

## Screening Assessment for the Challenge

### Chemical Abstracts Service Registry Number

**6407-74-5**

3H-Pyrazol-3-one, 4-[(2-chlorophenyl)azo]-2,4-dihydro-5-methyl-2-phenyl-  
(Pigment Yellow 60)

### Chemical Abstracts Service Registry Number

**6407-78-9**

3H-Pyrazol-3-one, 4-[(2,4-dimethylphenyl)azo]-2,4-dihydro-5-methyl-2-phenyl-  
(Solvent Yellow 18)

### Chemical Abstracts Service Registry Number

**29398-96-7**

[1,1'-Biphenyl]-4,4'-diamine, *N,N'*-bis(2,4-dinitrophenyl)-3,3'-dimethoxy-  
(Pigment Brown 22)

### Chemical Abstracts Service Registry Number

**1325-86-6**

1-Naphthalenemethanol,  $\alpha,\alpha$ -bis[4-(diethylamino)phenyl]-4-(ethylamino)-  
(Solvent Blue 5)

### Chemical Abstracts Service Registry Number

**6786-83-0**

1-Naphthalenemethanol,  $\alpha,\alpha$ -bis[4-(dimethylamino)phenyl]-4-(phenylamino)-  
(Solvent Blue 4)

**Environment Canada  
Health Canada**

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## Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or human health. Based on the results of a screening assessment, the Ministers can propose to take no further action with respect to the substance, to add the substance to the Priority Substances List (PSL) for further assessment, or to recommend that the substance be added to the List of Toxic Substances in Schedule 1 of the Act and, where applicable, the implementation of virtual elimination.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce in Canada; and/or
- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE), and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The Ministers therefore published a notice of intent in the *Canada Gazette*, Part I, on December 9, 2006 (Canada 2006a), that challenged industry and other interested stakeholders to submit, within specified timelines, specific information that may be used to inform risk assessment, and to develop and benchmark best practices for the risk management and product stewardship of these substances identified as high priorities.

The substances listed below were identified as high priorities for screening assessment and were included in the Ministerial Challenge because they were found to meet the ecological categorization criteria for persistence, bioaccumulation potential and inherent toxicity to non-human organisms and were believed to be in commerce in Canada. These substances are not considered to be a high priority for assessment of potential risks to human health, based upon application of the simple exposure and hazard tools developed by Health Canada for categorization of substances on the Domestic Substances List (DSL).

CAS RN*	DSL Name
6407-74-5	3H-Pyrazol-3-one, 4-[(2-chlorophenyl)azo]-2,4-dihydro-5-methyl-2-phenyl-
6407-78-9	3H-Pyrazol-3-one,4-[(2,4-dimethylphenyl)azo]-2,4-dihydro-5-methyl-2-phenyl-
29398-96-7	[1,1'-Biphenyl]-4,4'-diamine, N,N'-bis(2,4-dinitrophenyl)-3,3'-dimethoxy-
1325-86-6	1-Naphthalenemethanol, $\alpha,\alpha$ -bis[4-(diethylamino)phenyl]-4-(ethylamino)-
6786-83-0	1-Naphthalenemethanol, $\alpha,\alpha$ -bis[4-(dimethylamino)phenyl]-4-(phenylamino)-

\*CAS RN = Chemical Abstracts Service Registry Number

Screening assessments focus on information critical to determining whether a substance meets the criteria for defining a chemical as toxic as set out in section 64 of CEPA 1999. Screening assessments examine scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution.

The Notice for the Challenge for the above substances was published in the *Canada Gazette* on August 30, 2008 (Canada 2008). Substance Profiles were released at the same time. The Substance Profiles presented the technical information available prior to December 2005 that formed the basis for categorization of these substances. Based on the outcome of the Challenge, the Ministers of the Environment and of Health have conducted the screening assessment below.

### Summary of Information Used as Basis for this Draft Screening Assessment

Based on categorization results, the substances listed in this report have been found to meet the ecological criteria for persistence, bioaccumulation and inherent toxicity to non-human organisms (PBiT). These substances were not found to meet the human health categorization criteria (Environment Canada 2006).

To establish whether certain high priority substances, including PBiT substances, were currently being manufactured in or imported into Canada, a survey was conducted by issuing a *Notice with Respect to Selected Substances Identified as Priority for Action* pursuant to paragraphs 71(1)(a) and (b) of CEPA 1999. The Notice was published in Part I of the *Canada Gazette* on March 4, 2006 (Canada 2006b). In response to this notice, there were no reports of industrial activity (import or manufacture) with respect to these substances in Canada, above the reporting threshold of 100 kg, for the specified reporting year of 2005. However, some companies did identify themselves as having a stakeholder interest in these substances. Therefore, these substances were believed to be potentially in commerce in Canada and were included in the Challenge.

Results from a similar notice issued under paragraph 71(1)(b) of CEPA 1999 on August 30, 2008, as part of the Challenge (Canada 2008) also resulted in no reports of industrial activity (import or manufacture with respect to these substances in Canada, above the reporting threshold of 100 kg, for

the specified reporting year of 2006. These results indicate that currently these substances are not in use above the specified reporting threshold, and therefore the likelihood of exposure to these substances in Canada resulting from commercial activity is low. Other sources of entry into the environment have not been identified at this time. However, there is a potential that some general uses of these substances in finished products and articles noted in readily available reference sources may also be found in Canada.

These substances can be grouped into three chemical classes of toxicological concern for human health. CAS RN 6407-78-9 and CAS RN 6407-74-5 belong to the class of azo colorants, CAS RN 1325-86-6 and CAS RN 6786-83-0 belong to the class of triarylmethane colorants and 29398-96-7 contains a structural moiety that may produce a benzidine congener of demonstrated carcinogenicity.

Limited empirical toxicity data are available for CAS RN 6407-74-5 and CAS RN 6407-78-9, however, these substances belong to the class of azo colorants that may generate aromatic amines by reductive cleavage of the azo linkage mediated by azoreductase enzymes found in mammalian tissues as well as bacteria of the intestine and skin (Platzek 1999; Golka et al. 2004; Chen 2006; Xu et al. 2007; Stingley et al. 2010). The collective toxicity database for aromatic amines as a chemical class (Vineis and Pirastu 1997; Benigni and Passerini 2002; Talaska 2003) suggests that there may be a potential concern for these substances. While it is recognized that the degree of azo reduction is likely influenced by various factors (e.g., solubility of parent, presence and position of molecular substituents), in the absence of chemical-specific data, it is assumed that exposure to an azo colorant may also result in exposure to its corresponding azo cleavage products, typically aromatic amines. The predicted azo cleavage products of CAS RN 6407-74-5 and CAS RN 6407-78-9 include 2-chloroaniline (CAS RN 95-51-2) and toluene-2,5-diamine (CAS RN 95-70-5), respectively, both of which have empirical toxicity data available suggesting potential hazards (2-chloroaniline: NTP 2009; toluene-2,5-diamine: SCCP 2007). Therefore, although data on the parental substances are limited, there may be potential hazards associated with their predicted azo cleavage products.

CAS RN 1325-86-6 and CAS RN 6786-83-0 belong to the class of triarylmethane colorants, where some members of which have demonstrated concerns for carcinogenicity as well as reproductive and developmental toxicity (IARC 1993; US EPA 2002). While these substances have limited empirical toxicity data available, there may be potential hazards associated with these chemicals by analogy to related triarylmethane substances of known toxicity.

CAS RN 29398-96-7 was positive for sister chromatid exchange in Chinese hamster bone marrow following intraperitoneal injection and also tested positive for mutagenicity in *Salmonella typhimurium* (Ciba Geigy Corp. 1992). 29398-96-7 contains a structural moiety that may produce a benzidine congener of demonstrated carcinogenicity: 3,3'-dimethoxybenzidine or 3,3'-DMOB (NTP 2005). While 3,3'-DMOB moiety is bonded by amino rather than more labile azo linkages, the potential for 29398-96-7 to release this moiety during metabolism is not known. Based on limited empirical toxicity data and the presence of a structural moiety of known carcinogenicity (3,3'-DMOB), there may be potential hazards associated with this substance.

While limited data and information on the classes of substances described above may suggest potential hazardous properties associated with these substances, exposure of the general population in Canada is expected to be low to negligible, and therefore the risk to human health is considered to be low. Confidence in the toxicity database is considered to be low.

Responses to the above notices and the accompanying questionnaire (Canada 2006b; Canada 2008) also revealed no new information relevant to the PBiT properties of these substances. Given the lack of any significant commercial activity for this substance, no further collection or analysis relevant to the persistence, bioaccumulation and ecological effects of this substance, beyond what was done for categorization, has been conducted. Therefore, the decisions on PBiT properties made during categorization remain unchanged. These substances are thus considered to be highly hazardous to aquatic organisms ( $LC_{50}/EC_{50} \leq 1$  mg/L). They are also considered to meet the criteria for both persistence and bioaccumulation as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

## Conclusion

Based on available information, and until new information is received indicating that these substances are entering, or may enter the environment from commercial activity or from other sources, it is concluded that the above substances are currently not entering, nor are likely to enter 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 constitute a danger to the environment on which life depends or that constitute a danger in Canada to human life or health. Therefore, it is proposed that these substances do not meet the criteria set out in section 64 of CEPA 1999.

As substances listed on the DSL, import and manufacture of these substances in Canada are not currently subject to notification under subsection 81(1). Given their potential hazardous properties, there is concern that new activities for the above substances which have not been identified or assessed under CEPA 1999 could lead to the substances meeting the criteria set out in section 64 of the Act. Therefore it is recommended that the above substances be subject to the Significant New Activity provisions specified under subsection 81(3) of the Act, to ensure that any new manufacture, import or use of these substances in quantities greater than 100 kg/year is notified and will undergo ecological and human health risk assessments as specified in section 83 of the Act, prior to the substances being introduced into Canada.

In addition and where relevant, research and monitoring will support verification of assumptions used during this screening assessment.

### Considerations for Follow-up

These substances belong to three chemical classes of toxicological concern for human health; CAS RN 6407-74-5 and CAS RN 6407-78-9 belong to the class of azo colorants, CAS RN 1325-86-6 and CAS RN 6786-83-0 belong to the class of triarylmethane colorants and CAS RN 29398-96-7 contains a structural moiety that may produce a benzidine congener of demonstrated carcinogenicity.

Given the potential hazardous properties of the classes of substances, additional activity (e.g., research, assessment, monitoring and surveillance) may be undertaken to characterize the risk to human health in Canada of these broader groups of substances.

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