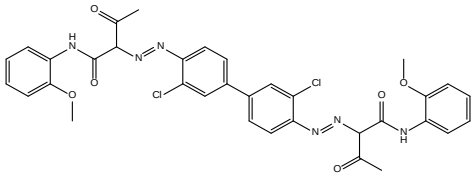
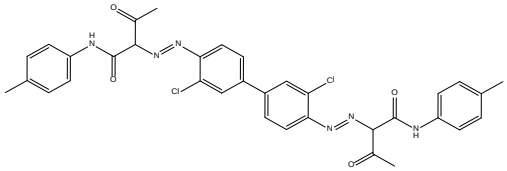
**Table 2-3. Identity of the five analogues**

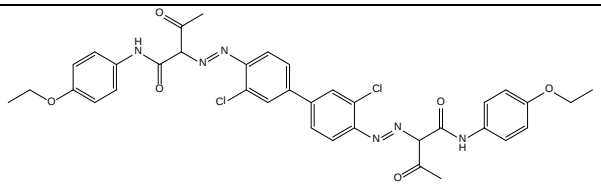
| CAS RN | DSL name (English) | C.I. generic name (C.I. constitution number) | Chemical acronym |
|---|---|---|---|
| 4531-49-1 | Butanamide, 2,2′-[(3,3′-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(2-methoxyphenyl)-3-oxo- | Pigment Yellow 17 (C.I. 21105) | PY17 |
| 5468-75-7 | Butanamide, 2,2′-[(3,3′-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxo- | Pigment Yellow 14 (C.I. 21095) | PY14 |
| 6358-37-8 | Butanamide, 2,2′-[(3,3′-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(4-methylphenyl)-3-oxo- | Pigment Yellow 55 (C.I. 21096) | PY55 |
| 7147-42-4 | Butanamide, 2,2′-[(3,3′-dimethoxy[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxo- | C.I. name and number not available | BPAOPB |
| 31775-20-9 | Butanamide, 2,2′-[(3,3′-dichloro[1,1′-biphenyl]-4,4′-diyl)bis(azo)]bis[N-(4-ethoxyphenyl)-3-oxo- (NDSL name) | Pigment Yellow 152 (C.I. 21111) | PY152 |

The structural identities (chemical structures, chemical formulas and molecular masses) of the five analogues of the diarylide yellow pigments are presented in Table 2-4.

**Table 2-4. Chemical structures, molecular formulas and molecular masses for the five analogues**

| Substance | Chemical structure and chemical formula[1] | Molecular mass (g/mol) |
|---|---|---|
| BPAOPB |  $C_{36}H_{36}N_6O_6$ | 649 |

| Substance | Chemical structure and chemical formula[1] | Molecular mass (g/mol) |
|---|---|---|
| | | |
| PY14 |  $C_{34}H_{30}Cl_2N_6O_4$ | 658 |
| PY17 |  $C_{34}H_{30}Cl_2N_6O_6$ | 690 |
| PY55 |  $C_{34}H_{30}Cl_2N_6O_4$ | 658 |
| PY152 | | 718 |

| Substance | Chemical structure and chemical formula[1] | Molecular mass (g/mol) |
|---|---|---|
| |  $C_{36}H_{34}Cl_2N_6O_6$ | |

## 2.2 Impurities

The purities of PY12, PY13 and PY83 were reported in a draft assessment of diarylide pigments by the Organisation for Economic Co-operation and Development (OECD) (OECD 2003a) to be >96%, with expected impurities consisting primarily of the respective acetoacetanilide derivative coupling components at levels ranging from 0.5 to 2% (i.e., CAS RNs 102-01-2, 97-36-9 and 4433-79-8, respectively). The levels of residual 3,3′-DCB for these three diarylide yellow pigments were also reported to be < 25 parts per million (ppm) (OECD 2003a) while a recent source also indicated 3,3'-DCB impurity of 10 ppm from a tattoo ink containing PY13 (Hauri 2013). It is expected that the other diarylide yellow pigments included in this Screening Assessment will also contain residues of their respective unreacted acetoacetanilide derivative coupling component along with the 3,3′-DCB/3,3′-dimethoxybenzidine (3,3′-DMOB) residual. In the European marketplace, PY13 and PY83 are allowed for use in rinse-off cosmetic products under the condition that the concentration of 3,3′-dimethylbenzidine (3'3-DMB) in the colouring agent is no more than 5 ppm according to the European Union 2010 Cosmetics Directive Annex IV, a list of colouring agents that are allowed for use in cosmetic products under certain conditions (EU 2010). While 3,3'-DMB is cited in Annex IV as the restricted impurity for PY13 and PY83, the residual benzidine derivative for these substances would be 3,3'-DCB and therefore the citation in Annex IV is presumed to be an administrative error.

In addition, the presence of a soluble 3,3′-DCB-based monoazo compound at a concentration of 220 ppm (i.e., 0.022%) has been reported in purified PY13 (Sagelsdorff et al. 1996), while a similar impurity was suggested in an OECD assessment (OECD, 2003a) to have been present in a study on PY17 (Zwirner-Baier and Neumann 1994), although the concentration of the suspected 3,3′-DCB-containing impurity was not indicated. No further details on the nature or identity of the soluble 3,3′-DCB-based impurities were provided in the references available.

Some substances, such as resins, rosins and aliphatic amines, and some other compounds, including surfactants, dispersing agents and coupling agents, are common

additives used in pigment preparation, depending on the application of the pigments. It is impossible to remove such impurities by pigment filtration and intensive washing, and even the effect of hot extraction procedures tends to be slow and unsatisfactory (Herbst and Hunger, 2004). It is possible that certain amounts of these substances were present in some pigments that were tested. If so, this could cause data variability and inconsistency between studies (e.g., biodegradability and water solubility studies).

Polychlorinated biphenyls (PCBs) are known to be found as inadvertent impurities in various classes of pigments including azo pigments (ETAD 2011; Grossman 2013). In Canada, the levels of incidentally-produced PCBs in colouring pigments are regulated under Sections 11 and 35 of the *PCB Regulations*. The regulations limit the annual maximum concentration of PCBs, produced incidentally in colouring pigments, to less than 50 mg/kg (ppm), and an annual average PCB concentration in pigments of not more than 25 mg/kg (ppm). Reported PCB levels in some diarylide yellow pigments used in Canada are well below the maximum limits set out in these regulations. For example, reported PCB levels in PY12 range from 0.04 - 1.5 ppm for reporting years 2009-2011, and for PY83 the reported PCB levels range from 0.02 - 9 ppm for reporting years 2008-2012 (personal communication, email from Waste Reduction and Management Division [Environment Canada] to Existing Substances Risk Assessment Bureau [Health Canada], dated 2014; unreferenced).

There is some uncertainty regarding whether the data above fully represents the range of purity for different grades of diarylide yellow pigments available in consumer products in Canada. It is therefore possible that use of lower-quality grades of diarylide yellow pigments could result in exposure to these and other potential impurities at levels higher than reported here.

# 3. Physical and Chemical Properties

A summary of experimental physical and chemical properties that play a critical role in determining the environmental fate and biological effects of diarylide yellow pigments is presented in Table 3-1. Detailed substance-specific information on these pigments and their analogues can be found in Appendix A of this report. The general assumption was that the properties of pigments depend strongly on the manner in which they have been prepared by manufacturers.

Experimental data on vapour pressure and Henry's Law constants are not available for most of the pigments. However, since the diarylide yellow pigments are similar in molecular size and complexity to some disperse dyes, they can be expected to have vapour pressures in the same range as values reported for disperse dyes (i.e., 10−11 to 10−19 Pa; Baughman and Perenich 1988). Similarly, all diarylide yellow pigments are also expected to have very low Henry's Law constant values. Therefore, exposure vapour phase is expected to be of low environmental relevance for this subgroup. However, airborne exposure to diarylide yellow pigments as dusts or particulates may be possible, especially for some consumer products.

Due to a lack of ionizable groups, dissociation of diarylide yellow pigments is expected to be negligible. Ionization or acid dissociation constants ($K_a$, $pK_a$) are therefore not considered relevant to the environmental fate and ecotoxicity of these pigments. Also, these diarylide yellow pigments decompose before boiling, so a boiling point is not applicable for these substances.

**Table 3-1. Experimental physical and chemical properties (at standard temperature of approximately 25°C where applicable) of PY12, PY13, PY83 and PY176 and their analogues**

| **Property** | **Property acronym used in the text** | **Range** | **Mean (number of data points)** |
|---|---|---|---|
| Melting point (°C) | MP | 306–323 | 314 (n = 6) |
| Decomposition temperature (°C) | DT | 300–339 | 317 (n = 8) |
| Particle size distribution (mass median diameter, µm) | $D_{50}$ | 2–8.5 | 4.0 (n = 8) |
| Density (g/cm$^3$) | | 1.26–1.50 | 1.38 (n = 4) |
| Water solubility (µg/L) | WS; $S_w$ | 0.35–10.6 | 3.4 (n = 9) |
| Solubility in n-octanol (µg/L) | $S_{oct}$ | 2.6–140 | 41 (n = 11) |
| Quotient logarithm of the molar solute concentrations in octanol and water (dimensionless) | log ($S_{oct}/S_w$) | 0.4–2.1 | 1.5 (n = 8) |
| Effective molecular diameter | $D_{eff}$ | 1.14–1.29 | 1.23 (n = 6) |

| Property | Property acronym used in the text | Range | Mean (number of data points) |
|---|---|---|---|
| (calculated average; nm) | | | |
| Maximum molecular diameter (calculated average; nm) | $D_{max}$ | 2.19–2.53 | 2.42 (n = 6) |

## 3.1 Particle Size Distribution and Density

The majority of organic pigments generally do not exist as individual molecules but are principally particles in the sub- or low micrometre size range. The pigment powder is typically composed of primary particles (i.e., the crystal lattice of a pigment), aggregates and agglomerates. Manufacturers usually provide the physical specifications of their pigments, which include the average particle size of the pigment powder. Users can then determine which pigment is the most appropriate to colour their products, since performance is chiefly controlled by the particle size distribution (Herbst and Hunger 2004). In terms of the particle size distribution, reported data on mass median diameter ($D_{50}$) were taken from information reported in the REACH registration dossiers for these substances, available from the European Chemicals Agency (ECHA 2012). The particle size data presented in Table 3-1 indicate that for this group of pigments, the $D_{50}$ values vary within a relatively narrow range of 2–8.5 µm (i.e., 50% of the total mass of particles are smaller than 2–8.5 µm).

In terms other than mass-dependent particle size distribution, some authors have reported particle sizes for diarylide yellow pigments to be very small, often below 1 µm. For example, while an inhalation toxicity study using PY13 showed the majority of particle diameters to be between 1 and 7 µm, roughly 10–20% of particles were less than 1 µm (Ciba Geigy Corp. 1979). Bäumler et al. (2000) reported sub-micrometre particle sizes of azo pigments (including several diarylide yellow pigments[4]) in tattoo inks ranging from 20 to 900 nm. While not specifically measuring diarylide yellow pigments, the work of Bäumler et al. (2000) is supported by a study by Høgsberg et al. (2011), which demonstrated tattoo inks containing red and yellow azo pigments of monoazo class and disazo dichlorobenzidine-based pyrazolone class exhibiting particle size ranges from < 100 to 1000 nm.As well, a technical paper illustrated that two different preparation methods for PY12 (micro-mixer vs. batch process) resulted in

[4] Diarylide yellow pigments cited in Bäumler et al. (2000) included PY14, PY55, PY83 and Pigment Yellow 87 (PY87; CAS RN 15110-84-6).

different particle size distributions, ranging from well below 1 µm to > 100 µm (Pennemann et al. 2005). Therefore, it should be considered that the particle size range of diarylide yellow pigments could be broad, including very small particles in the sub-micrometre (< 1 µm) and even nanoscale particle size range (1–100 nm; Canada 2007; Health Canada 2011a), and may be a factor in potential uptake and absorption as the insoluble particulate form (discussed further in the respective sections on ecological and human health assessment).

The density of diarylide yellow pigments varies within a relatively narrow range (from ~1.3 to 1.5 g/cm$^3$), which is higher than the density of water. Therefore, when released to water, the pigments, being relatively heavy particles, are expected to deposit and further reside in sediments, with eventual burial to deeper sediments.

## 3.2 Melting and Decomposition Temperatures

Results indicate that melting points are just slightly below the decomposition temperatures (314ºC and 317ºC, respectively). In some tests with the diarylide yellow pigments, decomposition of the substances started without discernible melting (see Appendix A for more details).

## 3.3 Solubility in Water and Octanol

Most of the data show that the diarylide yellow pigments in this Screening Assessment are characterized by very low water solubility—from less than 1 µg/L to 10.6 µg/L (Table A-1; Appendix A); the reported solubilities in octanol are relatively higher than that in water (2.6–140 µg/L). Both water and octanol solubilities for the diarylide yellow pigments are considered very low in absolute terms and also relatively low compared with the solubilities reported for some other azo pigments of different structural classes (Anliker and Moser 1987).

The low solubility of organic pigments is a result of the inherent design of colorants, which have strong interactive forces between molecules, achieved by the introduction of substituents such as –CONH– in the molecule (Lincke 2003; Herbst and Hunger 2004). The resulting intermolecular bonding in turn generates a crystal structure that lends stability to organic pigments (Lincke 2003). Panina (2009) emphasized that due to the molecular structure features, organic pigments tend to form highly crystalline solids; very typical structural motifs are π-π stacking of conjugated rings and intermolecular hydrogen bonds C=O…H–N. Such strong intermolecular interactions inside the crystal structure lead to a high lattice energy and, often as a consequence, a very low solubility. (It should, however, also be mentioned that all azo pigments exist in crystal form as solid particulate with hydrogen bonding, yet there might be substantial differences in solubility in water and octanol between diarylide and some monoazo pigments; therefore, some major differences in apparent stability of the crystal also have to be taken into account.) Such differences in water and octanol solubilities have been observed for azo pigments of different structural classes (Anliker and Moser 1987;).

## 3.4 Octanol–Water Partition Coefficient

No experimental data on octanol–water partition coefficients ($K_{ow}$) are available for the diarylide yellow pigments. The $K_{ow}$ values derived from fragment-based models such as KOWWIN (2010) often overestimate the actual $K_{ow}$ of sparingly soluble substances such as pigments. For example, for PY12 and PY13, Koch (2008) reported KOWWIN-estimated log $K_{ow}$ values of 7 and 8.1, respectively, and indicated that for organic pigments, KOWWIN far overestimates the "true" $K_{ow}$ values in most cases. At the Environment Canada–sponsored QSAR Workshop in 1999, invited modelling experts identified many structural classes of pigments and dyes as "difficult to model" using most QSARs (Environment Canada 2000). The physical and chemical properties of many of the structural classes of pigments and dyes are often not amenable to model prediction because they are typically considered out of the model domain of applicability (e.g., structural and/or property parameter domains).

According to the European Chemicals Agency's Guidance on Information Requirements and Chemical Safety Assessment (ECHA 2008), in order to overcome the difficulties in measuring the $K_{ow}$, the solubilities in octanol and water may be determined in separate tests. With these solubilities, the quotient of solubilities in octanol and in water ($S_{oct}/S_w$) can be calculated. Although the European Chemicals Agency notes that this quotient is not exactly identical to log $K_{ow}$, as the latter is related to the partitioning of the substance in water-saturated octanol and octanol-saturated water, it recommends that this method be considered for sparingly soluble substances.

Therefore, it is considered that a $S_{oct}/S_w$ parameter would reasonably represent the octanol–water partition coefficient for organic pigments. This approach has been used in previous screening assessments on pigments (e.g., see Environment Canada and Health Canada 2009a, b) and is also used in this report. For diarylide yellow pigments, the log ($S_{oct}/S_w$) values, based on experimental solubility values in water and in octanol, vary within a reasonably narrow range of 0.4–2.1, with the mean value being 1.5 (Table 3-1); therefore, low bioaccumulation of these substances in organisms is expected.

## 3.5 Cross-sectional Diameter

Average effective cross-sectional diameters of molecules of diarylide yellow pigments are greater than 1.1 nm, while average maximum diameters can reach 2.5 nm. Since this parameter is important in terms of the permeation of substances through biological membranes, detailed discussion on cross-sectional diameters of these pigments is presented in the Potential for Bioaccumulation section.

## 3.6 Data Outliers

Table 3-1 does not contain the data that are considered to be obvious outliers. For example, an unusually high solubility value of 8 900 µg/L (PY83), a very high solubility

in octanol value of 500 mg/L (PY12), an abnormally low decomposition temperature (200°C) and unusually high melting points (360–400°C) are not presented in Table 3-1; however, all these atypical data can be found in Appendix A of this report.

Some of the abnormal physical and chemical property values may be typographical errors, but most likely these atypical values reported in the studies were from testing of relatively low-purity pigments; the unexpectedly high solubility values or unusual melting and/or decomposition temperatures can likely be attributed to the impurities and/or additives (formulants) contained in the pigments' final products. For example, large amounts of additives such as rosin are frequently used in manufacturing highly transparent types of azo pigments for application in process colour printing inks (Herbst and Hunger 2004). These substances are largely adsorbed on the surface of the pigment particles. The extent to which measurement results can be distorted by additives is particularly severe in the case of disazo yellow pigments, whose preparation involves fatty amines (Herbst and Hunger 2004).

# 4. Sources and Uses

## 4.1 Sources

All five diarylide yellow pigments are anthropogenically produced; they are not expected to occur naturally in the environment.

In recent years, the five diarylide yellow pigments and the analogue BPAOPB have been included in industry surveys issued pursuant to section 71 of CEPA 1999. Four substances (PY83, PY176, CPAOBP and the analogue BPAOPB) were included in a survey conducted pursuant to section 71 of CEPA 1999 for the 2005 calendar year (Canada 2006), one substance (the analogue BPAOPB) was included in a survey conducted pursuant to section 71 for the 2006 calendar year under the Government of Canada's Challenge Initiative (Canada 2008), and four substances (PY12, PY13, PY83 and PY176) were included in a survey conducted pursuant to section 71 of CEPA 1999 for the 2010 calendar year (Canada 2011a).

Based on the most recent information submitted via the section 71 survey (Canada 2011a), four of the five diarylide yellow pigments assessed in this report (PY12, PY13, PY83 and PY176) as well as BPAOPB are imported or manufactured in quantities greater than 100 kg/year. The total manufacture and import quantity for these substances is in the range of 100 to 1 000 tonnes. In addition, stakeholder interest in these substances was declared by several companies, although the activities of these substances did not meet the mandatory reporting requirements at the time of the survey.

Elsewhere, four of the five diarylide yellow pigments are found in the European Chemical Substances Information System (ESIS). PY12, PY13 and PY83 are reported as high production volume (HPV) substances, while PY176 is reported as a low production volume (LPV) chemical (see Table 4-1).

PY12, PY13 and PY83 have also been reported in the Inventory Update Reporting (IUR) (US EPA 2006) Modifications Rule under the *Toxic Substances Control Act* (TSCA) in the United States. The aggregated national production volumes of these substances in the year 2006 are presented in Table 4-1.

During the last several years, PY12, PY13, PY83 and PY176 were also used in Denmark, Norway and/or Sweden. The quantities of these substances used, for example, in the year 2010 (see Table 4-1) can be found in the Substances in Preparations in Nordic Countries (SPIN) database, which is based on data from the product registries of Norway, Sweden, Denmark and Finland and supported by the Nordic Council of Ministers.

**Table 4-1. Production volumes of diarylide yellow pigments identified in ESIS, TSCA IUR and SPIN databases**

| Substance | ESIS (©1995–2012) | IUR (2006) | SPIN (2010) |
|---|---|---|---|
| PY12 | HPV substance | 10 to < 50 million pounds<br><br>(i.e., 4 500 to < 22 700 tonnes) | 600 tonnes (Sweden and Denmark) |
| PY13 | HPV substance | 1 to < 10 million pounds<br><br>(i.e., 454 to < 4 500 tonnes) | 192 tonnes (Sweden, Denmark and Norway) |
| PY83 | HPV substance | 1 to < 10 million pounds<br><br>(i.e., 454 to < 4 500 tonnes) | 131 tonnes (Sweden, Denmark and Norway) |
| PY176 | LPV substance | No data | 14 tonnes (Sweden) |
| CPAOBP | Not found in ESIS | No data | No data |

Abbreviations: HPV, high production volume; LPV, low production volume; ESIS, European Chemical Substances Information System; IUR, Inventory Update Reporting ;SPIN, Substances in Preparations in Nordic Countries.

## 4.2 Uses

The five diarylide yellow pigments evaluated in this assessment (PY12, PY13, PY83, PY176 and CPAOBP) are used in various sectors, such as “Ink, toner and colorants,” “Paints and coatings,” “Fabric, textile and leather articles” and “Plastic and rubber materials.” Linak et al. (2011) indicated that diarylide yellow pigments are popular with ink makers because of their bright shades and their outstanding tinting strength. They have good printing qualities and are economical on the basis of cost per unit of tinting strength. Although semi-opaque, they can be resinated to produce transparent grades for three- and four-colour printing processes. With the largest volume of all organic pigments, PY12 is used in lithographic, letterpress and publication gravure inks. Some diarylide yellow pigments (e.g., PY13 and PY83) can also be used for textile printing, and PY83 is also used in the paints and coatings sector, replacing lead chromate yellow pigments (Linak et al. 2011).

### 4.2.1 Uses in Canada

Table 4-2 presents a summary of the major uses of the four diarylide yellow pigments used in Canada (Environment Canada 2012) based on the section 71 survey conducted under CEPA 1999 (Canada 2011a) and/or Phase 1 of the DSL Inventory Update (Canada 2009). No uses were reported from section 71 surveys for CPAOBP.

**Table 4-2. Summary of the major uses of diarylide yellow pigments in Canada submitted in response to section 71 surveys (Environment Canada 2012)**

| Substance | Ink, toner, and colorants | Paints and coatings | Plastic and rubber | Textile and leather |
|---|---|---|---|---|
| PY12 | X | - | - | - |
| PY13 | X | X | X | X |
| PY83 | X | X | X | X |
| PY176 | X | - | - | - |

Section 71 data indicate that the “Ink, toner, and colorants” sector is the major sector for the diarylide yellow pigment group of substances. Information available for four pigments from this group of substances shows that all five pigments are used in the “Ink, toner, and colorants” sector—i.e., as “substances in ink, toners and colorants used for writing, printing, creating an image on paper; or as substances contained in other substrates or applied to substrates to change their colour or hide images”—with 86% of the total declared quantities (Canada 2011a; Environment Canada 2012). The second major use is “Paints and coatings” (8% of the total declared quantities), followed by the “Plastic and rubber” sector (3%).

PY12 is also known to be used in cosmetics, metal and paper (HSDB 1983–; Lewis 2001; INCI 2004). Based on notifications submitted under the *Cosmetic Regulations* to Health Canada, it is used in certain cosmetic products in Canada such as, bath salts for infants, face makeup, hair dye, mascara, nail polish and bath showering products (personal communication, email from the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced).

PY13 is used in the textile and leather, plastic and rubber, and paints and coatings packaging sectors(Environment Canada 2012) , as well as in cosmetics and paper (HSDB 1983–; INCI 2004; SPIN 2010; SRD 2010).

More than five uses have been reported for PY83 (Environment Canada 2012); therefore, only the top uses (reflecting the top use-based quantities in the reporting year) for this substance, are presented in Table 4-2. PY83 has additional uses in building materials (the volume of this use is almost identical to the “textile and leather” use pattern). It is also known to be used in cosmetics and paper (HSDB 1983–; INCI 2004) and based on notifications submitted under the *Cosmetic Regulations* to Health Canada, it is used in certain cosmetic products in Canada such as foundation, hair dye, hair grooming products, lipstick, mascara and nail polish (personal communication, email from the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced).

Based on notifications submitted under the *Cosmetic Regulations* to Health Canada, PY12 and PY83 are used in permanent tattoo inks (personal communication, email from

the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced). The diarylide pigment PY83 is also listed as an ingredient in the MSDS sheets of two brands of tattoo inks available internationally including Canada (SkinCandy 2013; Starbrite 2013). The Color Pigment Manufacturers Association (CPMA), representing importers and manufacturers of diarylide pigments in Canada, have indicated that in Canada, their members do not supply these substances for use in tattoo inks (CPMA 2013).

No uses for CPAOBP were reported in the section 71 survey (Environment Canada 2005), although other sources have identified its use in textiles (OTA 2003).

In Canada, food colouring agents to be added directly to food are regulated as food additives under the *Food and Drug Regulations* (Canada [1978]). Colours that are permitted for use in food are included in the *List of Permitted Colouring Agents*, incorporated by reference in the *Marketing Authorization for Food Additives that May be Used As Colouring Agents*, issued under the authority of the *Food and Drugs Act* (Canada 1985). None of the five diarylide yellow pigments in this Screening Assessment are included on the *List of Permitted Colouring Agents* as a permitted food colourant.

PY12, PY13 and PY83 are identified for use in food packaging materials, as components of inks not intended to have direct contact with food. In addition, PY13 and PY83 were identified as components of colour concentrates also for use in food packaging with few applications in direct contact with food (July and September 2011 emails from the Food Directorate, Health Canada to the Risk Management Bureau, Health Canada; unreferenced).

Colourants that are permitted to be used in drugs in Canada are regulated under Part C, Division 1, of the *Food and Drug Regulations* (Canada [1978]). None of the five diarylide yellow pigments are listed as a permitted drug colourant, nor have any been identified to be present in pharmaceuticals, veterinary drugs or biologics in Canada (personal communication, email from the Therapeutic Products Directorate [Health Canada] to the Risk Management Bureau [Health Canada], dated 2011; unreferenced; personal communication, email from the Veterinary Drugs Directorate [Health Canada] to the Risk Management Bureau [Health Canada], dated 2011; unreferenced; personal communication, email from the Biologics and Genetic Therapies Directorate [Health Canada] to the Risk Management Bureau [Health Canada], dated 2011; unreferenced).

PY13 is listed in the Natural Health Products Ingredients Database (NHPID 2011) with a non-medicinal ingredient role (colour additive) for topical use only. However, PY13 is not present in any currently licensed natural health products (Licensed Natural Health Products Database (LNHPD 2011). None of the remaining four diarylide yellow pigments are listed in the NHPID, or are listed in the LNHPD to be present in currently licensed natural health products (NHPID 2011; LNHPD 2011).

None of the five diarylide yellow pigments are included on the List of Prohibited and Restricted Cosmetic Ingredients (more commonly referred to as the Cosmetic Ingredient Hotlist or simply the "Hotlist"), an administrative tool that Health Canada uses to communicate to manufacturers and others that certain substances, when present in a cosmetic, may contravene the general prohibition found in section 16 of the *Food and Drugs Act* or a provision of the *Cosmetic Regulations* (Health Canada 2011b).

None of the five diarylide yellow pigments were identified as a formulant in pest control products registered in Canada (personal communication, email from the Pest Management Regulatory Agency [Health Canada] to the Risk Management Bureau [Health Canada], dated 2011; unreferenced).

### 4.2.2 Other Jurisdictions

PY12, PY13 and PY83 have been reported in the IUR (US EPA 2006) Modifications Rule under the TSCA in the United States. In 2006, the industrial sectors (based on the North American Industry Classification System) involved included "Printing," "Printing ink manufacturing," "Synthetic dye and pigment manufacturing," "Paint and coating manufacturing" and "Plastics product manufacturing." "Coloring agents, pigments" was the only industrial function of these substances.

During the last several years, PY12, PY13, PY83 and PY176 were also used in Denmark, Norway and/or Sweden. The industrial use and use category quantities of these substances can be found in the SPIN database, which is based on data from the product registries of Norway, Sweden, Denmark and Finland and supported by the Nordic Council of Ministers. For example, in the year 2010, some industrial uses of these substances included "Publishing, printing and reproduction of recorded media," "Manufacture of paper and paper products," "Manufacture of fabricated metal products," "Manufacture of rubber and plastic products" and "Manufacture of textiles." "Colouring agents," "Paints, lacquers, and varnishes" and "Reprographic agents" were the major use categories of PY12, PY13 and PY83, while "Reprographic agents" was the only use category of PY176.The use in tattoo inks of several diarylide yellow pigments, including PY13, PY14, PY55, PY83 and PY87, and Pigment Orange 16 (PO16), has been reported in studies from Europe (Bäumler et al. 2000; De Cuyper and D'hollander 2010; KEMI 2010; Hauri 2011, 2013; Danish EPA 2012) and Australia (Poon et al. 2008). The diarylide pigment PO16 is also listed as an ingredient in the MSDS sheets of two brands of tattoo inks available internationally (SkinCandy 2013; Starbrite 2013). Collectively, this information indicates that there is a potential for exposure to diarylide yellow pigments through use in tattoos.

# 5. Environmental Fate

The environmental fate of chemicals describes the processes by which chemicals move and are transformed in the environment. Environmental fate processes that are usually addressed include, for example, persistence of the substances in environmental compartments, their degradation, distribution among media, migration in groundwater, removal from effluents by standard wastewater treatment methods and bioaccumulation in organisms.

However, the combination of variability among chemicals and variability among environments creates complexity that it is challenging to readily survey a set of properties and forecast how a specific chemical is likely to behave (Mackay et al. 2001). While certain attributes of chemicals in the environment (e.g., concentrations) can be measured directly, other attributes (e.g., evaporation rates or distance travelled) cannot be measured directly and can only be estimated using models. However, present models do not always satisfactorily address some chemicals, including pigments (Mackay et al. 2009).

It must also be emphasized that the majority of organic pigments generally do not exist as individual molecules but are principally particles in the sub- or low micrometre size range. The pigment powder is typically composed of primary particles (i.e., the crystal lattice of a pigment), aggregates and agglomerates.

Taking these considerations into account, fugacity modelling for describing the distribution of these substances among environmental compartments would not be applicable for the model-difficult pigments. It was also considered that reasonably reliable conclusions on the environmental fate of diarylide yellow pigments could be made on the basis of available experimental information on the physical and chemical properties of these pigments.

As has been already mentioned, diarylide yellow pigments have very low water solubility – in the sub- or low micrograms per litre range (see Table 3-1). Taking this into account, as well as the fact that these pigments are principally particles in the sub- or low micrometre size range, it may be supposed that when released into water, these substances would be mostly present as particles or adsorbed to other suspended solids and, therefore, would be expected to eventually sink to bed sediments.

Direct releases of diarylide yellow pigments to air are not expected to be significant, but even if they occur, these substances are not expected to reside in this environmental compartment. Indeed, even in a worst-case theoretical scenario, if pigments are released as molecules, not as particles, they, being large, complex molecules, can be expected to have very low vapour pressures. While experimental data on vapour pressure are not available for most of the pigments, these substances can be expected to have vapour pressures similar to those of similarly large and complex azo disperse dyes (i.e., from $10^{-11}$ to $10^{-19}$ Pa, as indicated by Baughman and Perenich 1988).

Another reason for volatilization to be unlikely for the uncharged pigments is that the escaping tendency or fugacity that drives volatilization is also the driving force for both sorption and bioconcentration (Baughman and Perenich 1988).

The particulate character of diarylide yellow pigments should have a key influence on their fate in the environment. This, together with their density (higher than the density of water), high chemical stability and extremely low aqueous solubility, suggests that diarylide yellow pigments will partition by gravity to sediments if released to surface waters and will tend to remain in soils if released to terrestrial environments.

Therefore, for this group of diarylide yellow pigments, soil and sediments are expected to be the two major environmental media of concern.

It should also be noted that, based on the information on the physical and chemical properties and uses of diarylide yellow pigments, air emissions of these substances are not expected to occur. Therefore, the potentials for long-range atmospheric transport of these substances from their emission sources were not calculated.

## 5.1 Environmental Persistence

In order to evaluate the environmental persistence of the substances in the diarylide yellow pigments group, empirical data, modelled data and available information for structural analogues were considered.

It was expected that the characteristics imparted to pigments would result in the diarylide yellow pigments being persistent in the environment. For example, the Color Pigments Manufacturers Association has indicated that pigments are designed to be durable or persistent in the environment in order to provide colour to finished products (e.g., coatings, inks, paints and others) (CPMA 2003).

### 5.1.1 Biodegradation in the Aquatic Environment

The results of multiple biodegradation studies are available for some of the substances in this group of diarylide yellow pigments (see Appendix B for detailed, substance-specific information). The range of biodegradation values for these substances in water is very large – from 0% to 83% (Appendix B). Three major factors probably explain such significant data variations given the similar structures of substances in this group, as described below.

#### 5.1.1.1 Pigments' purity

Substance-specific information on the biodegradation of diarylide yellow pigments (see Appendix B) indicates that in some tests, pigment formulations have been used instead of high-purity pigments. For example, in two tests with PY83, 40% and 52%

formulations were tested, with the biodegradation values being 65% and 83%, respectively.

Therefore, two different summary tables with the results of studies of the biodegradation of diarylide yellow pigments are presented in this report. The first table, Table 5-1, shows the results of the studies where “pure” pigments (i.e., not pigment formulations or final products) have been tested.

**Table 5-1. Biodegradation of diarylide yellow pigments: pure pigments tested**

| Substance | Biodegradation (%) | Test duration (days) | Degradation type (ready or inherent) | Reference |
|---|---|---|---|---|
| PY12 | 0 | 14 | Ready | J-CHECK 2012 |
| PY13 | Not readily biodegradable | 28 | Ready | US EPA 2010 |
| PY83 | 6 | 28 | Ready | J-CHECK 2012 |
| PY14 (analogue) | 2; 4 | 28 | Ready | J-CHECK 2012 |
| Group submission for diarylide yellow pigments: PY12, PY13, PY83, PY176; PY14 (analogue) | 1 | 28 | Ready | ECHA 2012 |

The results of ready biodegradability studies clearly indicate that under aerobic conditions, diarylide yellow pigments are not readily biodegradable (0–6% biodegradation). Therefore, based on the experimental data presented in Table 5-1, it may be concluded that this group of substances is expected to be persistent in water under aerobic conditions.

The second table, Table 5-2, shows the results of the biodegradation studies in which pigment formulations have been tested. The results of three studies show very high biodegradation potential of the tested substances (65–83%). One study, however, has a relatively low biodegradation value of 16%. At the same time, the study contains the statement that “only 70% of the total carbon in the tested product is contained in the pigment. Assuming that the pigment component was stable, the observed BOD (biological oxygen demand) of 16% indicates that, besides carbon assimilation by the microorganisms, 53% of the additives were mineralized during the test” (see also Appendix B). Therefore, the results of the study may suggest that the higher than expected (for the pigment) biodegradation value of 16% can be attributed to biodegradation of additives or formulants rather than to the pigment itself. It may be supposed that if the amounts of additives in this pigment formulation were lower, the

biodegradation value in this study would also be lower (or much lower) than 16%. However, there is some uncertainty here, since this is a ready—not inherent—biodegradability study. (Inherent vs. ready biodegradation issues are discussed in the next part of this section.)

**Table 5-2. Biodegradation of diarylide yellow pigments: pigment formulations tested**

| Substance | Biodegradation (%) | Test duration (days) | Degradation type (ready or inherent) | Reference |
|---|---|---|---|---|
| PY12 | 81 | 15 | Inherent | European Commission ©2000b |
| PY83 | 65; 83 | 15 | Inherent | European Commission ©2000a |
| Group submission for diarylide yellow pigments: PY12, PY13, PY83, PY176; PY14 (analogue) | 16 | 28 | Ready | ECHA 2012 |

It should be noted that even in the tests with the pure pigments (see Table 5-1), the biodegradation values of 4–6% could probably be attributed to the additives rather than to the pigment component itself. Indeed, azo pigments are very difficult to purify; in particular, it is impossible to remove some impurities by pigment filtration and intensive washing, and even the effect of hot extraction procedures tends to be slow and unsatisfactory. Considerable amounts of such soluble species may remain within the pigment even after hours of refluxing and repeated filtration with freshly distilled water (Herbst and Hunger 2004). Another example would be highly transparent pigments (e.g., PY83), which are almost exclusively resinated. However, considerable amounts of resin remain on the pigment surface, even after repeated washing with petrol ether (Herbst and Hunger 2004).

Resins, rosins, aliphatic amines and other compounds, such as surfactants, dispersing agents and coupling agents, are common additives used in pigment preparation, depending on the application of the pigments (Herbst and Hunger 2004), and their biodegradation in the biodegradability studies may result in higher than expected biodegradation values.

However, the purity of the pigments may not be the only reason for the unexpected high biodegradation values in some studies.

#### 5.1.1.2 Inherent biodegradability vs. ready biodegradability

Some of the studies represent the results of ready biodegradability tests, while others are inherent biodegradation studies (see Table 5-1and Table 5-2 and Appendix B). Data indicate that in the ready biodegradation tests, the biodegradation values do not exceed 16%, while in the inherent biodegradation studies, some biodegradation values were greater than 80%. These differences can be explained by the differences in the test procedures of these two types of biodegradability tests.

Indeed, the ready biodegradability tests are stringent screening tests, conducted under aerobic conditions, in which the inoculum should not have been pre-adapted to degradation of the test substance by previous exposure to the test substance or structurally related chemicals. On the contrary, inherent biodegradability tests allow prolonged exposure of the test substance to microorganisms and a low ratio of test substance to biomass, which offers a better chance to obtain a positive result compared with tests for ready biodegradability. Some of these tests may be conducted using microorganisms that have previously been exposed to the test substance, which frequently results in adaptation, leading to a significant increase in the degradation rate (OECD 2005). As a result, biodegradation values from inherent biodegradability studies are usually higher (and sometimes much higher) than those from ready biodegradation tests.

Therefore, it may be supposed that in the inherent biodegradation studies—i.e., under the most favourable conditions—with the pigment formulations, the additives/formulants may quickly degrade, and high biodegradation values in these studies do not reflect actual degradability of the pigment component.

#### 5.1.1.3 Adsorption of pigments on the inoculum matrix (sludge)

Adsorption of pigments on the sludge (used as inoculum, i.e., the source of microorganisms in the test) could be another explanation for the unusually high biodegradation values. Indeed, two studies with PY83 contained the important statement that 20% (one study) and 50% (another study) of the elimination of dissolved organic carbon “occurred due to adsorption on activated sludge, not due to biodegradation” (see Appendix B for more details).

Therefore, pigment purity (i.e., pure pigment vs. pigment formulation), the type of biodegradation test (i.e., inherent vs. ready biodegradability) and adsorption of pigments on the inoculum (sludge) are the major factors explaining the unusually high biodegradation values in some biodegradation tests with the diarylide yellow pigments in the water compartment. Therefore, the results of these tests with unexpectedly high biodegradation values cannot be considered applicable for the risk assessment of diarylide yellow pigments.

It may also be concluded that the multiple ready biodegradation studies with the pure diarylide yellow pigments indicate their very low biodegradation potential in water. Thus, considering all this information, it is expected that under aerobic conditions, diarylide yellow pigments will have long residence times in water.

The environmental persistence of disazo diarylide yellow pigments in anoxic environments is an important area of uncertainty, because of a lack of biodegradation data for the pigments. While some azo dyes are reported to be biodegradable in anoxic waters via anaerobic reduction of the azo bond (–N=N–), which results in releasing potentially harmful aromatic amines (Øllgaard et al. 1998), almost no documentation has been found regarding the potential for anaerobic degradation of azo pigments in aqueous environments. In principle, the pigment crystals would have to dissolve first, which would release the constituent molecules to the aqueous medium and make the azo bonds available for biotic reduction (Øllgaard et al. 1998). However, it may be expected that only a very small (if any) proportion of the disazo diarylide yellow pigments may be reduced in this manner, given their unique physical state (pigments are typically composed of primary particles —i.e., the crystal lattice of a pigment, as well as aggregates and agglomerates), along with their very low water solubility, which would limit the availability of the molecules for biotic reduction.

### 5.1.2 Biodegradation in Soil and Sediments

No studies on the biodegradation of diarylide yellow pigments in soils or sediments have been identified. However, the approach to estimating the required soil and sediment half-lives is to use the recommended values for water and extrapolate to the other media using scaling factors. Scaling factors are numbers that, when multiplied by a degradation rate constant or half-life for one set of environmental or test conditions, they yield a rate for a second, different set of conditions (US EPA 2000).

Boethling et al. (1995) collected measured half-life data for a wide variety of chemicals that had been tested in both soil and water samples collected from the environment and then calculated mean ratios of half-life in water to half-life in aerobic surface soil for 20 chemicals. It was suggested that for screening purposes, it is valid to assume that biodegradation in aerobic surface water is about as fast as degradation in aerobic surface soil and that sediment half-lives may be assumed to be 3–4 times longer (US EPA 2000).

Therefore, in terms of biodegradation half-life, using a water to soil to sediment extrapolation ratio of 1:1:4 (Boethling et al. 1995) and the ultimate biodegradation half-life in water of ≥ 182 days based on experimental biodegradation data of 0–6% (for pure pigments), it may be concluded that the ultimate biodegradation half-life of diarylide yellow pigments in aerobic soils is also expected to be ≥ 182 days, and the half-life in aerobic sediments is expected to be ≥ 365 days.

In anaerobic sediment conditions, there is the possibility that solubility-limited azo reduction may occur. However, given the unique physical and chemical characteristics of diarylide yellow pigments (particulate nature, extremely low solubility), it is expected that only a very small proportion of these pigments may be available to microorganisms for biotic reduction.

Therefore, taking into account that diarylide yellow pigments generally do not exist as individual molecules but are principally particles in the sub- or low micrometre size range, and that the water solubility of diarylide yellow pigments is very low (sub- to low micrograms per litre), it may be supposed that the bioavailability of these substances to microorganisms for biotransformation (biotic reduction) is very limited, which is confirmed by the results of multiple ready biodegradability studies (0–6% biodegradation in water) with the pure pigments (not pigment formulations). In soil and sediments, these substances are also expected to be not readily biodegradable.

### 5.1.3 Abiotic Degradation

No experimental data have been found for photodegradation of diarylide yellow pigments in air. The predictions using the AOPWIN model from EPISuite version 4.10 (AOPWIN 2010) indicate that calculated half-lives (indirect reaction with hydroxyl radicals based on a 12-hour day) were relatively short—only 1.7–4.9 hours. These results are consistent with the fact that these pigments are generally not used in artists' colours, since diarylide yellow pigments have significantly reduced light-fastness (Herbst and Hunger 2004; MacEvoy 2008).

Diarylide yellow pigments are expected to be hydrolytically stable, as indicated in a study on PY83 that did not detect hydrolysis in a 56-day experiment (European Commission ©2000a).

### 5.1.4 Summary of Persistence in the Environment

Based on empirical data (Table 5-1 and Appendix B) and the above-mentioned considerations, it is expected that under aerobic conditions, diarylide yellow pigments will have long residence times in water, soil, and sediment.

## 5.2 Potential for Bioaccumulation

In order to evaluate the bioaccumulation potential of substances in this group of diarylide yellow pigments, only empirical data were considered, given the high level of uncertainty associated with modelling the bioaccumulation of this substance group.

### 5.2.1 Octanol–Water Partition Coefficient

As indicated in the Physical and Chemical Properties section of this report, a $S_{oct}/S_w$ parameter can represent octanol–water partition coefficient for organic pigments. For

diarylide yellow pigments, the log ($S_{oct}/S_w$) values, based on experimental solubility values in water and in octanol, vary within a reasonably narrow range of 0.4–2.1, with a mean value of 1.5 (see Table 3-1), which is significantly lower than the criterion of $K_{ow}$ for bioaccumulation (log $K_{ow} \geq 5$) when neither a bioaccumulation factor (BAF) nor a bioconcentration factor (BCF) of the substance can be determined in accordance with a method referred to in section 5 of the *Persistence and Bioaccumulation Regulations* (Canada 2000). Therefore, based on the experimental log ($S_{oct}/S_w$) values, diarylide yellow pigments have a low potential to bioaccumulate in organisms.

Other physiological parameters and processes, such as metabolism, are important to consider along with information on octanol–water partition coefficients (indeed, the substance may be characterized by a high $K_{ow}$ and, at the same time, quickly metabolized or biotransformed in the organism). Therefore, octanol–water partition coefficient data have to ideally be considered along with other information related to the bioaccumulation of these substances.

### 5.2.2 Bioconcentration Factor (BCF)

For the group of diarylide yellow pigments, several experimental BCF studies have been identified. The results of these studies are presented in Table 5-3.

**Table 5-3. Experimental BCF data for diarylide yellow pigments in common carp (Cyprinus carpio)**

| Substance | BCF (L/kg) | Test conditions | Reference |
|---|---|---|---|
| PY12 | 2.4–5.4 (at 0.01 mg/L) | Test duration 6 weeks; lipid level in fish 2.8% | MITI 1992; J-CHECK 2012 |
| PY12 | 0.38–3.2 (at 0.1 mg/L) | Test duration 6 weeks; lipid level in fish 2.8% | MITI 1992; J-CHECK 2012 |
| PY14 (analogue) | < 4.9 (at 0.1 mg/L) | Test duration 6 weeks; lipid level in fish 3.8% | J-CHECK 2012 |
| PY14 (analogue) | ≤ 0.5–0.6 (at 1 mg/L) | Test duration 6 weeks; lipid level in fish 3.8% | J-CHECK 2012 |
| Group submission for diarylide yellow pigments: PY12, PY13, PY83, PY176; PY14 (analogue) | ≤ 6.2 (at 0.09 mg/L) | Test duration 28 days; lipid level in fish 1.69% | ECHA 2012 |

Data show that for the diarylide yellow pigments, all available BCF values do not exceed 6.2 L/kg in common carp (the highest definitive experimental BCF value was 5.4 L/kg), indicating that these diarylide yellow pigments have a low potential to bioconcentrate from water in fish.

In the scientific literature and recommendations from international jurisdictions, there are some data regarding bioaccumulation of pigments. In particular, ECHA (2008) presented a weight of evidence approach for PY12. Based on low solubility in octanol and low log ($S_{oct}/S_w$), as well as on pharmacokinetic data (14C pharmacokinetic rat study showing no uptake from food and complete excretion of PY12 through feces), ECHA (2008) concluded that PY12 is not a bioaccumulative substance.

Anliker and Moser (1987) studied the limits of bioconcentration of azo pigments in fish and their relation to the partition coefficient and solubilities in water and octanol. Despite a high calculated log $K_{ow}$ for two pigments, the experimentally determined log BCFs were low. The explanation for this apparent inconsistency is the very limited fat (lipid) storage potential of these pigments, as indicated by their low solubility in n-octanol (< 1 and < 0.1 mg/L) and their large molecular size (cross-sectional diameters of 0.97 and 1.68 nm).

In another study, Anliker et al. (1988) assessed different dyes and pigments, including two organic pigments, for which the experimental BCFs in fish were known (16 halogenated aromatic hydrocarbons were included for comparison). None of the disperse dyestuffs, even the highly lipophilic colorants with log $K_{ow}$ > 3, accumulated significantly in fish. The authors suggested that the large molecular size of the colorants prevented their effective permeation through biological membranes and thus limited their uptake during the time of exposure. Anliker et al. (1988) proposed that a cross-sectional diameter of more than 1.05 nm with a molecular weight of greater than 450 g/mol would suggest a lack of bioconcentration for organic colorants.

Molecular size and cross-sectional diameter are commonly used by international jurisdictions in weight of evidence for conclusions on bioaccumulation potential. For example, ECHA (2008), describing “Indicators for limited bioaccumulation,” showed that some additional indicators for low bioaccumulation potential might be applicable for substances with low solubility in octanol and water. In particular, an average $D_{max}$ of > 1.7 nm may be considered as one of these additional indicators.

Investigations relating fish BCF data and molecular size parameters (Dimitrov et al. 2002, 2005) suggest that the probability of a molecule crossing cell membranes as a result of passive diffusion declines significantly with increasing maximum diameter ($D_{max}$). The probability of passive diffusion decreases appreciably when the maximum diameter is greater than approximately 1.5 nm, and much more so for molecules having a maximum diameter of greater than 1.7 nm. Sakuratani et al. (2008) also investigated the effect of cross-sectional diameter on passive diffusion in a BCF test set of about 1200 new and existing chemicals. They observed that substances that do not have a

very high bioconcentration potential (i.e., BCF < 5000) often have a $D_{max}$ of greater than 2.0 nm and an effective diameter ($D_{eff}$) of greater than 1.1 nm.

Table 3-1 in the Physical and Chemical Properties section presents estimates of the ranges and averages of maximum diameters ($D_{max}$) and effective diameters ($D_{eff}$) of diarylide yellow pigments performed by the BCFmax model with mitigating factors (Dimitrov et al. 2005). The statistics for calculations of cross-sectional diameters of diarylide yellow pigments include the consideration of conformational analysis for up to 30 conformers.

Average effective cross-sectional diameters of molecules of diarylide yellow pigments are greater than 1.1 nm, while average maximum diameters can reach 2.5 nm. Since all these values exceed the threshold values recommended by Dimitrov et al. (2002, 2005) and Sakuratani et al. (2008), it can be supposed that diarylide yellow pigments will likely experience restricted uptake from steric effects at the gill surface of fish, which helps explain the low observed empirical BCF values (≤ 6.2 L/kg) for these substances.

It should, however, be noted that according to Arnot et al. (2010), there are some uncertainties associated with the thresholds proposed by Dimitrov et al. (2002, 2005) and Sakuratani et al. (2008), since the bioaccumulation studies used to derive them were not always critically evaluated. Arnot et al. (2010) pointed out that molecular size influences solubility and diffusivity in water and organic phases (membranes), and larger molecules may have slower uptake rates. However, these same kinetic constraints apply to diffusive routes of chemical elimination (i.e., slow uptake = slow elimination). Thus, significant bioaccumulation potential may remain for substances that are subject to slow absorption processes, if they are slowly biotransformed or slowly eliminated by other processes. However, if the rate of gill uptake is sufficiently mitigated by steric hindrance to the point that the rate of elimination exceeds uptake, bioconcentration will be lowered.

Steric effects, however, cannot be considered directly applicable to dietary exposure studies (e.g., studies on biomagnification factor). The “transepithelial electrical resistance” of fish intestines compared with gills is 2 orders of magnitude lower (Arnot et al. 2010), which suggests that the permeability of chemicals from the gastrointestinal tract is likely much greater than that from the gill; thus, dietary uptake cannot be explained by the studies relating molecular size to BCF.

Another aspect of bioavailability and bioaccumulation of pigments in non-human organisms may also be considered. Many pigments have a particle size in the low sub-micrometre range and therefore potentially fall partially within the “nanoscale” size range (i.e., 1–100 nm; Canada 2007; Health Canada 2011a). Lynch et al. (2006), Rothen-Rutishauser et al. (2006), Smart et al. (2006) and others indicate that nanoparticles can be taken up by different types of mammalian cells and are able to cross the cell membrane and become internalized. Importantly, the interaction of nanoparticles with the cells and their uptake are size dependent (Limbach et al. 2005;

Chithrani et al. 2006) and shape dependent (Pal et al. 2007), and uptake occurs via endocytosis or phagocytosis in specialized cells.

Passive diffusion is considered the predominant mechanism for the transport of substances across epithelia for most pharmaceuticals and environmental organic contaminants, although facilitated, active, paracellular and phagocytosis (pinocytosis and endocytosis) transport mechanisms can be important for certain substances (DeVito 2000). Passive diffusion rather than a facilitated process controls the absorption of hydrophobic persistent organic pollutants (Kelly et al. 2004).

At the same time, bioaccumulation studies in which the endocytosis or phagocytosis mechanism could be reliably confirmed could not be identified for the diarylide yellow pigments. If this mechanism was typical (or significant) for diarylide yellow pigments, the results of bioaccumulation studies—namely, high (or relatively high) BCF values—would reflect the existence of this phenomenon in terms of the pigments' uptake. However, all available experimental BCF values show that diarylide yellow pigments have a very low potential to bioconcentrate from water in fish.

The results of ecotoxicity studies, which are discussed in the next section of this report, indicate that aqueous dispersions of diarylide yellow pigments do not cause noticeable biological effects. This indicates that the bioavailability of these substances is limited, and phagocytosis most likely does not play a significant role in the uptake of diarylide yellow pigments.

### 5.2.3 Summary of Bioaccumulation Potential

Based on the consistency of various lines of evidence, including low experimental log ($S_{oct}/S_w$) values of approximately 1.5 (mean), low experimental solubility in octanol (mean ~40 µg/L), large molecular cross-sectional diameter (average $D_{eff}$ of 1.1–1.3 nm and $D_{max}$ of 2.2–2.5 nm) and very low experimental BCF values (≤ 6.2 L/kg), it is expected that the substances in the diarylide yellow pigments group will have low bioaccumulation potential in aquatic organisms.

# 6. Potential to Cause Ecological Harm

## 6.1 Ecological effects assessment

In order to provide the best possible weight of evidence for assessing the ecological effects of substances in the diarylide yellow pigments group, only empirical data were considered, given the high level of uncertainty associated with modelling the ecotoxicity of this substance group.

### 6.1.1 Aquatic Environment

Both acute and chronic aquatic toxicity studies are available for this group of diarylide yellow pigments. Table 6-1 presents a summary of available empirical ecotoxicity data for the diarylide yellow pigments and one of their structural analogues, while Appendix C contains more detailed, substance-specific information on the specific studies.

**Table 6-1. Summary of empirical data for aquatic toxicity of diarylide yellow pigments**

| Substance | Test type | Organism | Endpoint, value | Details | Reference |
|---|---|---|---|---|---|
| PY12 | Chronic (72 h) | Alga (*Selenastrum capricornutum*) | NOEC > 100 mg/L | NA- | CPMA 2009 |
| PY12 | Acute (72 h) | Water flea (*Daphnia magna*) | $EC_{50}$ > 100 mg/L | Effects: immobilization; high-purity test substance (98%) | US EPA 2006 |
| PY12 | Acute (48 h) | Zebrafish (*Brachydanio rerio*) | $LC_{50}$ = 5–22 mg/L; $LC_{100}$ = 10–22 mg/L | 55% and 63% formulations; TWEEN 80 (polyethylene sorbitol ester) added | European Commission ©2000a |
| PY12 | Acute (48 h, 96 h) | Ide (*Leuciscus idus*) | $LC_{50}$ > 500 mg/L; $LC_{50}$ > 1 000 mg/L | 35% solution in water | European Commission ©2000a |
| PY12 | Acute | Ide (*Leuciscus idus*) | $LC_{50}$ = 10–100 mg/L | 81% solution; acetone added | European Commissio |

| Substance | Test type | Organism | Endpoint, value | Details | Reference |
|---|---|---|---|---|---|
| | (96 h) | | | | n ©2000a |
| PY12 | Acute (48 h) | Medaka (*Oryzias latipes*) | $LC_{50}$ > 420 mg/L | NA | MITI 1992 |
| PY13 | Chronic (21 days) | Water flea (*Daphnia magna*) | NOEC = 1 mg/L | Effects: immobilization, reproduction; high-purity test substance (99.7%) | US EPA 2006 |
| PY83 | Chronic (72 h) | Alga (*Selenastrum capricornutum*) | $EC_{50}$ = 190 mg/L | High-purity test substance (94.5%) | US EPA 2006 |
| PY83 | Acute (96 h) | Zebrafish (*Brachydanio rerio*) | $LC_{50}$ > 100 mg/L | High-purity test substance (94.5%) | US EPA 2006 |
| PY83 | Acute (48 h) | Fish (*Phoxinus phoxinus*; *Oncorhynchus mykiss*; *Leuciscus idus*) | $LC_{50}$ = 18–80 mg/L[1]; $LC_{100}$ = 100–200 mg/L | Aqueous ethylene glycol preparation (concentration of ethylene glycol not reported) | Hamburger et al. 1977 |
| Group submission for diaryl pigments[2] | Chronic (72 h) | Alga (*Desmodesmus subspicatus*; *Selenastrum capricornutum*) | NOEC = 100 mg/L | Effects: growth inhibition, growth rate reduction; filtered solution was prepared at 100 mg/L of pigment | ECHA 2012 |
| Group submission for diaryl pigments[2] | Acute (48 h) | Water flea (*Daphnia magna*) | NOEC = 100 mg/L; $EC_{50}$ > 1 000 mg/L | Effects: immobilization; filtered solution (at a loading of 100 mg/L of the substance) or aqueous dispersion of the substance (loading rate of 1000 mg/L) | ECHA 2012 |
| Group submission for diaryl pigments[2] | Chronic (21 days) | Water flea (*Daphnia magna*) | NOEC = 10 mg/L | Effects: reproduction, mortality, body weight, length, | ECHA 2012 |

| Substance | Test type | Organism | Endpoint, value | Details | Reference |
|---|---|---|---|---|---|
| | | | | etc.; centrifuged solution (loading of 10 mg/L of pigment) | |
| Group submission for diaryl pigments[2] | Acute<br><br>(96 h) | Rainbow trout (*Oncorhynchus mykiss*) | $LC_{50}$ = 124 mg/L | Aqueous suspension; the $LC_{50}$ of 124 mg/L equals 49 mg/L of test substance (far above solubility limit) | ECHA 2012 |

Abbreviations: CTV, critical toxicity value; EC50, effective concentration for 50% of test organisms; LCx, lethal concentration for x% of test organisms; NOEC, no-observed-effect concentration ; NA, not available
1 $LC_{50}$ of 18 mg/L from this study was selected as the CTV.
2 Submission for a group of diaryl yellow pigments from ECHA 2012 includes experimental data on pigments PY12, PY13, PY83, PY176, and PY14.

It should first be noted that the results of all these studies are based on loading rates, and no studies with measured or nominal concentrations have been identified. For aquatic tests, the nominal concentration is the concentration that would exist if all test material added to the test solution was completely dissolved and did not dissipate (US EPA 1996). Although many of these studies refer to "nominal concentrations," they appear to be using this terminology as a synonym for "loading rate" or "non-measured concentration," which, strictly speaking, is not necessarily the same. Particularly in studies in which solvents or dispersants were not applied, the reported values (e.g., NOEC = 10 mg/L, $LC_{50}$ > 1 000 mg/L) were 4–6 orders of magnitude above the water solubility limits of the tested pigments, suggesting that the test solution was not completely dissolved and that these were, in fact, loading rates. Consequently, in studies in which the loading rates exponentially exceeded the water solubility limits of the pigments (when solvents or dispersants were not applied), the endpoints probably should have been more accurately reported as $EL_{50}$ (loading rate causing adverse effect in 50% of exposed organisms) instead of $EC_{50}$, or as $LL_{50}$ (loading rate causing mortality of 50% of exposed organisms) instead of $LC_{50}$, and NOELR (no-observed-effect loading rate) instead of NOEC (no-observed-effect concentration). However, there appear to be differing opinions in the literature. The OECD's Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (OECD 2000), in which the water accommodated fractions (WAF) protocol is discussed, indicates that "WAFs may be thus considered analogous to the term 'nominal concentration' used for typical test substances, with all the limitations inherent to that term." It is further stated that "$LL_{50}$ or $EL_{50}$ values are comparable to $LC_{50}$ or $EC_{50}$ values determined for pure substances tested within their solubility range."

Nonetheless, the results presented in Table 6-1 are considered somewhat questionable in those cases where the concentrations are exponentially higher than the water

solubility limits for the pigments. It may therefore be concluded that in all aquatic tests with the diarylide yellow pigments where solvents or dispersants were not applied (see Table 6-1 and Appendix C) and where the toxicity values were far above the water solubility values of the substances, the results can only be, strictly speaking, interpreted as “not toxic at saturation” or “no effect at saturation” (i.e., at water solubility limits).

It must also be mentioned that in aquatic tests where solvents or dispersants were used, very significant biological effects (such as mortality of 50% and even 100% of test organisms) have been reported, and some toxicity values are at relatively low concentrations (e.g., $LC_{50}$ of 18–80 mg/L for PY83 or $LC_{100}$ of 10–22 mg/L for PY12; see Table 6-1 and Appendix C), which, according to ecotoxicity classification schemes, indicate that the tested pigments can be considered as moderately toxic (i.e., $EC_{50}$ or $LC_{50}$ from 1 to 100 mg/L). Unfortunately, similar to the above-mentioned studies without solvents, no measured concentrations were reported in these studies.

There are different reasons for such pronounced biological effects in the studies with solvents or dispersants. The first reason is that diarylide yellow pigments might theoretically be potentially moderately toxic substances—that is, when their solubility limits are substantially increased to certain levels (by using the solvents or dispersants), these substances can cause adverse effects.

Herbst and Hunger (2004) indicated that although, according to definition, the ideal pigment is practically insoluble in its medium of application, organic pigments may, in reality, deviate more or less from this postulate of insolubility. Since a pigment that is to a certain extent soluble in its carrier is expected to perform poorly and may even recrystallize, bleed or bloom, it is important to prevent pigment dissolution. There are even certain accepted tests used to determine the extent to which a given organic pigment tolerates solvents. The results of these tests, for example, indicate that, compared with other diarylide yellow pigments, PY12 is only moderately fast to organic solvents (Herbst and Hunger 2004).

Therefore, it may be supposed that in the aquatic toxicity tests with dispersants and solvents (see Table 6-1 and Appendix C), the solubility of pigments is very likely to have been increased from the low microgram per litre range to the low milligram per litre range.

There is also an opinion (Rufli et al. 1998) that dispersants, even if non-toxic, may have a pronounced effect on the physical form of the hydrophobic test substances in the test medium and may thereby influence their bioavailability. Thus, results from a test involving a dispersant may be specific for a defined substance–dispersant system, and it may be difficult to extrapolate to other exposure conditions. Rufli et al. (1998) believed that controls containing dispersant only can identify dispersant-related effects, but not dispersant–substance interactions.

In addition, test concentrations far above the water solubility of the test substance can contain more soluble impurities whose effects might also confuse the interpretation of true substance toxicity (Weyman et al. 2012). Weyman et al. (2012) indicated that when a solvent is used, but the test substance is not completely dissolved, undissolved material present in the test media has the potential to exert adverse (physical) effects on test organisms, such as blocking of fish gill membranes, encapsulation/entrapment of daphnids or the reduction of light intensity in algal tests.

If studies with the pure pigments only—not pigment formulations—are considered, the important question would probably be whether the no effect at saturation situations occurred due to the low bioavailability of the pigments or their low inherent toxicity, or both. To answer this question, a critical body burden (CBB), or internal critical concentration (ICC), approach can be applied where the acute external effect concentrations of pigments causing the mortality of organisms can be calculated and compared with the results of ecotoxicity studies with pronounced biological effects (i.e., tests with solvents or dispersants), and are also compared with the cut-off values of ecotoxicity classification schemes (i.e., $LC_{50}$/$EC_{50}$ values reflecting low, moderate or high aquatic toxicity levels).

Calculated data indicate that to reach the CBB threshold levels for the acute endpoints (mortality), the external $LC_{50}$ values of diarylide yellow pigments should be in the range of 565–803 mg/L, which suggests that these pigments are of low toxicity. This is also in line with the low bioaccumulation potential of these substances in fish. Indeed, very low BCFs (i.e., little uptake) of these substances of a particulate nature with low solubility in water and octanol mean low risk of toxic effects, which is confirmed by the above-mentioned CBB-based external effect concentrations and by the lack of significant adverse effects observed in any of the bioconcentration tests.

It should, however, be noted that the calculated external effect concentrations are higher than the $LC_{50}$ values of 5–22 mg/L (PY12) and 18–80 mg/L (PY83) that were reported in the studies in which solvents or dispersants were used (see Table 6-1). The apparent discrepancy between the observed toxicity as indicated by the $LC_{50}$ in water and the calculated CBB-based toxicity values may be due to toxic effects caused by impurities (contained in the tested pigments) and different additives (contained in the pigment formulations), the dispersant–pigment (or solvent–pigment) interactions, as well as a mode of toxic action not predictable by the CBB approach.

Regarding the experimental $LC_{50}$ values of 5–22 mg/L (PY12) and 18–80 mg/L (PY83) in aquatic tests in which solvents or dispersants were used to enhance the apparent water solubility above the maximum thermodynamic equilibrium solubility in water, it should be emphasized that reaching such high concentrations (in molecular form) of diarylide yellow pigments is not likely realistic in the Canadian environment. It is acknowledged that in the realistic aquatic environment and in laboratory studies, water solubility values will rarely be identical. Indeed, laboratory tests are conducted under conditions that do not take into account the various co-solvents that exist in the

environment, which may ultimately affect the solubility and bioavailability of a substance. Temperature, pressure and surfactants (which may be present in the aquatic environments) are other important factors that may affect the solubility of chemicals in the environment. At the same time, water solubility enhancement in the environment would not, probably, be as high as 4–5 orders of magnitude over solubility under laboratory conditions.

Accordingly, studies without strong solvents and dispersants have greater inference, as they are more environmentally relevant. In these studies, the no effect at saturation situations occurred due to the very low bioavailability of the diarylide yellow pigments. Therefore, it is expected that diarylide yellow pigments will not be harmful to aquatic organisms, due to the very limited bioavailability of these substances under realistic environmental conditions.

Finally, it should be noted that the absence of effects in short-term studies does not necessarily mean that the substance would not be toxic during longer-term exposure. For diarylide yellow pigments, two chronic studies (21-day tests with *Daphnia magna*) are available (see Table 6-1 and Appendix C). In these studies, multiple endpoints have been studied, including (but not limited to) reproduction, mortality and immobilization of organisms, as well as their body weight and body length. No adverse effects were observed at loading rates of 1 and 10 mg/L (i.e., no effect at saturation).

The above information allows one to conclude that no effect at saturation situations in both acute and chronic studies occurred due to the low bioavailability of the pigments and their low inherent toxicity. All the results therefore support the conclusion that diarylide yellow pigments are of low inherent toxicity to aquatic organisms.

### 6.1.2 Other Environmental Compartments

In order to provide the best possible weight of evidence for assessing the ecological effects of substances in the diarylide yellow pigments group, empirical data for soil and sediments were also considered. It should be emphasized that, in terms of environmental fate, these two environmental compartments are critical, because the substances from this group are expected to almost solely reside in soils or sediments (depending on the exposure scenario). Therefore, soil and sediment toxicity data are highly relevant to the diarylide yellow pigments group.

One study on soil toxicity and one study on sediment toxicity are available for diarylide yellow pigments (group submission for PY12, PY13, PY83, PY176, and PY14, see Table 6-2). Data show that at a loading rate of 1 000 mg/kg of soil or sediment, no effects (e.g., mortality, behaviour, reproduction and biomass of organisms) were observed in chronic toxicity studies.

**Table 6-2. Empirical data for ecotoxicity of diarylide yellow pigments in sediment and soil**

| Test type | Organism | Endpoint, value | Details | Reference |
|---|---|---|---|---|
| Sediment toxicity, long-term (28 days) | Freshwater oligochaete (*Lumbriculus variegatus*) | NOEC = 1 000 mg/kg sediment (dry weight) | Effects: biomass, mortality, behaviour, reproduction; spiking the test item (1 000 mg/kg) into sediment | ECHA 2012 |
| Soil toxicity, long-term (56 days) | Earthworm (*Eisenia fetida*) | NOEC = 1 000 mg/kg soil (dry weight) | Effects: reproduction, mortality, body weight; test item (1 000 mg/kg) was mixed with soil | ECHA 2012 |

Therefore, it may be concluded that diarylide yellow pigments are of low inherent toxicity to soil- or sediment-dwelling organisms, which can most likely be explained by the very low bioavailability of these substances.

### 6.1.3 Derivation of the Predicted No Effects Concentration (PNEC) for Water

As has already been mentioned, multiple experimental toxicity data from acute and chronic aquatic ecotoxicity studies are available for this group of substances (see Table 6-1 and Appendix C). The range of empirical acute toxicity values from these studies is quite significant—from 5 mg/L to more than 1 000 mg/L. It has already been noted that in most studies, loading rates were reported, and very often the toxicity data were expressed as ranges, not as definitive values (e.g., $LC_{50}$ > 100 mg/L).

For deriving a PNEC value, it was decided to use the study with obvious biological effect (e.g., mortality) and a conservative exposure scenario (i.e., the use of dispersant or solubilizer to significantly increase the bioavailability of the pigment) instead of studies with “no effect at saturation” results. One study (Hamburger et al. 1977; see Table 6-1 and Appendix C), containing one of the lowest definitive acute toxicity values available for this group of substances (namely, $LC_{50}$ of 18 mg/L), has been critically reviewed and is considered to be a high-quality study; therefore, the toxicity value of 18 mg/L was selected as the critical toxicity value (CTV), which is also consistent with other risk assessments on azo-colorants. For example, this toxicity value of 18 mg/L was also chosen for calculation of the aquatic PNEC in the Danish Environmental Protection Agency’s Survey of Azo-colorants in Denmark (Øllgaard et al. 1998) and in the screening assessment for the Challenge on the diarylide yellow pigment analogue BPAOPB (Environment Canada and Health Canada 2011).

Therefore, the aquatic PNEC of 180 µg/L was derived based on the CTV of 18 mg/L and an assessment (safety) factor of 100 to account for interspecies and intraspecies variability in sensitivity and to estimate a long-term no-effect concentration.

### 6.1.4 Derivation of the PNECs for Soil and Sediment

One study on sediment toxicity and one study on soil toxicity are available for a group of diarylide yellow pigments (see Table 6-2). These two studies have been considered as key, high-quality studies, and the toxicity values (NOEC) of 1 000 mg/kg sediment (dry weight) and 1 000 mg/kg soil (dry weight) were selected as the CTVs. Importantly, the European Chemicals Agency has also considered these tests as key studies for a group of diarylide yellow pigments (ECHA 2012).

Taking into account that the CTVs were based on NOEC values in long-term studies, where no lethal or sublethal adverse effects (including sensitive endpoints, such as reproduction) were found at the loading concentration of 1 000 mg/kg sediment or soil, an application factor of 10 was used to account for inter- and intra-species variability in sensitivity only. A PNEC for sediment or soil of 100 mg/kg soil (dry weight) was calculated.

It should also be mentioned that the soil toxicity study was conducted with earthworms, which are excellent model organisms in ecotoxicity studies due to their exposure to soil contaminants via both ingestion and passive absorption through their skin. Since no adverse biological effects were observed in this study, it was considered that a safety factor of 100 would be overly conservative for calculation of a PNEC value.

Therefore, for characterization of ecological risk in different environmental compartments, the following PNEC values will be used: aquatic PNEC, 180 µg/L; soil PNEC, 100 mg/kg; and sediment PNEC, 100 mg/kg.

### 6.1.5 Ecological Effects Summary

Based on various lines of evidence involving empirical ecotoxicity data in various environmental compartments, it may be concluded that diarylide yellow pigments are not expected to cause harm to aquatic or soil- and sediment-dwelling organisms at low concentrations. It should be emphasized that this conclusion does not contradict the relatively low aquatic CTV of 18 mg/L, because this CTV is very conservative, assuming very high bioavailability (provided by the use of a solvent in the aquatic ecotoxicity study), which is not expected in the realistic environment.

Empirical data allowed derivation of the PNEC values for water, soil and sediments for further characterization of the ecological risk of diarylide yellow pigments in different environmental compartments.

## 6.2 Ecological exposure assessment

### 6.2.1 Releases to the Environment

No data on measured environmental concentrations (in water, soils or sediments) of the five diarylide yellow pigments in Canada have been identified. Environmental concentrations have therefore been estimated from available information.

Anthropogenic releases of a substance to the environment depend upon various losses that occur during the manufacture, industrial use, consumer/commercial use and disposal of the substance. In order to estimate releases to the environment occurring at different stages of the life cycle of the diarylide yellow pigments, Environment Canada compiled information on the relevant sectors and product lines as well as emission factors[5] to wastewater, land and air at different life cycle stages in order to identify the life cycle stages that are the largest contributors to environmental concentrations. Recycling activities and transfer to waste disposal sites (landfill, incineration) were also considered. However, releases to the environment from disposal were not quantitatively accounted for unless reliable specific information on the rate of (or potential for) release from landfills and incinerators was available.

Factors relevant to the life cycle of these substances have been considered, uncertainties have been recognized, and assumptions may be made during each stage, depending on information available. Exposure scenarios for the uses and media of concern have been developed, including the determination of applicable predicted environmental concentrations (PECs).

In order to evaluate potential exposures to the diarylide yellow pigments in the environment, environmental concentrations are estimated from available information on substance quantities, industrial use patterns, estimated release rates, characteristics of wastewater treatment systems and characteristics of the receiving environment.

[5] An emission factor is generally expressed as the fraction of a substance released to a given medium, such as wastewater, land or air, during a life cycle stage, such as manufacture, processing, industrial application or commercial/consumer use. Sources of emission factors include emission scenario documents developed under the auspices of the OECD, data reported to Environment Canada's National Pollutant Release Inventory, industry-generated data and monitoring data.

In order to characterize the ecological exposure to diarylide yellow pigments, the sector or use likely to be responsible for the highest potential releases in Canada was identified, and a conservative exposure scenario was developed. When a sector or use with the highest potential releases is determined to present low ecological concern, then all other sectors or uses are also considered to be of low concern due to the lower potential releases, i.e., no further analysis is necessary. However, additional sectors or activities may be examined if there is cause for concern to determine the extent of the ecological risk.

In the case of diarylide yellow pigments, the recycled paper deinking sector has been determined to incur the highest potential environmental releases among all sectors or uses identified from the survey data for the diarylide yellow pigments. This is supported by data compiled from the 2006 and 2010 section 71 surveys, which show that the use as ink, toner and colorants represented the majority (in the range of 100 000 – 500 000 kg/yr) of the diarylide yellow pigments reported. The other uses reported (paints and coatings; food and beverage packaging applications; plastics and rubber; textile and leather; building materials; automotive industry; adhesive sealants) accounted for lower total quantities (10 000 – 100 000 kg). An approach focusing on the recycled paper deinking sector was taken based on this information, which represents the scenario with highest expected exposure.

PY12 is the dominant substance with respect to volume used under the code “Ink, toner and colorants” and is known, along with other diarylide yellow pigments, to be used for printing on both paper and plastic film according to the information provided by major pigment producers and ink/toner formulators. It was therefore induced that the entire quantity of diarylide yellow pigments, formulated into inks and toners, ended up on printed paper and plastic film. Although the proportions of these pigments between the two substrates were unknown, a substantial quantity was expected to be used on the paper substrate. Considering this and a large recycled portion of the printed paper, it was expected that a significant quantity of the ink/toner-destined diarylide yellow pigments was subject to deinking.

For pigments in general, the emission factor to wastewater was estimated to be 20% from deinking operations (see Appendix D), while the emission factor from any other sector or use is much lower, ranging from 2.5% for plastics manufacture (OECD 2009c) and 3% from the formulation of paints and coatings (OECD 2009b) to 5% from printing (Baumann et al. 2001). The combination of a high emission factor of 20% and more than 50% of the total quantity potentially reaching deinking facilities resulted in the recycled paper deinking sector being chosen as the highest potential release source.

### 6.2.2 Aquatic Exposure from Recycled Paper Deinking Operations

Fifteen facilities were identified as sites that perform recycled paper deinking operations from three reference sources: MacDonald (2013), Lockwood-Post Directory (Dyer 2001 and Jones et al 2011) and FisherSolve (2012). Of these 15 facilities, sufficient

information was available for 6 facilities to permit aquatic exposure analyses, while there were insufficient data related to the remaining 9 facilities. Nevertheless, these six facilities were judged to be a good representation of the Canadian deinking operations sector.

The six recycled paper deinking facilities generate and treat their respective wastewater on site and subsequently discharge directly to receiving water. An aquatic PEC was estimated for each facility based on the quantity of the diarylide yellow pigments entering the facility, the emission factor to wastewater, the wastewater volume, the removal efficiency of the on-site wastewater treatment and the dilution of the receiving water. These PECs are considered conservative, since the total quantity of the diarylide yellow pigments used for paper printing is assumed to be 500 000 kg/year, and this quantity is higher than the quantity reported to the 2006 and 2010 section 71 surveys. At one of the sites, the highest PEC value of 28.5 µg/L was derived for the deinking sector. This highest PEC represents the greatest potential for exposure for the deinking sector, since the facility is estimated to receive the highest quantity of the diarylide yellow pigments while generating the lowest wastewater volume, both on a per tonne of pulp basis. This combination of having the highest quantity of the pigments and the lowest wastewater volume results in the highest concentration in receiving water, when all other parameters (emission factor to wastewater, removal efficiency of on-site wastewater treatment and receiving water dilution) used in PEC calculations, are assumed to be the same between facilities. For the other five facilities, lower PEC values (0.2–3.8 µg/L) were derived because they receive lower quantities of the diarylide yellow pigments and have higher wastewater dilution volumes.

More detailed calculations are provided and explained in Appendix D.

### 6.2.3 Sediment Exposure from Recycled Paper Deinking Operations

The European Chemicals Agency (ECHA 2010) suggests using the concentration of a substance in freshly deposited sediment to evaluate its risk to sediment-dwelling organisms. This approach implies that the concentration in suspended sediment instead of bottom sediment should be used in PEC and risk quotient calculations. This approach is used in estimating the concentration of the diarylide yellow pigments in sediment.

The concentration of the diarylide yellow pigments in suspended sediment or the sediment PEC is estimated based on equilibrium partitioning between the aqueous phase and suspended sediment. The method used for this estimate is discussed in detail by Gobas (2007, 2010). The resulting sediment PEC is estimated as 0.15 mg/kg—at the same site where the highest aquatic PEC of 28.5 µg/L was derived. This estimate is conservative, because not only the highest aquatic PEC is used, but also a conservative log ($S_{oct}/S_w$) value (representing octanol–water partition coefficient for pigments as described in the Physical and Chemical Properties section) is selected for the diarylide yellow pigments.

Detailed calculations are provided and explained in Appendix D of this report.

### 6.2.4 Soil Exposure from Recycled Paper Deinking Operations

The soil exposure to the diarylide yellow pigments is estimated under a conservative scenario. In this scenario, it is assumed that pigment-containing biosolids generated from the deinking sector are applied on agricultural lands at the maximum allowable rate of 4.4 t/ha (Crechem 2005) over a substantial number of years (i.e., 10 years). It is also assumed that the pigments are accumulated in soil and do not incur any degradation, volatilization, soil runoff or leaching losses. This conservative scenario yields a soil PEC of 6.8 mg/kg.

Detailed calculations are provided and explained in Appendix D of this report.

## 6.3 Characterization of Ecological Risk

The approach taken in this ecological screening assessment was to examine various supporting information and develop conclusions based on a weight of evidence approach, and using precaution as required under CEPA 1999. Lines of evidence considered include results from a conservative risk quotient analysis, as well as information on physical and chemical properties, environmental fate, ecotoxicity and sources of the diarylide yellow pigments.

### 6.3.1 Risk Quotient Analysis

As a line of evidence to support the ecological risk characterization of diarylide yellow pigments, risk quotients (RQ) were calculated for relevant exposure scenarios by dividing the PEC values with the corresponding PNEC values.

The following PNEC values (see Ecological Effects Assessment section of this report) were used for the calculation of risk quotients:

- aquatic PNEC = 180 µg/L;
- soil PNEC = 100 mg/kg soil (dry weight);
- sediment PNEC = 100 mg/kg sediment (dry weight).

The aquatic risk quotients from deinking vary from only 0.001 to 0.158. The highest risk quotient estimate was 0.158 (at the site where the highest aquatic PEC was derived), representing the worst-case aquatic exposure scenario. All seven facilities are estimated to have RQ values below (or well below) 0.1.

The sediment risk quotient is calculated by dividing the sediment PEC by the sediment PNEC of 100 mg/kg. A sediment RQ of 0.0015 was calculated.

The soil risk quotient is determined by dividing the soil PEC by the soil PNEC. A soil RQ of 0.07 was calculated.

Therefore, for the deinking operations scenario, all RQ values for diarylide yellow pigments in water, sediment and soil are well below one which suggests a very low risk.

Due to their lower releases, all other sectors or uses are not expected to cause ecological concern and were, therefore, not a subject to further analysis.

### 6.3.2 Consideration of Lines of Evidence and Conclusion

Diarylide yellow pigments are anthropogenically produced; they are not expected to occur naturally in the environment. According to recent surveys, four of the five pigments in this grouping have been found to be in Canadian commerce. No data concerning concentrations of these substances in the Canadian environment have been identified.

Diarylide yellow pigments do not exist as individual molecules; they are principally particles in the sub- or low micrometre size range, and the pigment powder is typically composed of primary particles (i.e., the crystal lattice of a pigment), aggregates and agglomerates. In terms of the distribution among environmental compartments, the physical and chemical properties and the particulate nature of these substances suggest that soil and sediments are expected to be the two major media where diarylide yellow pigments may be found in the environment.

Diarylide yellow pigments are expected to be persistent in the environment based on the available multiple experimental biodegradation data for the pigments from this group of substances as well as their analogues, using a category approach for pigments. High persistence of these substances is also supported by experimental physical and chemical properties of pigments (e.g., particulate nature of pigments, their high density, high chemical and hydraulic stability, and very low aqueous solubility). Indeed, pigments are expected to be durable, given their intended use as colorants in finished products. Physical-chemical properties, experimental degradation data and medium-to-medium half-life extrapolations indicate that under aerobic conditions, diarylide yellow pigments are expected to be persistent not only in water, but also in soil and sediments.

The bioavailability of diarylide yellow pigments is expected to be very low based on the particulate character of these substances, their very low solubility in both water and octanol, and the high molecular weight and large cross-sectional diameter of molecules of these substances. As a result, the potential to bioaccumulate in aquatic organisms is expected to be low, which is confirmed by the results of bioconcentration studies.

Due to the limited bioavailability of diarylide yellow pigments, no effects were found in chronic soil and sediment toxicity studies at the concentration of 1 000 mg/kg soil or sediment (dry weight). In terms of biological effects on aquatic organisms, these

pigments showed no effect at saturation (i.e., at water solubility limits) in acute and chronic aquatic ecotoxicity studies where solvents were not used. The results of these studies allowed the conclusion that diarylide yellow pigments are not expected to be inherently toxic to aquatic, soil-dwelling or sediment-dwelling organisms at low concentrations.

To evaluate potential exposures to diarylide yellow pigments in the environment, environmental concentrations were estimated (PECs) from available information on substance quantities, industrial use patterns, estimated release rates, characteristics of on-site or municipal treatment plants and characteristics of the receiving environment. The industrial release scenario chosen to evaluate the potential exposure to these substances relates to the major use of these pigments as “Ink, toner and colorants.”

Risk quotient analyses compare PEC with the appropriate predicted no-effect concentration (PNEC) values in order to evaluate potential risks. The PEC in water, soil and sediments for the group of diarylide yellow pigments were well below the respective PNEC for sensitive aquatic, soil-dwelling and sediment-dwelling organisms, resulting in risk quotients of much lower than 1.

Overall, the results of this assessment lead to the conclusion that the five diarylide yellow pigments have a low potential to cause ecological harm in Canada.

### 6.3.3 Uncertainties in the Evaluation of Ecological Risk

There were some uncertainties associated with the assessment of diarylide yellow pigments. For example, pigment concentrations associated with toxicity for aquatic organisms may have a source of uncertainty in the studies where these concentrations exceeded the water solubility limits of pigments, or when dispersants or solvents were used in aquatic toxicity tests. For instance, calculations based on a CBB approach indicated that diarylide yellow pigments are not expected to be acutely toxic to aquatic organisms; however, some experimental acute toxicity studies in which dispersants or solvents were used (to increase the solubility of diarylide yellow pigments) suggested otherwise, showing pronounced biological effects at moderate concentrations (e.g., ~20 mg/L). The apparent data discrepancy may be attributed to toxic effects caused by impurities (contained in the tested pigments) and different additives (contained in the pigment formulations), dispersant–pigment (or solvent–pigment) interactions or a mode of toxic action that is not predictable by the CBB approach. There might also be uncertainty in the aquatic toxicity studies even without solvents, because in all these studies with diarylide yellow pigments, only loading rates were reported, and no information on measured concentrations was provided.

In this risk assessment, there are two areas of uncertainty associated with the purity of diarylide yellow pigments. The first relates to the purity itself, because many substances (e.g., resins, rosins, different surfactants, dispersing agents, coupling agents) are used in pigment preparation, and it is impossible to remove such impurities by even intensive

washing and hot extraction procedures. As a result, certain amounts of these substances can most likely be found even in pigments of relatively high-quality grade. Another area of uncertainty is that instead of pure pigments, pigment formulations (i.e., final products) were tested. In both cases, impurities and additives may affect physical and chemical properties, persistence and biological effects of pigments.

Another area of uncertainty relates to the degradation of diarylide yellow pigments. Because of a lack of experimental data, there is uncertainty as to the rate and extent to which degradation of diarylide yellow pigments occurs in anaerobic environments and whether those degradation products (e.g., aromatic amines) could ever become biologically available. (It may be expected, however, that the unique physical state of diarylide yellow pigments [particles] along with their very low water solubility would limit the availability of the molecules for biotic reduction, so that the formation of degradation products will also be very limited.)

In terms of the bioavailability and bioaccumulation of pigments, there is also some uncertainty. Since many azo pigments have particle sizes in the low sub-micrometre range, a portion of the size distribution may fall partially in the “nanoparticle” domain. Some nanoparticles can be taken up by different types of cells and are able to cross the cell membrane and become internalized. Importantly, the interaction of nanoparticles with the cells and their uptake can occur via, for example, endocytosis or phagocytosis in specialized cells. (It should be noted, however, that no bioaccumulation studies with diarylide yellow pigments where these mechanisms could be reliably confirmed have been identified.)

Uncertainties are also associated with the lack of information on environmental concentrations of the diarylide yellow pigments in Canada. It is also recognized that releases from waste disposal sites are possible, although difficult to quantify due to the lack of data, and would contribute to overall environmental concentrations.

It is anticipated that the proportions of diarylide yellow pigments released to the various environmental media would not be significantly different from those estimated here, given the conservative assumptions used in the exposure analysis.

# 7. Potential to Cause Harm to Human Health

## 7.1 Exposure Assessment

### Environmental Media

Empirical data on concentrations of the five diarylide yellow pigments in environmental media in Canada or elsewhere were not identified. Due to the very low volatility and water solubility of diarylide yellow pigments, these substances are expected to be adsorbed onto soil and sediments when released to the environment and not partition into water. Therefore exposure for the general population to diarylide yellow pigments through drinking water is not expected. Due to the very low expected vapour pressures of these substances, inhalation of the volatile fraction via air is not expected to be a significant route of exposure (refer to Environmental Fate section). Thus, environmental media are not expected to be a significant source of exposure for these substances for the general population of Canada.

As summarized in the Uses section, three of the five diarylide yellow pigments were identified to be used in food packaging applications. Minimal potential for direct food contact is expected; therefore, food is not considered as a significant source of exposure to the diarylide yellow pigments evaluated in this assessment.

### Consumer Products

Four of the diarylide yellow pigments (PY12, PY13, PY83 and PY176) are known to be used as colourants in a variety of consumer products in Canada (Canada 2011b; Environment Canada 2012) which may lead to exposure for the general population during use of these products through the oral, inhalation, and dermal routes. A summary of estimates of oral and inhalation exposure to consumer products containing PY12, PY13, PY83 and PY176 is provided in Table 7-1. However, these estimates no not reflect the limited systemic exposure to diarylide yellow pigments expected due to very low absorption of these substances from the oral and inhalation routes (see Health Effects Assessment section for study details). Also, while topical exposures to the diarylide yellow pigments can occur from uses of these substances in consumer products and cosmetics, systemic exposure is not expected from the dermal route since dermal absorption of the predominantly insoluble diarylide yellow pigment particles is considered to be negligible. Therefore, dermal estimates of exposure were not derived.

Based on the use information obtained specific to the Canadian market, exposure estimates for oral ingestion of lipstick and finger paint, as well as mouthing of a painted toy car were derived (Table 7-1). PY83 was identified at a maximum concentration of 0.1% by weight in a lipstick (personal communication, email from the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced), resulting in a daily oral exposure estimate of $3.4 \times 10^{-4}$ mg/kg-bw per day for an adult (20–59 years of age).

As a conservative approach, oral exposure to these substances for younger age groups (0.5-4 years old) for finger painting was estimated. Available information indicates that it is foreseeable for PY12, PY13 and PY83 to be used in finger paints (Clariant 2010; BS 2002). Another source indicates pigments are generally found at concentration ranges of 1 – 3% by weight in finger paints (Delta Creative 2008). This range is consistent with the levels of monoazo pigments in finger paints (personal communication, email from Duke University Toxicology Program to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2013; unreferenced). A generic approach was taken to apply the information to the four diarylide yellow pigments (PY12, PY13, PY83 and PY176) and the range of oral exposures were estimated to be 0.87 - 2.6 mg/kg-bw per event for incidental ingestion during finger painting (refer to Appendix E for details).

**Table 7-1. Upper-bounding estimates of oral exposure and acute inhalation exposure to PY12, PY13, PY83 and PY176**

| Consumer product | Age range (years) | Pigment | Concentration range (% w/w) | Oral (daily) (mg/kg-bw per day) | Oral (per event) (mg/kg-bw per event) | Inhalation ($mg/m^3$) |
|---|---|---|---|---|---|---|
| Hair dyes (spray) | 5–11 | PY83 | 0.1–3[a] | N/A | N/A | $4.1 \times 10^{-6}$ – $1.2 \times 10^{-4}$ |
| Hair dyes (spray) | 5–11 | PY12 | 0.1–0.3[a] | N/A | N/A | $4.1 \times 10^{-6}$ – $1.2 \times 10^{-5}$ |
| Spray paint | 20–59 | PY12, Y13, PY83, PY176 | 3–60[b] | N/A | N/A | 0.008–0.15[c] |
| Lipstick | 20–59 | PY83 | 0.1[a] | $3.4 \times 10^{-4}$ | N/A | N/A |
| Finger paint | 0.5–4 | PY12, PY13, PY83, PY176 | 1–3[b] | | 0.87 - 2.6 | N/A |
| Hair spray | 20–59 | PY83 | 0.1 | $4.2 \times 10^{-4}$ | N/A | $6.1 \times 10^{-6}$ |

Abbreviation: N/A, not applicable

[a] Personal communication, email from the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced

[b] Delta Creative (2008); 2013 personal communication from Duke University Toxicology Program to Health Canada regarding concentrations of monoazo pigments in finger paints (unreferenced).

[c] An airless wall sprayer was considered relevant due to the generation of respirable paint aerosols. An airless wall sprayer is a typical product available for spray painting walls. However, the use of an airless wall sprayer by homeowners/consumers is not expected to be common.

Inhalation exposure to diarylide yellow pigments is expected via aerosol particles only, due to the very low vapour pressures of these substances (i.e., $< 10^{-11}$ to $10^{-9}$ Pa) (Baughman and Perenich 1988). PY83 and PY12 were identified in hair dyes at concentration ranges of 0.1–3% by weight and 0.1–0.3% by weight, respectively (personal communication, email from the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced). Exposure to PY83 and PY12 from the use of a temporary hair dye spray was considered due to the potential for application in aerosol form and the potential for use by younger age groups. Inhalation exposure estimates, expressed as mean concentration ranges on the day of exposure to these substances, were $4.1 \times 10^{-6}$ – $1.2 \times 10^{-4}$ $mg/m^3$ and $4.1 \times 10^{-6}$ – $1.2 \times 10^{-5}$ $mg/m^3$ for a child (5–11 years of age), for PY83 and PY12, respectively. PY83 was identified at a maximum concentration of 0.1%

by weight in a hair spray product (personal communication, email from the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced), which results in an inhalation exposure estimate expressed as a mean concentration on the day of exposure of $6.1\times10^{-6}$ mg/m$^3$ for an adult (20–59 years of age). In addition, an oral daily exposure to the non-respirable fraction for PY83 of $4.2\times10^{-4}$ mg/kg-bw per day was determined for adults (20–59 years of age). PY12, PY13, PY83 and PY176 are known to be used in paints at concentrations of 3–60% by weight (IARC 2010a). For this product category for inhalation exposure, an airless wall sprayer was considered relevant due to the generation of respirable paint aerosols. The inhalation mean event concentration range for PY12, PY13, PY83 and PY176 was estimated to be 0.008–0.15 mg/m$^3$ for an adult (20–59 years of age). The details of the inhalation exposure scenarios are summarized in Appendix E.

PY12 and PY83 were identified as being present in permanent tattoo inks in Canada (personal communication, email from the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced). Therefore, the exposure potential of diarylide yellow pigments from use in tattoos is considered.

Permanent tattoos are a potential source of exposure, as they are injected into the dermis, below the epidermal–dermal junction at a depth of 1–2 mm (Lea and Pawlowski 1987; Sperry 1992). Therefore, in contrast to dermal exposures to diarylide yellow pigments, where dermal absorption is expected to be negligible, intradermal injection of tattoo ink is considered to be a route of systemic exposure to these substances.

After injection of tattoo ink into the dermis, the fate of the pigment particles is expected to follow one of three paths (Danish EPA 2012). First, injected pigment may migrate upward through the individual needle tracts into the epidermis where it is sloughed off (epidermal removal)(Lea and Pawlowski 1987). Second, removal of the injected pigment can occur over the short-term (first few weeks after injection) by macrophages into the lymphatic system due to the dermal inflammatory response (Sperry 1992). Finally, the injected tattoo pigment which is retained in the dermis forms the stable tattoo by which the pigment is sequestered into secondary lysosomes after being engulfed by dermal fibroblasts and macrophages (Bäumler et al. 2000). The fractions of injected pigment making up the short-term removal and the stable tattoo are together considered potential sources of systemic exposure from a single tattoo.

For the fraction of the tattoo subject to lymphatic removal over the short-term, a short-term exposure estimate for the diarylide yellow pigments in tattoo inks was based mainly on the results of Engel et al. (2009), an *in vivo* study of mice that were injected with monoazo Pigment Red 22 into their dermis. The short-term daily systemic exposure was estimated to range from 0.12 mg/kg-bw per day - 1.1 mg/kg-bw per day for an adult (refer to Appendix G for details).

For the fraction of injected tattoo pigment forming the stable tattoo, the long-term *in vivo* fate of this injected material is largely unknown. While fading of tattoos over time is known to occur (Lehner et al. 2011), several mechanisms may be responsible including: ongoing phagocytosis and translocation via lymphatic system (Gopee et al. 2005, Jemec 2010), photodegradation of the pigment at the tattoo site (Doll et al. 2008, Kuramoto et al. 1996, Engel et al. 2007, 2009; Cui et al. 2004; Vasold et al. 2004; Bäumler et al. 2000, 2004; Hauri 2013), *in vivo* metabolism, and removal via venous drainage (Danish EPA 2012). The Danish EPA (2012) stated that regarding tattoo exposure, "the current knowledge is considered as being insufficient for a valid quantitative exposure assessment". Accordingly, an estimate of long-term systemic exposure from certain azo pigments in permanent tattoo inks has not been derived.

## 7.2 Health Effects Assessment

Reviews of the health effects data for diarylide yellow pigments have previously been published, including a draft OECD assessment(OECD 2003a, b), and a more recent Screening-Level Hazard Characterization by the US Environmental Protection Agency (US EPA 2010) and a Screening Assessment for the Challenge under Canada's CMP (Environment Canada and Health Canada 2011). The available studies on the critical health effects for the five substances, as well as analogues, are presented below. The interpretation of these studies by other organizations (e.g. OECD, US EPA) has also been taken into consideration. Overviews of other endpoints are briefly summarized based on descriptions from secondary sources (BIBRA 1991, 1996a, b; OECD 2003a, b; US EPA 2010).

A key consideration in the potential health effects of aromatic azo and benzidine-based substances in general is the potential generation of aromatic amine metabolites following reduction of the azo bond (Environment Canada and Health Canada 2013). While biological azo bond cleavage is generally considered an important metabolic reaction for more soluble aromatic azo and benzidine-based substances, it is not considered to apply to the same magnitude for poorly soluble azo pigments (Golka et al. 2004). However, given the high hazard potential of the benzidine derivative structural moiety found in diarylide yellow pigments (i.e. 3,3′-DCB), the potential for absorption, azo bond cleavage and metabolism of these substances was evaluated.

The information available in support of the negligible absorption, azo bond cleavage potential and low hazard for the diarylide yellow pigments are summarized in subsequent sections based on the following lines of evidence:

- negligible absorption of the parent diarylide yellow pigment and/or azo cleavage products as generated by the intestinal bacteria or by tissues *in vivo*;
- lack of evidence for adverse effects, including no evidence for carcinogenicity from repeated-dose studies primarily from the oral route;
- negative results in Prival-modified Ames assays and other standard *in vivo* and *in vitro* genotoxicity tests;

- low hazard potential from acute toxicity studies; and
- other information, including mechanistic data and low solubility in both water and octanol.

**Absorption Potential**

*In vivo* absorption and metabolism studies provide direct evidence to evaluate azo bond cleavage in the gastro-intestinal tract (GIT) or by mammalian tissues following absorption of aromatic azo and benzidine-based substances. There are several *in vivo* absorption and/or metabolism studies available for the diarylide yellow pigments, primarily for the oral route (Table 7-2), while single studies following each of inhalation (Table 7-3) and dermal exposure (Table 7-4) were also identified. Other studies by intra-tracheal instillation provide supporting data (Table 7-5). These data are summarized in the sections below.

The evidence of potential azo bond cleavage or absorption of diarylide yellow pigments was first reported by Akiyama (1970), where free 3,3′-DCB was detected in the urine samples of rabbits orally exposed to a single gavage dose of PY13 as "purified benzidine yellow" (recovered 3,3′-DCB approximately 0.05% of the 50 mg dose, equivalent to 0.025 mg) (Table 7-2). The small portion of free 3,3′-DCB recovered in the urine may have been due to azo bond cleavage and absorption of free 3,3′-DCB in the GIT. It could also be due to residual 3,3′-DCB in the dosage formulation, since the detection limit of free 3,3′-DCB in the "purified benzidine yellow" was not indicated. The observation in this study, however, was not supported by several subsequent follow-up oral studies by other authors on various species and diarylide yellow pigments, with higher tested doses, repeated exposures and more sensitive detection methods (Table 7-2). Thus, in light of these subsequent studies, the findings reported by Akiyama (1970) are uncertain and therefore considered equivocal. An inhalation study on PY17 looking at 3,3′-DCB and conjugates in urine and serum (Table 7-3) as well as a dermal study with [$^{14}$C]DCB-labelled PY12 (Table 7-4) also did not demonstrate evidence of azo bond cleavage or absorption of these substances, further supporting the overall evidence of limited bioavailability for the diarylide yellow pigments.

**Table 7-2. Oral metabolism/absorption of diarylide yellow pigments**

| Species | Substance tested | Tissue | Analyte | Exposure | Dose (mg/kg-bw per day) | Evidence[a] for absorption/ azo bond cleavage |
|---|---|---|---|---|---|---|
| rabbit[b] | PY13 | urine | DCB | single dose gavage | 20 | +/- |
| rat[c] | PY12, PY83 | urine | DCB | 6 & 23 month diet | 630 | - |
| rabbit[c] | PY13 | urine | DCB | single dose | 50 | - |

| Species | Substance tested | Tissue | Analyte | Exposure | Dose (mg/kg-bw per day) | Evidence[a] for absorption/ azo bond cleavage |
|---|---|---|---|---|---|---|
| | | | | gavage | | |
| rabbit[d], rat, monkey | PY13 | urine | DCB or conjugates | single dose gavage | 20-400 | - |
| hamster[e] | PY12 | urine | DCB or conjugates | single dose gavage | 100 | - |
| rat[f] | PY12 | blood, liver, urine | [$^{14}$C]DCB | single dose gavage | 1.1 | - |
| rat[g] | PY13, PY174 | liver | DCB-DNA adducts | single dose gavage | 400 | - |
| rat[g] | PY13, PY174 | urine | DCB or conjugates | single dose gavage | 400 | - |
| rat[h] | PY17 | blood | DCB- & mNAcDCB-Hb adducts | single dose gavage | 138 | - |
| rat[h] | PY17 | blood | DCB- & mNAcDCB-Hb adducts | 4wk diet | 100 | +/- |
| rat[i] | PY13, PY17 | blood | DCB- & mNAcDCB-Hb adducts | 4wk diet | 165-170 | +/- (PY13)<br>- (PY17) |
| rat[i] | PY13, PY17 | liver | DCB-DNA adducts | 4wk diet | 165-170 | +/- (PY13)<br>- (PY17) |

Abbreviations: DCB, 3,3′-dichlorobenzidine; DNA, deoxyribonucleic acid; dNAcDCB, di-N,N-acetyl-3,3′-dichlorobenzidine; Hb, hemoglobin; mNAcDCB, mono-N-acetyl-3,3′-dichlorobenzidine

[a] Evidence for absorption/azo cleavage: + (positive), +/− (equivocal), − (negative at limit of detection).

[b] Akiyama 1970

[c] Leuschner 1978

[d] Mondino et al. 1978

[e] Nony et al.1979; 1980

[f] Decad, et al. 1983

[g] Sagelsdorff et al. 1990

[h] Zwirner-Baier & Neuman 1994

[l] Sagelsdorff et al 1996

**Table 7-3. Inhalation metabolism/absorption of diarylide yellow pigments (Hofman and Schmidt 1993)**

| Species | Substance tested | Tissue | Analyte | Exposure | Dose (mg/kg-bw per day) | Evidence[a] for absorption/ azo bond cleavage |
|---|---|---|---|---|---|---|
| rat | PY17 | urine, serum | DCB or conjugates | 4hr | 230 ($mg/m^3$) | - |

Abbreviations: DCB, 3,3′-dichlorobenzidine

[a] Evidence for absorption/azo cleavage: − (negative at limit of detection).

**Table 7-4. Dermal metabolism/absorption of diarylide yellow pigments (Decad et al. 1983)**

| Species | Substance tested | Tissue | Analyte | Exposure | Dose (mg/kg-bw per day) | Evidence[a] for absorption/ azo bond cleavage |
|---|---|---|---|---|---|---|
| rat | PY12 | blood liver urine | [$^{14}$C]DCB | 24hr | dose not provided | - |

Abbreviations: DCB, 3,3′-dichlorobenzidine

[a] Evidence for absorption/azo cleavage: − (negative at limit of detection).

**Table 7-5. Intra-tracheal metabolism/absorption of diarylide yellow pigments**

| Species | Substance tested | Tissue | Analyte | Exposure | Dose (mg/kg-bw per day) | Evidence[a] for absorption/ azo bond cleavage |
|---|---|---|---|---|---|---|
| rat[b] | PY17, PY83 | blood | DCB-Hb adducts | 5 exposures over 4wk | 10-20 | +/- (PY83) - (PY17) |
| rat[b] | PY17, PY83 | urine | DCB | 5 exposures over 4wk | 10-20 | +/- (PY83) - (PY17) |
| rat[c] | PY17 | blood | DCB-Hb, mNAcDCB-Hb adducts | single exposure | 13.8-69 | +/- |

Abbreviations: DCB, 3,3′-dichlorobenzidine; Hb, hemoglobin; mNAcDCB, mono-N-acetyl-3,3′-dichlorobenzidine

[a] Evidence for absorption/azo cleavage: +/− (equivocal), − (negative at limit of detection).

[b] Bartsch et al. 2001

[c] Zwirner-Baier & Neuman 1994

However, two studies by Zwirner-Baier and Neumann (1994) and Sagelsdorff et al. (1996) did report detectable 3,3′-DCB adducts in hemoglobin and liver deoxyribonucleic acid (DNA) of rats exposed for 4 weeks in the diet to PY17 and PY13 respectively (Table 7-2). In both studies, levels of 3,3′-DCB adducts of hemoglobin (Hb) and liver

DNA were relatively low and slightly above the analytical method of detection. The tested pigments were both reported to have relatively low levels of free 3,3′-DCB (< 5 ppm for PY17, < 0.1 ppm for PY13), which suggests that 3,3′-DCB impurity was not the source of the adducts. While a low level of azo bond cleavage of the tested diarylide yellow pigments may have occurred, the presence of soluble 3,3′-DCB-containing impurities has been suggested as the potential source of the 3,3′-DCB adducts observed (OECD 2003a). A “readily soluble” “monoazo compound” was reported to be present at relatively high levels in PY13 (220 ppm) compared with a lower level in PY17 (21 ppm) in the study by Sagelsdorff et al. (1996) and was considered to be the explanation for the 3,3′-DCB adducts in Hb and liver produced by PY13 but not PY17 in this study (OECD 2003a). Similarly, the draft OECD assessment (OECD 2003a) reported a follow-up communication with the study authors of Zwirner-Baier and Neumann (1994), which indicated the presence of a “soluble extractable impurity” that was also present in the sample of PY17 tested and may possibly explain the Hb-adducts detected in that study. No more information was available on the nature and identity of these putative 3,3′-DCB-based impurities. Similar low levels of 3,3′-DCB in urine and Hb-adducts were reported in rats during repeated intratracheal instillations of PY83 but not PY17 over a 4-week period (Bartsch et al. 2001). However, since no 3,3′-DCB or Hb-adducts were detected in the 4-week recovery period, the study authors stated that “no unequivocal proof of the bioavailability” of PY83 could be concluded from this study.

Some evidence of limited uptake for the diarylide yellow pigments was reported, based on an inhalation study of PY13 and an intratracheal dosing study of PY17 and PY83, as well as two repeated-dose oral studies on PY12. Accumulation of pigment particles in lung-associated lymphatic tissue of rats was observed in an inhalation study of PY13 (Table 7-3) and following intratracheal instillation of PY17 and PY83 (Table 7-5). From the oral studies on PY12 (Table 7-2), observations of faint yellow discoloration of organs and internal mucosal surfaces were reported in all exposure groups of rats and mice in a chronic dietary study (NCI 1978), and some discoloration was observed in parents and pups in a reproductive/developmental toxicity screening study (Frieling 2001). It was suggested that impurities (e.g., monoazo substances) or contamination during necropsy may have been the reason for the observations in the oral studies (OEDC 2003a, b; US EPA 2010); however, another explanation may be low-level absorption of insoluble diarylide yellow pigment particles from the intestine. Low levels of uptake and systemic distribution to local lymph nodes and other distal tissues have been described for other insoluble microparticles and nanoparticles administered to the lungs and GIT (Oberdörster et al. 2005; Carr et al. 2012). Given the likelihood of some of the diarylide yellow pigments in these studies to have been in the sub-micrometre size range (see section on Particle Size Distribution and Density), it is reasonably expected that similar uptake of insoluble diarylide yellow pigment particles would occur for the oral and inhalation routes. Therefore, it is possible that small amounts of parent diarylide yellow pigments are absorbed systemically in the particle form following oral and inhalation exposure; however, the fraction of the total administered dose that could be absorbed in this way is expected to be low.

The potential for dermal absorption of diarlyide yellow pigments was investigated in rats using [$^{14}$C]-DCB-labelled PY12 (Decad et al. 1983). Briefly, three to six male F344 rats were exposed to the [$^{14}$C]-PY12 on the shaved dorsal area which was occluded with aluminum foil for up to one day. The [$^{14}$C]-PY12 was applied in a 1:1 solution of Emulphor EL 620/ethanol and distilled water to a 4x4 cm$^2$ area at a dose of radio-label of 2.57-2.95 µCi/rat (application volume and concentration of [$^{14}$C]-PY12 was not provided in the study). Blood collected at intervals from 10 minutes to 8 hours and liver homogenate and collected urine did not show radioactivity above background levels after 1 day of exposure. The applied dose of radioactivity was fully accounted from the skin application site, aluminum patch, and pipet tip. This data provide evidence of negligible systemic absorption of PY12 or its metabolites from the dermal route of application. Although the dermal study by Decad et al. (1983) has limitations (only 3–6 replicates, only PY12 tested), the evidence for negligible oral absorption outlined in Table 7-2 supports a similar expectation for the dermal route. In addition, the low water and octanol solubility of diarylide yellow pigments suggests that these substances would exist almost entirely as insoluble particles in dermal applications further limiting their potential dermal absorption, thus dermal absorption is expected to be negligible.

Overall, the *in vivo* metabolism and absorption studies on diarylide yellow pigments generally demonstrated negligible absorption and/or azo bond cleavage of the parent diarylide yellow pigments investigated. The presence of impurities (residual 3,3′-DCB and/or undefined soluble “monoazo impurity”) may also have been responsible for some of the results observed in these studies, while limited uptake of diarylide yellow pigments in particle form cannot be excluded.

**Repeated-dose Studies**

The available repeated-dose data are primarily oral studies on PY12 and PY83, with one short-term inhalation study on PY13. These studies are summarized in this section, with all dose conversions from dietary concentration to milligrams per kilogram of body weight per day (mg/kg-bw/day) using values by Health Canada (1994) unless otherwise noted.

In chronic dietary studies conducted by the US National Cancer Institute (NCI), there was no significant positive correlation between dosage and tumour incidence observed in Fischer 344 rats or B6C3F1 mice (n = 50/sex) administered concentrations of 0, 2.5 or 5% PY12 in the diet for 78 weeks (dose equivalents of 0, 1250 and 2500 mg/kg-bw per day in rats and 0, 3 250 and 6 500 mg/kg-bw per day in mice) followed by a 28-week observation period (NCI 1978). The precise purity of the test material was not indicated in the study report; however, the melting point range between 311°C and 320ºC “suggested the presence of impurities” (NCI 1978). The body weight changes for the control and exposed groups of rats of both sexes were generally equivalent throughout the dosing period. No statistically significant positive association between dose and mortality in rats was observed. Faint yellow discoloration of internal organ mucosa was observed at all dose levels in both rats and mice, indicating some possible

systemic absorption of either the parent PY12 or an impurity (refer to Absorption Potential section). No differences in non-cancer effects were generally observed between control and exposure groups in this study. However, exposure-related basophilic cytoplasm changes in hepatocytes of low and high dose groups of both sexes of rats were observed in this study and were noted by the NCI study authors as the “the only clinical sign or pathologic lesion observed” in the study (NCI 1978). While hepatocytes with basophilic cytoplasm are common in older F344 rats (Ward 1981), these changes were generally limited to the exposure groups in this study, and displayed dose-dependent increase in both sexes (females: control 2/48, low dose 42/49, high dose 40/48; males: control 0/50, low dose 5/49, high dose 11/47) and are therefore considered to be exposure related. While hepatocellular basophilic cell foci are generally regarded as a proliferative lesion in the liver (Goodman et al. 1994, Thoolen et al. 2010), the toxicological significance and adversity of these findings in the NCI study are uncertain based on the absence of other reported effects. Therefore, this effect from the NCI study is being treated as a lowest-observed-effect level (LOEL) (1 250 mg/kg-bw per day, lowest dose tested) rather than a lowest-observed-adverse-effect level (LOAEL). While the highest doses tested were considered by the US EPA (2010) and OECD (2003a) to be the no-observed-adverse-effect levels (NOAELs) for mice and rats in these studies, a discussion of the significance (or lack) of the basophilic hepatocellular changes in rats in the NCI study was absent from these assessments. An 8-week subchronic dose-finding study by NCI also showed no apparent changes in body weights, mortality, feed consumption or gross abnormalities in mice or rats (n = 5/sex/dose) at dietary concentrations up to 3% (dose conversion equivalents are 2 500 mg/kg-bw per day in rats and 3 900 mg/kg-bw per day in mice).

In a chronic oral study in which groups of 50 Sprague-Dawley rats or NMRI mice of each sex were administered PY83 (< 0.5 ppm 3.3′-DCB and < 20 ppm acetoacetanilide derivatives) or PY12 (< 20 ppm 3,3′-DCB, < 20 ppm acetoacetanilide derivatives and < 0.005% 2,5-dimethoxy-4-chloroaniline) in the diet at doses of 0, 68, 205 or 630 mg/kg-bw per day in rats and 0, 215, 650 or 1 960 mg/kg-bw per day in mice for 104 weeks. No evidence of a significant correlation between exposure and tumour incidence was found. Feed consumption and water consumption were within the normal range for the strains used, and data analyses showed no exposure-related statistically significant increase in mortality rate for either male or female rats and mice. The study authors reported that gross examinations of the surviving animals at week 104 showed no pathological conditions that were unusual or that could be related to the exposure. Subsequent histological examinations did not provide evidence for any cellular changes caused by the pigment exposures (Leuschner 1978). However it should be noted that unlike the full study report by the NCI (1978), limited pathology results were shown in the Leuchner study adding uncertainty when interpreting the study author’s conclusions.

Freiling (2001) reported no observed changes in reproductive parameters in rats exposed to PY12 at 0, 50, 200 or 1 000 mg/kg-bw/day via gavage for 4 weeks (males) or 6 to 7 weeks (females). The NOAEL for parental and reproductive toxicity was greater than 1 000 mg/kg-bw per day, based on no exposure-related effects on

mortality, body weight or feed consumption in female rats in the study. All females, including controls, showed diarrhea, feces discoloration was observed in all treated females, while no exposure-related organ weight changes or histopathological effects were observed in male and female parents (Frieling 2001). Some “staining” of parents and pups was reported for this study, but the significance of this finding is unknown (refer to Absorption Potential section).

In a 21-day inhalation study, groups of 10 male and 10 female RAI fSPF rats were exposed to dusts of PY13 (Ciba Geigy Corp. 1979). This study was designed to generate a high proportion of respirable particles (80% < 7 µm) at concentrations of 0, 54, 157 and 410 mg/m$^3$ for 6 hours per day, 5 days per week. In the treated rats from all concentration level groups, yellowish or yellow discoloration of the lungs was seen at autopsy. Slight increases in both absolute and relative weights of the lungs of both sexes were reported, which showed a statistically significant difference from the control group (trend from control to high dose P = 0.01, control versus high dose P = 0.05). Accumulation of brown and yellow particles in the macrophages in the interstitium, alveoli, bronchi and lymphatic tissues was reported for rats in all exposure groups and appeared to be dose dependent. At the high dose, these observations were also associated with pneumoconiosis, focal accumulation of foamy pneumocytes in the alveoli and focal lymphohistiocytic infiltration. These effects were still noted in the high-dose group following a recovery period. No systemic effects were reported at the highest concentration tested. The study authors concluded that the no-observed-effect concentration (NOEC) for this study was below the lowest tested concentration of 54 mg/m$^3$. The lowest concentration of 54 mg/m$^3$ was considered to be a lowest-observed-effect concentration (LOEC) for local effects in the lung in this study (OECD 2003a) and is expected to be primarily due to the inhaled pigment particle rather than a sign of chemical-specific toxicity of PY13 or its metabolites.

Several other oral studies also indicated no evidence of carcinogenicity and other non-cancer effects from repeated-dose studies; however, these results were reported only very briefly from secondary sources (ICI 1973; Colipa 1984; Anliker 1990) and are therefore not considered as critical studies for informing the hazard profile of diarylide yellow pigments in this assessment. However, a short-term 28 day gavage study in rats using the analogue diarylide pigment PO16 also demonstrated low oral toxicity (JECDB 2013). With repeated doses of up to 1 000mg/kg per day in rats (5-10/sex/dose, Crj:CD(SD)IGS strain), there were no exposure-related changes observed in survival, organ weights, urine, hematologic parameters, or histopathology findings. This study further supports the overall low oral toxicity of diarylide yellow pigments.

**Modified Ames Assay and Other Genotoxicity Data**

Positive results of an Ames assay under reductive conditions (i.e. incubation with intestinal contents or Prival modification) are also considered as a line of evidence for cleavage of azo bonding of the parent substance into one or more mutagenic metabolites (i.e. 3,3’-DCB). Previous Ames tests conducted on PY12 and PY83 under

reductive conditions were negative for both substances (Prival et al. 1984; Reid et al. 1984; Kauffmann 2002). Recent Ames tests using reductive S9 with and without the reducing agent flavin mononucleotide (FMN) on PY83 and PY176 at concentrations up to 6 000 µg/plate were all negative (ILS 2011a, b). In addition, analogue 3,3′-DMOB-based diarylide pigments BPAOPB (previously evaluated in the Challenge) and PO16 were also not mutagenic in modified Ames assays (BF Goodrich Co. 1992; ILS 2011a). Overall, the results from the mutagenicity testing under reductive conditions for diarylide yellow pigments were negative. Given that the potential azo bond cleavage product 3,3′-DCB,is genotoxic (NTP 1990; IARC 2010b), azo bond cleavage would be expected to lead to a positive result in these modified Ames assays. Therefore, negative results from modified Ames assays for the diarylide yellow pigments provide evidence that a negligible azo bond cleavage did not allow for generation of 3,3′-DCB in amounts sufficient to elicit a positive response in this assay.

The available data on other genotoxicity endpoints (other than Prival-modified Ames assay) for the diarylide yellow pigments were negative overall. In an *in vivo* study with PY13, groups of 3–6 female rats were administered PY13 (containing 0.02% soluble monoazo substance) in the diet for four weeks; liver DNA adducts or Hb adducts were either not detected or detected at levels only slightly above the detection limits. The low level of adducts was considered to result from a small amount of the azo bond cleavage metabolite, 3,3′-DCB, released from the contaminated soluble monoazo substance (Sagelsdorff et al. 1996). While some individual genotoxicity assays showed some positive or mixed results (Møller et al. 1998; NTP 2006a, b), the overall weight of evidence of *in vitro* genotoxicity studies, including Ames tests under standard conditions, chromosomal aberrations and sister chromatid exchange, was negative for these diarylide yellow pigments (refer to references in OECD 2003a). Ambiguous results were observed in a mouse lymphoma assay, in which a positive response was seen in one of three replicates with induced S9, but the positive result was not confirmed in the following two replicates; overall, the US National Toxicology Program considered this study to be negative (NTP 2006a, 2012 email from the US NTP to the Existing Substances Risk Assessment Bureau, Health Canada, unreferenced). The analogue 3,3'DMOB-based diarylide pigment PO16 was also shown to be negative in a standard Ames assay and test for chromosome aberrations *in vitro* (JECDB 2013).

**Other Health Effects**

Diarylide yellow pigments are of very low acute toxicity to mammals, with the acute oral median lethal dose ($LD_{50}$) greater than 1 750 mg/kg-bw and acute dermal $LD_{50}$ greater than 3 000 mg/kg-bw, while the acute inhalation $LC_{50}$ was reported to be 4 448 mg/m$^3$ (OECD 2003a; US EPA 2010). The substances may be slightly irritating to the skin and eyes (BIBRA 1996a, b; European Commission 2000a, b, c; OECD 2003a; US EPA 2010). There was no indication of sensitizing potential for PY12, PY13 and PY83 in guinea pigs and humans reported in several studies (Thierbach et al. 1992; BIBRA 1996a, b; OECD 2003a; US EPA 2010); however, sensitizing effects of PY12 were

observed in humans and guinea pig patch tests and have also been reported in a case study (Sugai et al. 1977; Lovell and Peachey 1981; European Commission 2000b).

**Other Supporting Data**

The limited azo bond cleavage of diarylide yellow pigments has been suggested by several authors to be primarily explained by the low solubility of these substances, which makes them generally unavailable for biological azo bond cleavage (reviewed in Golka et al. 2004). To investigate this hypothesis, Decad et al. (1983) showed that "somewhat solubilized" PY12 (by addition of a sulfonate group on the benzene ring of each of the acetoacetanilide coupling components) was not appreciably absorbed in rats exposed orally, with only 0.02% of the applied radiolabelled dose detected in the urine and the rest of the dose excreted in the feces, presumably as unchanged PY12. In the same study, another 3,3′-DCB-based disazo non-diarylide type pigment, chlorodiane blue[6] (CAS RN 41709-76-6), had also been similarly "solubilized" with a sulfonate group added to the naphthol AS coupling component. Whereas both sulfonated 3,3′-DCB-based colourants were soluble in distilled water, neither was soluble in physiological saline, and both precipitated in the stomach of dosed rats. However, sulfonated chlorodiane blue showed approximately 200 times greater absorption with radiolabelled 3,3′-DCB or metabolites detected 1 day after dosing in blood (0.2%), liver (1.4%) and urine (2.6%); approximately half the radiolabel detected in urine was 3,3′-DCB acetate and glucuronide conjugates, suggesting azo bond cleavage in the GIT to release [$^{14}$C]3,3′-DCB, which was subsequently absorbed and metabolized (Decad et al. 1983). The explanation for the significantly lower relative amount of azo bond cleavage observed for sulfonated PY12 than for sulfonated chlorodiane blue is unclear, although it is possible that sulfonated PY12 was still relatively less soluble (no additional information was provided in this study).

Further support for the inluence of solubility on azo bond cleavage comes from studies using chemical reduction with sodium dithionite conducted by ETAD (2008), which demonstrated that all tested diarylide yellow pigments (including PY12, PY13, PY17, PY83, PY176 and PO16) did not release any benzidine derivatives or other aromatic amines examined at levels greater than 30 ppm. However, in this report, there were two monoazo pigments and one disazo 3,3′-DCB-based pyrazolone pigment, which did release aromatic amines at levels above 30 ppm. The study authors acknowledged that "some azo pigments are sufficiently soluble under the analytical test conditions to yield

[6] Chlorodiane blue is based on 3,3′-DCB fragment disazo coupled to naphthol AS derivatives rather than acetoacetanilide and is therefore not a diarylide yellow pigment.

detectable amounts of a listed amine" (ETAD 2008). In a recent survey of tattoo inks in Denmark (Danish EPA 2012) containing diarylide yellow pigments as a product label ingredient, the levels of measured 3,3′-DCB, while measurable in some cases, were not dramatically different before or following chemical azo reduction, suggesting that a limited amount is released from these substances under the test conditions. However, a recent study reported some instances of 3,3'-DCB released at levels of 34 to 36 ppm following azo cleavage of a tattoo ink containing PY13 (Hauri 2013). This information demonstrates that even low-solubility azo pigments can potentially release aromatic amines by reduction of the azo bond, although the release may be quite limited (Platzek 2010). Based on this premise, and given the large range of solubility observed for different structural classes of aromatic azo and benzidine-based substances, including within the azo pigment subgroup, a broad range of azo bond cleavage potentials would be expected, with diarylide yellow pigments placed near the very low end of the range as per their relative lower solubility compared with other azo substances.

Other authors suggest a structural basis for the negligible azo bond cleavage of diarylide yellow pigments and aromatic azo and benzidine-based substances, with β-diketone coupling, due to azo-hydrazone tautomerism, playing a role (US EPA 1979; De France et al. 1986; Brown and DeVito 1993). De France et al. (1986) demonstrated that benzidine and several benzidine derivatives (3,3′-DCB, 3,3′-DMOB), which were disazo coupled to diethyl malonate (a β-diketone), were not azo reduced following *in vitro* incubation with hamster liver S9 and FMN, nor were they mutagenic in the Prival-modified Ames assay, indicating no release of the mutagenic benzidine derivatives. These synthesized hydrazone substances were not water soluble. However, unlike diarylide yellow pigments, they were readily soluble in organic solvents, including the dimethyl sulfoxide vehicle used in these studies, thereby excluding the possibility of the substances not being available in solution. Nuclear magnetic resonance spectroscopy of these synthesized diethyl malonate benzidine-based substances verified that only the hydrazone tautomer was observed, while the azo tautomer was not detected (De France et al. 1986). The diarylide yellow pigments are also predominantly in the hydrazone tautomeric form, due to similar hydrogen bonding with the acetoacetanilide coupling components (Barrow et al. 2000, 2002, 2003). De France and colleagues (1986) speculated that hydrazone tautomers stabilized by the acetoacetanilide coupling components may contribute to the resistance of diarylide yellow pigments to undergo azo bond cleavage. While structural features are known to impact the rate and degree of azo bond cleavage in aromatic azo and benzidine-based substances in general (Environment Canada and Health Canada 2013), their significance for the diarylide yellow pigments is currently unclear.

Other information on azo bond cleavage and metabolism of diarylide yellow pigments comes from the empirical data on bacterial degradation in the environment and overall suggests that the diarylide yellow pigments are not likely to be biodegraded or are biodegraded at a very slow rate (refer to Ecological Effects Assessment section).

## 7.3 Human Health Risk Characterization

The available information indicates that azo bond cleavage following exposure to diarylide yellow pigments is unlikely and does not identify a genotoxicity or carcinogenity concern for these substances. Overall, it is expected that the five diarylide yellow pigments in this assessment, PY12, PY13, PY83, PY176 and CPAOBP, will pose a low hazard potential from the dermal, inhalation and oral routes of exposure. The lowest effect level from oral studies is based on observations of basophilic cytoplasm observed in hepatocytes of male and female rats in a chronic dietary study using PY12 (LOEL of 1 250 mg/kg-bw/day, the lowest dose tested; NCI 1978). The toxicological significance of the hepatocellular basophilic cytoplasm is uncertain in the context of the absence of other effects observed in repeated-dose studies for these substances, and therefore this effect is not considered to be adverse. In terms of the potential hazard from inhalation exposure, increased lung weights and diarylide yellow pigment particle deposition in the lungs were observed in an inhalation study in rats exposed to PY13 dusts (LOEC of 54 $mg/m^3$, lowest concentration tested; Ciba Giegy Corp. 1979) for 21 days. It is uncertain whether the increased lung weights were simply due to pigment deposition or associated with the inflammatory immune responses observed at the highest concentration tested in this study (410 $mg/m^3$). Therefore, while the 54 $mg/m^3$ concentration is considered a LOEC rather than a lowest-observed-adverse-effect concentration (LOAEC) for this study, clear adverse inflammatory responses at higher doses do indicate a potential inhalation hazard for these substances at elevated levels of inhalation exposure. No repeated-dose dermal toxicity data were identified for these substances, however dermal absorption of insoluble diarylide yellow pigment particles is considered to be negligible, and therefore systemic exposure is not expected following dermal applications.

In terms of risk characterization for the oral route of exposure, as a conservative approach, the LOEL of 1 250 mg/kg-bw per day (lowest dose tested) for changes in hepatocytes (basophilic cytoplasm, NCI 1978) was compared to daily oral exposure estimates to lipstick ($3.4\times10^{-4}$ mg/kg-bw per day), resulting in margins of exposure of more than 3 million which is considered adequate to address uncertainties in the health effects and exposure databases. For other scenarios that could result in repeated, but intermittent exposure in early childhood (finger painting and mouthing a painted object), the levels of exposure combined with the low hazard nature of these substances indicates a low concern for human health.

For the risk from inhalation exposure scenarios, a LOEC of 54 $mg/m^3$ (lowest concentration tested) has been selected as the critical effect level based on increased lung weights and deposition of particles in pulmonary tissues reported in a short-term (21 day) inhalation study in rats (Ciba Geigy Corp. 1979). This is considered a conservative approach for risk characterization, as it is likely that the effect is due to the pigment particle rather than a chemical-specific toxicity of the diarylide yellow pigment and/or metabolites. Margins of exposure resulting from a comparison of this effect level with mean event exposure estimates for inhalation for three consumer product

scenarios are presented in Table 7-3. Due to the conservative nature of both the hazard and exposure estimates, as well as they fact that two of the exposure scenarios are more acute in nature rather than repeated (hair dye and wall sprayer), the margins of exposure, ranging from 360 to greater than 13 million, are considered adequate to address uncertainties in the health effects and exposure databases.

As systemic exposure is not expected from the dermal route due to negligible dermal absorption, the risk from dermal exposure to these substances would be low.

While an upper-bounding daily systemic exposure to tattoo pigments has been presented in this assessment based on the available information (0.12 to 1.1 mg/kg-bw per day, Appendix G), no specific health effects data were identified for the intradermal exposure route with which to derive the associated MOEs. As the general lack of observed effects for the diarylide pigments from oral studies are considered primarily due to the limited absorption from this route, a comparison of the short-term tattoo exposure estimate with the oral chronic effect level (i.e., LOEL of 1250 mg/kg-bw per day) is considered not appropriate for tattoo exposure since systemic exposure is expected to occur from the intradermal injection route.

**Table 7-6. Margins of exposure for inhalation exposure scenarios**

| Short-term inhalation effect level | Inhalation exposure estimates | MOE |
|---|---|---|
| LOEC of 54 mg/m$^3$ | $4.1 \times 10^{-}$ – $1.2 \times 10^{--}$ mg/m$^3$ (temporary hair dye spray) | $0.5 \times 10^6$ to $> 13 \times 10^6$ |
| LOEC of 54 mg/m$^3$ | $6.1 \times 10^{-}$ mg/m$^3$ (hair spray) | $> 8 \times 10^6$ |
| LOEC of 54 mg/m$^3$ | 0.008–0.15 mg/m$^3$ (airless wall sprayer) | 360 – 6 800 |

**Uncertainties with Human Health Risk Characterization**

Uncertainty is recognized as to whether the limited observed absorption and health effects in some studies were the result of impurities, such as residual 3,3′-DCB or unidentified “soluble monoazo” substances, or the intact parent diarylide yellow pigment in a discrete molecular form or as an insoluble pigment particle.

Exposure estimates presented in this Screening Assessment are based on conservative assumptions. There is uncertainty pertaining to the specific types of paint products that contain some of the diarylide yellow pigments presented in this report. As a result, conservative inputs were selected in deriving exposure estimates. The exposure estimate derived for finger paint is based on the range of reported weight fractions of pigments in paint (IARC 2010) not specific to diarylide yellow pigments in finger paint. Therefore uncertainty is recognized with the assumption that finger paints contain the same range of diarylide yellow pigments evaluated in this Screening Assessment. Although the exposure factors used in this assessment are comparable to those used

by US EPA (2008) and RIVM (2002), using a lower ingestion quantity was recommended in more recent publication elsewhere (RIVM 2008). Considering these factors, confidence is high that oral exposure estimated for younger population during use of finger paints is a conservative estimate.

With respect to various routes of exposure to the diarylide yellow pigments, the limited effects from oral studies observed are considered primarily due to the negligible absorption from this route. While there were no dermal metabolism data, an available dermal absorption study did not show any evidence of absorption of radio-labelled PY12. Uncertainty is recognized around the dermal route of exposure in the absence of dermal toxicity studies identified for these substances; however, low oral hazard potential provides confidence that the potential dermal hazard would also be very low given that absorption is considered negligible from both oral and dermal routes. In addition, while low solubility may largely explain the low biological activity of these substances in the studies identified, the contribution from other potential factors is not well understood.

Information on tattoo exposure is limited, and high uncertainty is recognized in the potential exposure from the particular diarylide yellow pigments used in tattoo inks. The Danish EPA (2012) stated that regarding tattoo exposure, “the current knowledge is considered as being insufficient for a valid quantitative exposure assessment”. Accordingly, an estimate of long-term systemic exposure from certain azo pigments in injected tattoo inks has not been derived.

# 8. Conclusion

Considering all available lines of evidence presented in this Screening Assessment, there is low risk of harm to organisms and the broader integrity of the environment from the five diarylide yellow pigments evaluated in this assessment. It is concluded that the five diarylide pigments do not meet the criteria under paragraphs 64(*a*) or 64(*b*) of CEPA 1999 as they are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

Based on the information presented in this Screening Assessment, it is concluded that the diarylide yellow pigments evaluated in this assessment do not meet the criteria under paragraph 64*(c)* of CEPA 1999, as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is concluded that the five diarylide yellow pigments evaluated in this assessment do not meet any of the criteria set out in section 64 of CEPA 1999.

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# Appendices

## Appendix A: Experimental Physical and Chemical Properties

**Table A-1: Experimental Physical and Chemical Properties (at Normal Temperature) of Diarylide Yellow Pigments**

| Chemical name | Property | Value | Reference |
|---|---|---|---|
| PY12 | Melting point (ºC) | 317 | Lide 2003 |
| PY12 | Melting point (ºC) | 320 | US EPA 2006 |
| PY12 | Melting point (ºC) | 320°C. Decomposition starts at ~200°C (i.e., measured melting point may not be true melting point, but rather the final decomposition temperature). | US EPA 2010 |
| PY12 | Melting point (ºC) | 306°C. Decomposition starts at 310°C. | ECHA 2012 |
| PY12 | Particle size distribution: $D_{50}$ (mass median diameter, µm) | 4.8 | ECHA 2012 |
| PY12 | Density (g/cm$^3$) | 1.39 | ECHA 2012 |
| PY12 | Water solubility (µg/L) | 0.4 | ECHA 2012; CPMA 2009, 2011 |
| PY12 | Water solubility (µg/L) | < 20 | OECD 2003b |
| PY12 | Solubility in *n*-octanol (µg/L) | 500. This value is significantly higher than the values from other studies (e.g., ECHA 2012). | Anliker and Moser 1987 |
| PY12 | Solubility in *n*-octanol (µg/L) | 49 | CPMA 2009, 2011 |
| PY12 | Log ($S_{oct}/S_w$) (dimensionless) | 2.1 (calculated from equilibrium concentrations in water and in octanol) | ECHA 2012; CPMA 2009, 2011 |
| PY13 | Melting point (ºC) | 350 | US EPA 2006 |
| PY13 | Melting point (ºC) | Decomposition starts at ~200°C | US EPA 2010 |
| PY13 | Melting point (ºC) | Decomposition starts at 330°C without discernible melting | ECHA 2012 |
| PY13 | Particle size distribution: $D_{50}$ (mass median diameter, µm) | 3 | ECHA 2012 |
| PY13 | Density (g/cm$^3$) | 1.36 | ECHA 2012 |
| PY13 | Water solubility (µg/L) | < 20 | Clariant 2003 |
| PY13 | Water solubility (µg/L) | 0.35 | ECHA 2012 |
| PY13 | Water solubility (µg/L) | 0.8 | CPMA 2009, 2011 |
| PY13 | Solubility in *n*-octanol (µg/L) | < 20 | Clariant 2003; OECD 2003b |
| PY13 | Solubility in *n*-octanol (µg/L) | 22 | CPMA 2009, 2011 |
| PY13 | Log ($S_{oct}/S_w$) (dimensionless) | 1.44 (calculated from equilibrium concentrations in water and in octanol) | CPMA 2009, 2011 |
| PY13 | Log ($S_{oct}/S_w$) (dimensionless) | 1.8 (calculated from equilibrium concentrations in water and in octanol) | ECHA 2012 |
| PY83 | Melting point (ºC) | 400 | US EPA 2006 |
| PY83 | Melting point (ºC) | 400°C. Decomposition starts at ~200°C | US EPA 2010 |

| Chemical name | Property | Value | Reference |
|---|---|---|---|
| | | (i.e., measured melting point may not be true melting point, but rather the final decomposition temperature). | |
| PY83 | Melting point (ºC) | Decomposition starts at 300°C without discernible melting | ECHA 2012 |
| PY83 | Particle size distribution: $D_{50}$ (mass median diameter, µm) | 2 | ECHA 2012 |
| PY83 | Density (g/cm$^3$) | 1.50 | ECHA 2012 |
| PY83 | Water solubility (µg/L) | < 20 | Clariant 2003; OECD 2003b |
| PY83 | Water solubility (µg/L) | 8.1 | ECHA 2012 |
| PY83 | Water solubility (µg/L) | 8900 µg/L. Note: In the US EPA Test Plan (US EPA 2006), this value is reported as 8.9 mg/L. However, in the screening-level hazard characterization (US EPA 2010), this value is not presented. Probably, it was a typo and was meant to be 8.9 µg/L instead of 8.9 mg/L. | US EPA 2006 |
| PY83 | Solubility in *n*-octanol (µg/L) | 20 | Clariant 2003 |
| PY83 | Solubility in *n*-octanol (µg/L) | 9.0 | CPMA 2011 |
| PY83 | Solubility in *n*-octanol (µg/L) | < 500 | Anliker and Moser 1987 |
| PY83 | Log ($S_{oct}/S_w$) (dimensionless) | 0.02 (calculated from equilibrium concentrations in water and in octanol) | ECHA 2012 |
| PY176 | Melting point (ºC) | Decomposition starts at 305°C without discernible melting | ECHA 2012 |
| PY176 | Particle size distribution: $D_{50}$ (mass median diameter, µm) | 4 | ECHA 2012 |
| PY176 | Water solubility (µg/L) | 2 | ECHA 2012 |
| PY176 | Density (g/cm$^3$) | 1.26 | ECHA 2012 |
| PY176 | Solubility in *n*-octanol (µg/L) | 41 | ECHA 2012 |
| PY176 | Log ($S_{oct}/S_w$) (dimensionless) | 1.3 (calculated from equilibrium concentrations in water and in octanol) | ECHA 2012 |
| PY14 (analogue) | Melting point (ºC) | 360°C. Decomposition begins at ~200°C (i.e., measured melting point may not be true melting point, but rather the final decomposition temperature). | US EPA 2006 |
| PY14 (analogue) | Melting point (ºC) | Decomposition starts at 308°C without discernible melting | ECHA 2012 |
| PY14 (analogue) | Particle size distribution: $D_{50}$ (mass median diameter, µm) | 3.5 | ECHA 2012 |
| PY14 (analogue) | Water solubility (µg/L) | 0.8 | ECHA 2012 |
| PY14 (analogue) | Solubility in *n*-octanol (µg/L) | 85 | Clariant 2003 |
| PY14 (analogue) | Solubility in *n*-octanol (µg/L) | 3.0 | CPMA 2011 |
| PY14 (analogue) | Solubility in *n*-octanol (µg/L) | 2.6 | ECHA 2012 |
| PY14 | Log ($S_{oct}/S_w$) (dimensionless) | 0.5 (calculated from equilibrium | ECHA 2012 |

| Chemical name | Property | Value | Reference |
|---|---|---|---|
| (analogue) | | concentrations in water and in octanol) | |
| PY17 (analogue) | Melting point (ºC) | 323ºC. Decomposition starts from the melting substance; the (exothermal) decomposition reaction shows an onset at 325°C (taken as decomposition temperature). | ECHA 2012 |
| PY17 (analogue) | Particle size distribution: $D_{50}$ (mass median diameter, µm) | 4.2 | ECHA 2012 |
| PY17 (analogue) | Water solubility (µg/L) | 2.6 | ECHA 2012 |
| PY17 (analogue) | Solubility in *n*-octanol (µg/L) | 6.8 | ECHA 2012 |
| PY17 (analogue) | Log ($S_{oct}/S_w$) (dimensionless) | 0.4 (calculated from equilibrium concentrations in water and in octanol) | ECHA 2012 |
| PY55 (analogue) | Melting point (ºC) | Decomposition starts at 339°C without discernible melting | ECHA 2012 |
| PY55 (analogue) | Particle size distribution: $D_{50}$ (mass median diameter, µm) | 8.5 | ECHA 2012 |
| PY55 (analogue) | Water solubility (µg/L) | 5.2 | ECHA 2012 |
| PY55 (analogue) | Solubility in *n*-octanol (µg/L) | 72 | ECHA 2012 |
| PY55 (analogue) | Log ($S_{oct}/S_w$) (dimensionless) | 1.1 (calculated from equilibrium concentrations in water and in octanol) | ECHA 2012 |
| PY152 (analogue) | Melting point (ºC) | 310°C with a decomposition temperature of 315°C | ECHA 2012 |
| PY152 (analogue) | Particle size distribution: $D_{50}$ (mass median diameter, µm) | 2.1 | ECHA 2012 |
| PY152 (analogue) | Water solubility (µg/L) | 10.6 | ECHA 2012 |
| PY152 (analogue) | Solubility in *n*-octanol (µg/L) | 140 | ECHA 2012 |
| PY152 (analogue) | Log ($S_{oct}/S_w$) (dimensionless) | 1.1 (calculated from equilibrium concentrations in water and in octanol) | ECHA 2012 |

# Appendix B: Experimental Data on Biodegradation

## Table B-1: Experimental Data on Biodegradation of Diarylide Yellow Pigments

| Chemical name | Biodegradation (%) | Test duration (days) | Details | Reference |
|---|---|---|---|---|
| PY12 | 0 | 14 | Ready biodegradation. | J-CHECK 2012 |
| PY12 | 81 | 15 | Inherent biodegradation. Multi-component final product (not pure pigment) was tested. | European Commission ©2000b |
| PY13 | Not readily biodegradable | 28 | Ready biodegradation. No quantitative results are available | US EPA 2010 |
| PY83 | 6 | 28 | Ready biodegradation. | J-CHECK 2012 |
| PY83 | 65 | 15 | Inherent biodegradation. 40% formulation (not a pure pigment) was tested. 20% of elimination of dissolved organic carbon occurred due to adsorption on activated sludge, not due to biodegradation. | European Commission ©2000a |
| PY83 | 83 | 15 | Inherent biodegradation. 52% formulation (i.e., not a pure pigment) was tested. 50% of elimination of dissolved organic carbon occurred due to adsorption on activated sludge, not due to biodegradation. | European Commission ©2000a |
| PY14 (analogue) | 2; 4 | 28 | Ready biodegradation. 2% biodegradation by BOD, 4% by weight. | J-CHECK 2012 |
| Group submission for diarylide yellow pigments[1] | 1 | 28 | Key study on ready biodegradability. It is impossible to reliably identify which diarylide pigments were tested. | ECHA 2012 |
| Group submission for diarylide yellow pigments[1] | 16 | 28 | Key study on ready biodegradability. Only 70% of the total carbon in the tested product is contained in the pigment. Assuming that the pigment component was stable, the observed BOD of 16% indicates that, besides carbon assimilation by the microorganisms, 53% of the additives were mineralized during the test. The HPLC analysis of the pigment and three possible degradation products indicated stability of the pigment during the test. | ECHA 2012 |

Abbreviations: BOD, biological oxygen demand; HPLC, high-performance liquid chromatography

[1] Submission for a group of diaryl yellow pigments from ECHA 2012 includes experimental data on pigments PY12, PY13, PY83, PY176, and PY14.

# Appendix C: Empirical Data for Aquatic Ecotoxicity

## Table C-1: Empirical Data for the Aquatic Ecotoxicity of Diarylide Yellow Pigments

| Chemical name | Test type | Organism | Endpoint, value | Details | Reference |
|---|---|---|---|---|---|
| PY12 | Acute (48 h) | Zebrafish (*Brachydanio rerio*) | $LC_{50}$ = 14.8 mg/L; $LC_{100}$ = 22 mg/L | ~55% and ~63% formulations; TWEEN 80 (polyethylene sorbitol ester) added | European Commission ©2000b |
| PY12 | Acute (48 h) | Zebrafish (*Brachydanio rerio*) | $LC_{50}$ = 5–10 mg/L; $LC_{100}$ = 22 mg/L | ~55% and ~63% formulations; TWEEN 80 (polyethylene sorbitol ester) added | European Commission ©2000b |
| PY12 | Acute (48 h) | Zebrafish (*Brachydanio rerio*) | $LC_{50}$ = 7.1 mg/L; $LC_{100}$ = 10 mg/L | ~55% and ~63% formulations; TWEEN 80 (polyethylene sorbitol ester) added | European Commission ©2000b |
| PY12 | Acute (48 h) | Zebrafish (*Brachydanio rerio*) | $LC_{50}$ = 10–22 mg/L; $LC_{100}$ = 22 mg/L | ~55% and ~63% formulations; TWEEN 80 (polyethylene sorbitol ester) added | European Commission ©2000b |
| PY12 | Acute (48 h) | Ide (*Leuciscus idus*) | $LC_{50}$ > 500 mg/L | 35% solution in water | European Commission ©2000b |
| PY12 | Acute (48 h) | Ide (*Leuciscus idus*) | $LC_{50}$ > 1000 mg/L | 35% solution in water | European Commission ©2000b |
| PY12 | Acute (96 h) | Ide (*Leuciscus idus*) | $LC_{50}$ = 10–100 mg/L | 81% formulation; acetone added | European Commission ©2000b |
| PY12 | Acute (96 h) | Ide (*Leuciscus idus*) | $LC_{50}$ > 500 mg/L | 35% solution in water | European Commission ©2000b |
| PY12 | Acute (72 h) | Water flea (*Daphnia magna*) | $EC_{50}$ > 100 mg/L | Effects: immobilization; substance purity: 98% | US EPA 2006 |
| PY12 | Acute (72 h) | Alga (*Selenastrum capricornutum*) | NOEC > 100 mg/L | | CPMA 2009 |
| PY12 | Acute | Medaka (*Oryzias latipes*) | $LC_{50}$ > 420 mg/L | | MITI 1992 |

| Chemical name | Test type | Organism | Endpoint, value | Details | Reference |
|---|---|---|---|---|---|
| | (48 h) | | | | |
| PY13 | Chronic (21 days) | Water flea (*Daphnia magna*) | NOEC = 1 mg/L | Effects: immobilization, reproduction; substance purity: 99.7% | US EPA 2006 |
| PY83 | Acute (96 h) | Zebrafish (*Brachydanio rerio*) | $LC_{50}$ > 100 mg/L | Substance purity: 94.5% | US EPA 2006 |
| PY83 | Acute (72 h) | Alga (*Selenastrum capricornutum*) | $EC_{50}$ = 190 mg/L | Substance purity: 94.5% | US EPA 2006 |
| PY83 | Acute (48 h) | Rainbow trout (*Salmo gairdneri*; new name *Oncorhynchus mykiss*) | $LC_{50}$ = 18 mg/L; $LC_{50}$ = 45 mg/L; $LC_{50}$ = 80 mg/L; $LC_{100}$ = 100 g/L; $LC_{100}$ = 200 mg/L | Aqueous ethylene glycol preparation (conc. of ethylene glycol not reported) | Hamburger et al. 1977 |
| PY83 | Acute (48 h) | Golden orfe (*Leuciscus idus*) | $LC_{50}$ = 45 mg/L; $LC_{50}$ = 70 mg/L; $LC_{50}$ = 75 mg/L; $LC_{100}$ = 100 mg/L | Aqueous ethylene glycol preparation (conc. of ethylene glycol not reported) | Hamburger et al. 1977 |
| PY83 | Acute (48 h) | Common minnow (*Phoxinus phoxinus*) | $LC_{50}$ = 45 mg/L; $LC_{100}$ = 100 mg/L | Aqueous ethylene glycol preparation (conc. of ethylene glycol not reported) | Hamburger et al. 1977 |
| Group submission for diarylide yellow pigments[1] | Acute (72 h) | Alga (*Desmodesmus subspicatus*) | NOEC = 100 mg/L | Effects: growth curve (biomass) and growth rate; filtered solution (visually clear) prepared at a loading of 100 mg/L of the substance | ECHA 2012 |
| Group submission for diarylide yellow pigments[1] | Acute (72 h) | Alga (*Selenastrum capricornutum*; new name *Pseudokirchneriella subcapitata*) | NOEC = 100 mg/L | Effects: growth inhibition, growth rate reduction; filtered solution (visually clear and colourless) was prepared at a loading of 100 mg/L of the substance | ECHA 2012 |
| Group submission for diarylide yellow pigments[1] | Acute (48 h) | Water flea (*Daphnia magna*) | NOEC = 100 mg/L | Effects: immobilization; a filtered solution was prepared at a loading of 100 mg/L of the substance | ECHA 2012 |

| Chemical name | Test type | Organism | Endpoint, value | Details | Reference |
|---|---|---|---|---|---|
| Group submission for diarylide yellow pigments[1] | Acute (24 h; 48 h) | Water flea (*Daphnia magna*) | $EC_{50}$ > 1000 mg/L | Effects: immobilization; the test item is 39.6% aqueous dispersion of the substance, so the results based on the content of the substance would be $EC_{50}$ > 396 mg/L | ECHA 2012 |
| Group submission for diarylide yellow pigments[1] | Chronic (21 days) | Water flea (*Daphnia magna*) | NOEC = 10 mg/L | Effects: reproduction, mortality, body weight, length, etc.; a solution (10 mg/L test item) was prepared with dilution water by shaking at 20 rpm for 48 h; undissolved particles were removed (10 min centrifugation at 10000 rpm) | ECHA 2012 |
| Group submission for diarylide yellow pigments[1] | Acute (96 h) | Rainbow trout (*Oncorhynchus mykiss*) | $LC_{50}$ = 124 mg/L | The test item contained 39.6% substance, so the effect concentration of 124 mg/L with regard to the substance is 49 mg/L; suspension of a nominal concentration far above the solubility limit had been prepared, and the study summary contains the statement that the results of the study are not reliable | ECHA 2012 |

Abbreviations: $EC_{50}$, effective concentration for 50% of test organisms; $LC_x$, lethal concentration for x% of test organisms; NOEC, no-observed-effect concentration; rpm, revolutions per minute

[1] Submission for a group of diaryl yellow pigments from ECHA 2012 includes experimental data on pigments PY12, PY13, PY83, PY176, and PY14.

# Appendix D: Exposures from Deinking Operations

## Aquatic Exposure Calculations for Deinking Operations

In total, 15 facilities were identified as performing recycled paper deinking operations from the Pulp and Paper Canada Directory (Macdonald 2013), the Lockwood-Post Directory (Dyer 2001; Jones2011) and FisherSolve (2012). Out of this total, six facilities are found to have sufficient information for aquatic exposure calculations. The six facilities are judged to be a good representation of the Canadian deinking sector.

The aquatic PEC is estimated for each of the six facilities. These facilities generate and treat their respective wastewater on site and subsequently discharge directly to receiving water. The aquatic PEC for each facility is estimated based on the quantity of the diarylide yellow pigments entering the facility, the emission factor to wastewater, the wastewater volume, the removal efficiency of the on-site wastewater treatment and the dilution of the receiving water.

The aquatic PEC values for the six facilities vary within 0.2-28.5 µg/L. These PECs are considered conservative, since the total quantity of the diarylide yellow pigments used for paper printing is assumed to be 500 000 kg/year, and this quantity is higher than the quantity reported to the 2006 and 2010 section 71 surveys.

A detailed explanation of the aquatic PEC calculations for the diarylide yellow pigments using the site in Alma, Quebec, as an example follows.

1. *Total quantity of diarylide yellow pigments*

   The total quantity of the diarylide yellow pigments imported to and manufactured in Canada is less than 500 000 kg/year for use as ink, toner and colorants based on the 2006 and 2010 section 71 surveys. This quantity is assumed to end up in paper products.

2. *Quantity of disposed paper*

   In Canada, in 2010, the paper recycling rate reached 69%, or 0.69 (Christine Burow Consulting 2011), which is 4 170 000 tonnes (2012 email from Christine Burow Consulting, unreferenced). These figures translate into 6 043 000 tonnes of waste paper products generated in 2010 in Canada:

   Quantity of waste paper generated: 4,170,000 tonnes/69% ≈ 6,043,000 tonnes

3. *Average pigment content*

The average content of the diarylide yellow pigments in printed paper products can therefore be estimated by dividing the total quantity of the pigments (500 000 kg/year) by the quantity of waste paper products (6 043 000 tonnes/year).

Average content of diarylide yellow pigments in paper: 500,000/6,043,000 t/yr = 0.0827 kg/t

*4. Annual pigment input*

This average content can be used to estimate the amount of the pigments entering a given deinking facility based on its deinking capacity. For example, the deinking capacity at Alma, Quebec, was 35 700 tonnes/year [see Lockwood-Post's Directory of Pulp & Paper Mills (Dyer 2001 and Jones et al 2011)]. The annual input of the pigments into the facility is then estimated as:

Annual input of diarylide yellow pigments: 0.0827 kg/tonne × 35 700 tonnes/year = 2952 kg/year

*5. Daily pigment input*

In general, deinking facilities operate 350 days/year on a continuous basis. On the basis of this operation, the daily input of the pigments into the facility in Alma, Quebec, can be estimated as:

Daily input of diarylide yellow pigments: 2,952 kg/yr/350 day/yr = 8.44 kg/day

*6. Emission factor to wastewater*

An experimental study by Körkkö et al. (2008) showed that the ink removal using a flotation process was in the range of 65–94%. Air flotation is commonly used for deinking in recycled paper mills. The waste paper tested in the study consisted of 50% newspapers and 50% magazines. The composition of this waste paper is assumed to be representative of the recycled paper processed by the Canadian deinking sector. The ink removal determined in the study refers to the fraction of the ink in feed that was collected in the flotation froth (reject). The reject is typically disposed of as a solid waste. Based on the range of 65–94% given in the study, an average ink removal rate is estimated as 80%. The reason for using an average is because varying deinking operations are used for different paper types across the deinking sector, and an average is judged to be statistically representative of these variations and differences. Since the remaining 20% remains in water and pulp, the maximum fraction entering wastewater would be 20%. This maximum is used as a conservative estimate for the emission factor to wastewater.

Therefore, the emission factor to wastewater: 20%

*7. Daily pigment release to raw wastewater*

The daily quantity of the diarylide yellow pigments emitted to raw wastewater at the facility in Alma, Quebec, is estimated based on the emission factor to wastewater (20%, or 0.2) and the daily input quantity into the facility (8.44 kg/day).

Daily emission of pigments to raw wastewater: 8.44 kg/day × 0.2 = 1.69 kg/day = $1.69 \times 10^9$ µg/day

*8. Water use rate*

To estimate the concentrations of the diarylide yellow pigments in raw and treated wastewater, the daily wastewater generation volume is required and can be estimated based on the per tonne water use rate, the per tonne water evaporation rate and the total pulp production.

The per tonne water use rate is derived from the water use volume and the total pulp production found in the Lockwood-Post Directory of the Pulp, Paper and Allied Trades (2002) book. For the same facility, which was then owned by Abitibi-Consolidated Inc. instead of the more recent company AbiBow Canada Inc., the daily water use volume was 7 570 000 L/day, and the total daily pulp capacity was 800 tonnes/day. The per tonne water use rate is then determined as:

Water use rate: 7,570,000 L/d/800 t/d = 9,643 L/t

This water use rate is in line with the range of 8000–16 000 L/tonne provided in the OECD emission scenario document on pulp and paper (OECD 2009a, p. 48) for deinking facilities.

*9. Water evaporation rate*

Water is lost to air via evaporation when pulp is dried via paper machines to produce paper. The per tonne water evaporation rate is relatively constant at 1500 L/tonne regardless of the type (deinked or virgin) of pulp (European Commission 2001). Therefore,

Water evaporation rate: 1500 L/tonne

*10. Wastewater generation rate*

The wastewater generation rate can then be determined as the difference between the per tonne water use rate and the per tonne water evaporation rate. For the facility in Alma, Quebec, this parameter is given as

Wastewater generation rate: 9463 L/tonne − 1500 L/tonne = 7963 L/tonne

*11. Total pulp production*

The total pulp production at a given facility includes all pulp types and can therefore be more than the production of deinked pulp only. These total production data can be found in Lockwood-Post Directory of Pulp & Paper Mills (Dyer 2001 and Jones et al 2011). For example, the total daily pulp production of the facility in Alma, Quebec, was 993 tonnes/day (total annual pulp capacity at 347 500 tonnes/year divided by a typical number of annual operation days at 350 days/year). This total capacity was much higher than the deinked pulp capacity at 102 tonnes/day.

Total pulp production: 993 tonnes/day

*12. Daily wastewater generation volume*

The daily wastewater generation volume is determined by multiplying the wastewater generation rate by the total pulp production. For the facility in Alma, Quebec, this parameter is, therefore, calculated as:

Daily wastewater generation volume: 7963 L/tonne × 993 tonnes/day = 7 907 259 L/day

*13. Pigment concentration in raw wastewater*

The concentration of the diarylide yellow pigments in raw wastewater is estimated by dividing the daily emission of pigments to wastewater by the daily wastewater generation volume. For the facility in Alma, Quebec, this concentration can be calculated as:

Concentration of pigments in raw wastewater: 1.69 kg/d x$10^9$ µg/kg/7,907,259 L/d = 214 µg/L

(where $10^9$ µg/kg is a conversion factor).

*14. Pigment concentration in treated wastewater*

Pigments with water solubility under 1 mg/L are expected to be removed by 90% (or 0.9) via primary sludge (OECD 2009, p. 58). Since all the diarylide yellow pigments have water solubility well below 1 mg/L and the wastewater generated from deinking facilities in Canada is subject to at least primary treatment, the reduction in the concentration of the diarylide yellow pigments would be even more than 90% through the wastewater treatment.

For the facility in Alma, Quebec, the maximum concentration of the diarylide yellow pigments in treated wastewater is estimated as:

Concentration of pigments in treated wastewater: 214 µg/L × (1−0.9) = 21.4 µg/L

*15. Pigment concentration in receiving water*

The receiving water for the facility in Alma, Quebec, is Petite-Decharge River, and its 10th percentile flow rate is 950 400 000 L/day. The full dilution capacity of the receiving water is estimated as the ratio of the 10th percentile flow to the daily wastewater volume, i.e.:

Receiving water full dilution capacity: 950,400,000 L/d/7,907,625 L/d = 120

In estimating the concentration of a chemical in receiving water, an appropriate dilution factor should be used to properly characterize the concentration near the discharge point. For the purpose of this risk assessment, 10-fold dilution is chosen to account for limited dilution near the discharge point when the full dilution capacity is over 10. For the facility in Alma, Quebec, the concentration of the diarylide yellow pigments in receiving water near the discharge point, or PEC, is therefore estimated as:

PEC of benzidine-based pigments: 21.4 µg/L/10 ≈ 2.1 µg/L

*16. Risk quotient (RQ)*

The aquatic risk quotient of the diarylide yellow pigments is then determined by dividing the PEC by the PNEC:

Aquatic RQ = PEC/PNEC = 2.1 µg/L/180 µg/L = 0.012

**Sediment Exposure Calculations for Deinking Operations**

The European Chemicals Agency (ECHA 2010, p. 64) suggests using the concentration of a substance in freshly deposited sediment to evaluate its risk to sediment-dwelling organisms. This suggested approach implies that the concentration in suspended sediment instead of bottom sediment should be used in exposure and risk quotient calculations. This approach is used below in estimating the concentration of the diarylide yellow pigments in sediment.

The concentration of the diarylide yellow pigments in suspended sediment or the sediment PEC is estimated based on equilibrium partitioning between the aqueous

phase and suspended sediment. At equilibrium partitioning, the sediment PEC can linearly correlate with the concentration in the aqueous phase as follows (Gobas 2007):

$$\text{Sediment PEC} = K_{sw} \times C_w$$

where $K_{sw}$ (L/kg) is the sediment–water partition coefficient and $C_w$ (mg/L) is the chemical concentration in the aqueous phase.

The aquatic PEC is normally higher than the chemical concentration in the aqueous phase ($C_w$) and can therefore be used as a conservative estimate for $C_w$. A conservative sediment PEC can then be estimated from the equation

$$\text{Sediment PEC} = K_{sw} \times PEC_{aquatic}$$

According to Gobas (2010), the sediment–water partition coefficient ($K_{sw}$, L/kg) can be estimated from the organic carbon (OC) fraction of suspended sediment ($F_{oc}$, kg OC/kg), the sorptive capacity of suspended sediment's organic carbon ($A_{oc}$, L/kg OC) and the octanol–water partition coefficient of the diarylide yellow pigments ($K_{ow}$, dimensionless):

$$K_{sw} = F_{oc} \times A_{oc} \times K_{ow}$$

Gobas (2010) suggested a value of 0.1 kg OC/kg for the OC fraction of suspended sediment (i.e., $F_{oc}$ = 0.1 kg OC/kg). Karickhoff (1981) proposed a value of 0.41 L/kg OC for the sorptive capacity of suspended sediment OC based on a set of 17 sediment and soil samples and various hydrophobic non-polar organic compounds. The log ($S_{oct}/S_w$) value, representing octanol–water partition coefficient for diarylide yellow pigments (as described in the Physical and Chemical Properties section), varies within 0.4–2.1 (see Table 5). The higher-end value of this range (log ($S_{oct}/S_w$) of 2.1, i.e., $S_{oct}/S_w$ of 126) is selected in order to derive a conservative sediment PEC. Based on these values, the sediment–water partition coefficient is estimated as:

$$K_{sw} = F_{oc} \times A_{oc} \times S_{oct}/S_w = 0.1 \text{ kg OC/kg} \times 0.41 \text{ L/kg OC} \times 126 = 5.2 \text{ L/kg}$$

As indicated in Ecological Exposure Assessment section, the highest aquatic PEC for the deinking sector is 28.5 µg/L. This value is used to derive the highest conservative sediment PEC:

$$\text{Sediment PEC} = K_{sw} \times PEC_{aquatic} = 5.2 \text{ L/kg} \times 28.5 \text{ µg/L} = 148 \text{ µg/kg} \approx 0.15 \text{ mg/kg}$$

The sediment risk quotient can therefore be calculated by dividing this PEC by the PNEC of 100 mg/kg:

$$\text{Sediment RQ} = \text{PEC/PNEC} = 0.15 \text{ mg/kg}/100 \text{ mg/kg} = 0.0015$$

**Soil Exposure Calculations for Deinking Operations**

The exposure to the diarylide yellow pigments in soil is estimated under a conservative scenario, i.e., assuming that the pigment-containing biosolids generated from the deinking sector are applied on agricultural land at the maximum allowable rate of 4.4 tonnes/ha (Crechem 2005) over a substantial number of years (i.e., 10 years), and also assuming that the pigments are accumulated in soil and do not incur any degradation, volatilization, soil runoff or leaching losses. This conservative scenario yields a soil PEC of 6.8 mg/kg and, therefore, a risk quotient of approximately 0.07 when compared with a PNEC of 100 mg/kg. Detailed calculations are presented below.

1. *Total annual quantity of diarylide yellow pigments*

   The total annual quantity of the diarylide yellow pigments imported to and manufactured in Canada is less than 500 000 kg/year for use as ink, toner and colorant based on the 2006 and 2010 section 71 surveys.

   Total annual quantity of diarylide yellow pigments: 500 000 kg/year

2. *Quantity of diarylide yellow pigments in recycled paper*

   According to the Pulp and Paper Products Council, in Canada, the paper recycling rate in 2010 was 69% (Christine Burow Consulting 2011). Based on this rate, the quantity of the diarylide yellow pigments in recycled paper can be estimated:

   Quantity of pigments in recycled paper: 500 000 kg/year × 0.69 = 345 000 kg/year

3. *Quantity of diarylide yellow pigments in biosolids*

   As a conservative estimate, it is assumed that the entire quantity of the diarylide yellow pigments in recycled paper ends up in biosolids.

   Quantity of diarylide yellow pigments in biosolids: 345 000 kg/year

4. *Fraction of deinked pulp in total pulp*

   The deinking sector processes two types of pulp: recycled pulp and virgin pulp. For these two types of pulp, the deinking and total pulp capacities of the seven deinking facilities evaluated for aquatic PECs (see Lockwood-Post Directory of Pulp and Paper Mills 2011) are found to be 1 081 300 tonnes/year and 2 357 100 tonnes/year,

respectively. The fraction of deinked pulp in total pulp for the Canadian deinking sector is thus estimated as:

Fraction of deinked pulp in total pulp: 1,081,300 t/yr/2,357,100 t/yr = 0.45 (or 45%)

*5. Paper production from deinking sector*

In 2010, the paper recycling rate in Canada reached 4 170 000 tonnes (2012 email from Christine Burow Consulting, unreferenced). Since this rate represents 45% of the total paper produced from the deinking sector, the latter can therefore be estimated as:

Total paper production: 4,170,000 t/yr/45% = 9,267,000 t/yr

*6. Sludge or biosolids quantity*

The sludge can be generated from various sources, such as on-site wastewater treatment and deinking operations. As a default value for assessment purposes, the sludge generation rate is 10% (or 0.1) of the paper production (OECD 2009, p. 63). The total annual quantity of sludge from deinking is then estimated as:

Total annual quantity of sludge: 9 267 000 tonnes/year × 0.1 = 926 700 tonnes/year

This sludge quantity is assumed to be equal to the biosolids quantity, i.e.:

Total annual quantity of biosolids = 926 700 tonnes/year

*7. Concentration of diarylide yellow pigments in biosolids*

The concentration of the diarylide yellow pigments in biosolids is estimated by dividing the quantity of the pigments in biosolids by the total biosolids quantity:

Concentration of pigments in biosolids: 345,000 kg/yr/926,700 t/yr = 0.37 kg/t = 370 mg/kg

*8. Land application rate*

In Canada, the land application rate of biosolids from publicly-owned wastewater systems is regulated by the provinces and territories. The allowable annual limits on a dry weight basis are 1.6 tonnes/ha in Ontario, 3.4 tonnes/ha in British Columbia and 4.4 tonnes/ha in Quebec (Crechem 2005). Considering that deinking mills are mainly located in Ontario and Quebec, and assuming that these application rates are applicable to biosolids generated from deinking activities, Quebec's annual

application rate of 4.4 tonnes/ha would be an appropriate conservative rate for use in the soil exposure assessment. Since 1 ha = 10 000 $m^2$ and 1 tonne = 1000 kg, the annual land application rate is:

Annual land application rate = 4.4 tonnes/ha = 0.44 kg/$m^2$

*9. Quantity of diarylide yellow pigments upon 10 years of biosolids application*

The European Chemicals Agency (ECHA 2010, p. 73) suggests using 10 consecutive years as a length of accumulation in evaluating soil exposure resulting from biosolids application. The quantity of the diarylide yellow pigments received per square metre of the amended soil during this 10-year period would be:

Quantity of pigments per square metre of soil = biosolids application rate × 10 years × concentration of pigments in biosolids = 0.44 kg/$m^2$ per year × 10 years × 370 mg/kg = 1628 mg/$m^2$

*10. Mass of ploughing-layer soil per square metre*

The European Chemicals Agency (ECHA 2010, p. 75) also suggests using 20 cm (i.e., 0.2 m) as the ploughing depth in determining a mixing layer. Using a dry soil density of 1200 kg/$m^3$ (Williams 1999), the mass of the top 20 cm soil layer per square metre is:

Mass of ploughing layer per square metre = 1200 kg/$m^3$ × 1 $m^2$ × 0.2 m = 240 kg

*11. Soil PEC*

The soil PEC is determined by dividing the quantity of the pigments upon 10-year land application by the mass of ploughing-layer soil per square metre:

Soil PEC = 1,628 mg/$m^2$/240 kg/$m^2$ = 6.8 mg/kg

*12. Risk quotient*

The risk quotient is determined by dividing the PEC by the PNEC:

Soil RQ = PEC/PNEC = 6.8 mg/kg/ 100 mg/kg = 0.07

## Appendix E: Upper-Bounding Estimates of Oral Exposure

**Table E-1: Upper-bounding estimates of oral exposure from ingestion of lipstick (adult)**

| | |
|---|---|
| **Substance** | PY83 (CAS RN 5567-15-7) |
| **Assumptions/ algorithm** | **(EF)** Exposure frequency: 2.4/day (Loretz et al. 2005)<br><br>**(PA)** Product amount: 0.01 g/application (Loretz et al. 2005)<br><br>**(BW)** Adult body weight (20–59 years): 70.9 kg-bw (Health Canada 1998)<br><br>**(WF)** Maximum weight fraction of PY83: 0.001 (personal communication, email from the Consumer Products Safety Directorate [Health Canada] to the Existing Substances Risk Assessment Bureau [Health Canada], dated 2011; unreferenced)<br><br>Exposure estimate (per event)<br><br>= [(PA) × (WF)] ÷ [BW]<br><br>= [0.01 g × 0.001] ÷ [70.9 kg-bw]<br><br>= 0.14 µg/kg-bw per event<br><br>Amortized exposure estimate (daily)<br><br>= [External exposure estimate (per event)] × [EF]<br><br>= (0.14 µg/kg-bw) × (2.4/day)<br><br>= 0.34 µg/kg-bw per day |
| **Exposure estimate** | **Oral exposure estimate (daily): 0.34 µg/kg-bw per day** |

**Table E-2: Upper-bounding estimates of oral exposure from ingestion of finger paint (toddler)**

| | |
|---|---|
| **Substances** | PY12 (CAS RN 6358-85-6); PY13 (CAS RN 5102-83-0); PY83 (CAS RN 5567-15-7); PY176 (CAS RN 90268-24-7) |

| | |
|---|---|
| **Assumptions/ algorithm** | **(ED)** Exposure duration: 45 min (Bremmer and van Veen 2002)<br><br>**(IR)** Ingestion rate: 30 mg/min (Bremmer and van Veen 2002)<br><br>**(WF)** Weight fraction of pigment: 0.01–0.03 (Delta Creative 2008)<br><br>**(BW)** Toddler body weight (0.5–4 years): 15.5 kg-bw (Health Canada 1998)<br><br>**(EF)** Exposure frequency: 0.27/day (i.e., 100/year; Bremmer and van Veen 2002)<br><br>Exposure estimate (per event)<br><br>= [(ED) × (IR) × (WF)] ÷ [BW]<br><br>= [(45 min) × (30 mg/min) × (0.01–0.03)] ÷ [15.5 kg-bw]<br><br>= 0.87 - 2.6 mg/kg-bw per event<br><br>Amortized exposure estimate (daily)<br><br>= [External exposure estimate (per event)] × [EF]<br><br>= [0.87 - 2.6 mg/kg-bw] × (0.27/day)<br><br>= 0.24 - 0.7 mg/kg-bw per day |

## Appendix F: Upper-Bounding Estimates of Inhalation Exposure

**Table F-1: Upper-bounding estimates of inhalation exposure from temporary hair dye spray (children)**

| | |
|---|---|
| **Substances** | PY12 (CAS RN 6358-85-6); PY83 (CAS RN 5567-15-7) |
| **Assumptions/ algorithm** | **Child body weight** (5–11 years): 31 kg-bw (Health Canada 1998)<br>**Exposure frequency**: 0.016/day (i.e., 6/year; Bremmer et al. 2006)<br>**Weight fraction of PY12**: 0.001–0.003 (CNS 2011)<br>**Weight fraction of PY83**: 0.001–0.03 (CNS 2011)<br><br>**Child inhalation rate** (5–11 years): 14.5 $m^3$/day (Health Canada 1998)<br>Temporary hair dye sprays may be particularly relevant to special occasions such as sporting events, carnivals and children's parties (Bremmer et al. 2006). As children may be exposed to such temporary hair dye sprays, a child body weight was assumed for this exposure scenario.<br><br>ConsExpo v4.1, a consumer product exposure model developed by the National Institute for Public Health and the Environment (RIVM) in the Netherlands, was used to determine the inhalation and oral (non-respirable) estimates of exposure to PY12 and PY83 in temporary hair dye spray (ConsExpo 2006).<br><br>***ConsExpo v4.1: "Exposure, spray model, spraying towards exposed person"***<br>Spray duration: 0.24 min (Bremmer et al. 2006)<br>Exposure duration: 5 min (Bremmer et al. 2006)<br>Room volume: 10 $m^3$ (Bremmer et al. 2006)<br>Room height: 2.5 m (Bremmer et al. 2006)<br>Ventilation rate: 2/h (Bremmer et al. 2006)<br>Cloud volume: 0.0625 $m^3$ (Bremmer et al. 2006)<br>Mean mass generation rate: 0.4 g/s (RIVM 2010)<br>Airborne fraction: 1 g/g (Bremmer et al. 2006)<br>Weight fraction non-volatile: 0.03 g/g (Bremmer et al. 2006)<br>Density non-volatile: 1.5 $g/cm^3$ (Bremmer et al. 2006)<br>Initial particle distribution median diameter (C.V.): 35 µm (Bremmer et al. 2006)<br>Inhalation cut-off diameter: 15 µm (Bremmer et al. 2006)<br><br>**Inhalation exposure estimates for PY12:**<br>Inhalation mean event concentration: $1.18 \times 10^{-3}$ to $3.53 \times 10^{-3}$ $mg/m^3$ |

| | |
|---|---|
| | Inhalation mean concentration on day of exposure: $4.08 \times 10^{-6}$ to $1.22 \times 10^{-5}$ mg/m$^3$<br><br>**Oral exposure estimate (non-respirable fraction) for PY12:**<br>Oral acute external dose: $5.78 \times 10^{-4}$ to $1.74 \times 10^{-3}$ mg/kg-bw<br><br>**Inhalation exposure estimates for PY83:**<br>Inhalation mean event concentration: $1.18 \times 10^{-3}$ to 0.0353 mg/m$^3$<br>Inhalation mean concentration on day of exposure: $4.08 \times 10^{-6}$ to $1.22 \times 10^{-4}$ mg/m$^3$<br><br>**Oral exposure estimate (non-respirable fraction) for PY83:**<br>Oral acute external dose: $5.78 \times 10^{-4}$ to 0.0173 mg/kg-bw |
| **Exposure estimates** | **Inhalation mean concentration of PY12 on day of exposure: $4.08 \times 10^{-6}$ to $1.22 \times 10^{-5}$ mg/m$^3$**<br><br>**Inhalation mean concentration of PY83 on day of exposure: $4.08 \times 10^{-6}$ to $1.22 \times 10^{-4}$ mg/m$^3$** |

**Table F-2: Upper-bounding estimates of inhalation exposure from hair spray (adult)**

| | |
|---|---|
| **Substance** | PY83 (CAS RN 5567-15-7) |
| **Assumptions/ algorithm** | **Adult body weight** (20–59 years): 70.9 kg-bw (Health Canada 1998)<br>**Exposure frequency**: 1.49/day (Loretz et al. 2006)<br>**Maximum weight fraction of PY83**: 0.001 (CNS 2011)<br>**Adult inhalation rate** (20–59 years): 16.2 m$^3$/day (Health Canada 1998)<br><br>ConsExpo v4.1, a consumer product exposure model developed by RIVM in the Netherlands, was used to determine the inhalation and oral (non-respirable) estimates of exposure to PY83 in hair spray (ConsExpo 2006).<br><br>***ConsExpo v4.1: "Exposure, spray model, spraying towards exposed person"***<br><br>Spray duration: 0.24 min (Bremmer et al. 2006)<br>Exposure duration: 5 min (Bremmer et al. 2006)<br>Room volume: 10 m$^3$ (Bremmer et al. 2006)<br>Room height: 2.5 m (Bremmer et al. 2006)<br>Ventilation rate: 2/h (Bremmer et al. 2006)<br>Cloud volume: 0.0625 m$^3$ (Bremmer et al. 2006)<br>Mean mass generation rate: 0.4 g/s (RIVM 2010)<br>Airborne fraction: 1 g/g (Bremmer et al. 2006) |

| | |
|---|---|
| | Weight fraction non-volatile: 0.03 g/g (Bremmer et al. 2006)<br>Density non-volatile: 1.5 g/cm$^3$ (Bremmer et al. 2006)<br>Initial particle distribution median diameter (C.V.): 35 µm (Bremmer et al. 2006)<br>Inhalation cut-off diameter: 15 µm (Bremmer et al. 2006)<br><br>**Inhalation exposure estimates for PY83:**<br>Inhalation mean event concentration: 1.18 × 10$^{-3}$ mg/m$^3$<br>Inhalation mean concentration on day of exposure: 6.08 × 10$^{-6}$ mg/m$^3$<br>Inhalation air concentration year average: 6.08 × 10$^{-6}$ mg/m$^3$ per day<br><br>**Oral exposure estimates (non-respirable fraction) for PY83:**<br>Oral acute dose: 2.82 × 10$^{-4}$ mg/kg-bw<br>Oral daily dose: 4.21 × 10$^{-4}$ mg/kg-bw per day |
| **Exposure estimates** | **Inhalation air concentration year average exposure: 6.08 × 10$^{-6}$ mg/m$^3$ per day**<br><br>**Oral chronic dose: 4.21 × 10$^{-4}$ mg/kg-bw per day** |

**Table F-3: Upper-bounding estimates of inhalation exposure from painting walls using an airless sprayer (adult)**

| | |
|---|---|
| **Substances** | PY12 (CAS RN 6358-85-6); PY13 (CAS RN 5102-83-0); PY83 (CAS RN 5567-15-7); PY176 (CAS RN 90268-24-7) |
| **Assumptions/ algorithm** | **(BW)** Adult body weight (20–59 years): 70.9 kg-bw (Health Canada 1998)<br>**(EF)** Exposure frequency: 0.0027/day (i.e., 1/year; Prud'homme de Lodder et al. 2006)<br>**(BZC)** Breathing zone concentration of respirable paint aerosols: 5.14 mg/m$^3$ (Reinhardt and Fendick 2004)<br>**(WF)** Weight fraction of pigment: 0.03–0.6 (IARC 2010a)<br>**(FPR)** Fraction of pigment remaining after use of particle filter: 0.05<br><br>Individuals applying paint through an airless sprayer were assumed to use a respirator with particle filter, removing 95% of respirable paint aerosol (PMRA 2000; 3M OHSD 2012). The use of appropriate respiratory protection is recommended for any spray application of paint.<br><br>Please note that the "inhalation mean event concentration" estimated below is the air concentration of pigment in inspired air, after 95% removal of respirable paint aerosol.<br><br>Inhalation mean event concentration<br>= [(BZC) × (WF) × (FPR)]<br>= [(5.14 mg/m$^3$) × (0.03–0.6) × (0.05)] |

| | |
|---|---|
| | = 0.008–0.15 mg/m$^3$ |
| **Exposure estimate** | **Inhalation mean event concentration: 0.008–0.15 mg/m$^3$** |

## Appendix G: Upper-Bounding Estimate of Short-Term Exposure from Tattoo Ink

**Table G-1: Upper-bounding estimate of short-term exposure from intra-dermal injection of tattoo ink**

| **Substances** | PY12 (CAS RN 6358-85-6); PY83 (CAS RN 5567-15-7) |
|---|---|
| **Assumptions/ algorithm** | Exposure factors were derived based on a study that examined the loss of a monoazo tattoo pigment from mouse skin *in vivo* due to biological dissemination and photochemical decomposition (Engel et al. 2009). While this study was specifically on Pigment Red 22 (PR22), a generic approach is taken as a conservative approach to estimate short-term exposure to any pigments including PY12 and PY83 in this assessment.<br><br>***Exposure scenario***<br>• Route of exposure: Injection into the dermis<br>• Average skin concentration: 2.53 mg pigment/cm$^2$ *ex vivo* human or pig skin (Engel et al. 2008; Danish EPA 2012)[1]<br>• Realistic worst-case skin concentration: 9.42 mg pigment/cm$^2$ (Danish EPA 2012)<br>• Skin area covered for average tattoo: 430 cm$^2$ (Danish EPA 2012)<br>• Skin area covered for realistic worst-case tattoo (i.e., whole back): 1090 cm$^2$ (Danish EPA 2012)<br>• **(AV)** Amount of azo pigment in average tattoo potentially available for absorption: 1.09 g (Danish EPA 2012)<br>• **(AW)** Amount of azo pigment in realistic worst-case tattoo potentially available for absorption: 10.3 g (Danish EPA 2012)<br>• **(BW)** Adult body weight: 70.9 kg-bw (Health Canada 1998)<br>• **(FP)** Fraction of intact pigment in dermis that is mobilized into the lymphatic system: 32% over 42 days (Engel et al. 2009) [1]<br><br>**Exposure to pigment**<br>= [(AV–AW) × (FP)] ÷ [(BW) × (Length of study)]<br>= [(1.09–10.3 g) × (0.32)] ÷ [(70.9 kg-bw) × (42 days)]<br>= 0.12–1.1 mg/kg-bw per day<br><br>Therefore, the short-term systemic daily exposure to PY12 and PY83 in tattooed individuals is assumed to be 0.12 mg/kg-bw per day on average and 1.1 mg/kg-bw per day as an upper-bounding estimate.<br><br>[1] In Engel et al. (2009), 19 hairless female SKH-1 mice, divided into four groups, were tattooed on their dorsa with PR22. Exposure to |

| | |
|---|---|
| | normal ambient light for 32 days after 10 days of recovery following the initial injection (total of 42 days) resulted in a 32% reduction of PR22 in skin. The loss percentage was considered predominantly attributable to biological dissemination of the tattoo pigment into the lymphatic system. A separate group of mice exposed to simulated solar radiation instead of normal ambient light resulted in a 60% reduction in the initial skin pigment concentration. The fraction of photodecomposed Pigment Red 22 that resulted in the formation of aromatic amines is unknown for simulated solar radiation. Therefore, this exposure scenario focuses on systemic exposures of the intact pigment only. |
| **Exposure estimate** | **0.12–1.1 mg/kg-bw per day** |