Draft Screening Assessment for the Challenge

β-Alanine, *N*-[4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl]-*N*-(3-methoxy-3-oxopropyl)-, methyl ester

Chemical Abstracts Service Registry Number
59709-38-5

Environment Canada
Health Canada

January 2011

Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment on β-Alanine, *N*-[4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl]-*N*-(3-methoxy-3-oxopropyl)-,methyl ester,Chemical Abstracts Service Registry Number* 59709-38-5; this substance will be referred to by its derived acronym, ANMOM, in the assessment. ANMOM was identified as a high priority for screening assessment and included in the Challenge initiative under the Chemicals Management Plan because it had been found to meet the ecological categorization criteria for persistence, bioaccumulation potential and inherent toxicity to non-human organisms and was believed to be in commerce in Canada.

This substance was 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. Therefore, this assessment focuses on information relevant to the evaluation of ecological risks.

β-Alanine, *N*-[4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl]-*N*-(3-methoxy-3-oxopropyl)-, methyl ester is an organic substance. In 2005, this substance was reported to be imported between 1001 and 100 000 kg into Canada primarily as a disperse dye in the finishing of textiles, fabrics and apparel. The substance is not naturally produced in the environment. It is not reported to be manufactured, used or imported into Canada for the 2006 reporting year.

Based on certain assumptions and reported use patterns in Canada, most of the substance ends up in wastewater effluent. ANMOM presents low experimental solubilities in n-octanol (1670 mg/L) and low predicted solubilities in water for the chemical analogues (ranges between 0.000938 and 0.07 mg/L). ANMOM is predicted to exist primarily as micro-particulate matter that is not volatile, is chemically stable under most conditions and has a tendency to partition by gravity to sediments if released to surface waters, and to soils if released to air.

Based on its physical and chemical properties, this substance is expected to be persistent in the environment. However, experimental data relating to its bioaccumulation in fish and its solubility in octanol and water suggest that this disperse dye has a low potential to accumulate in the lipid tissues of organisms. ANMOM therefore meets the persistence criteria but does not meet the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations*. In addition, experimental toxicity data for the chemical analogues, as well as toxicity predictions that take into account revised estimates of

bioaccumulation potential, suggest that saturated solutions of the substance do not cause acute harm to aquatic organisms.

For this screening assessment, a very conservative exposure scenario was selected in which an industrial operation (user of the disperse dye) discharges ANMOM into the aquatic environment. The predicted environmental concentration in water was below the predicted no-effect concentrations calculated for fish, daphnids and algae. Based on the information available, it is proposed that ANMOM is 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.

The potential for exposure of the general population in Canada to this substance from environmental media is expected to be low. Exposure to this substance from its potential use as a dye in textiles and fabrics is also expected to be low.

The limited empirical health effects data identified for this substance, its potential metabolites, and analogues, together with mixed quantitative structure-activity relationship predictions, suggest this substance may pose a potential hazard to human health. However, exposure for the general population of Canada to this substance is expected to be low, and consequently, the potential risk to human health is considered to be low at current potential levels of exposure. It is proposed that ANMOM does not constitute a danger in Canada to human life or health.

Based on the information available, ANMOM does not meet any of the criteria set out in section 64 of the *Canadian Environmental Protection Act, 1999*.

This substance will be considered for inclusion in the *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment.

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 to human health.

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 2006), 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 those substances identified as high priorities.

The substance was identified as a high priority for assessment of ecological risk as it was found to be persistent, bioaccumulative and inherently toxic to aquatic organisms and was believed to be in commerce in Canada. The Challenge for this substance was published in the *Canada Gazette* on December 26, 2009 (Canada 2009a, 2009b). A substance profile was released at the same time. The substance profile presented the technical information available prior to December 2005 that formed the basis for categorization of this substance. As a result of the Challenge, submissions of information pertaining to the properties, bioaccumulation potential, persistence, hazard, uses, and exposure of the substance were not received.

Although this substance was determined to be a high priority for assessment with respect to the environment, it did not meet the criteria for high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity. Therefore, this assessment focuses principally on information relevant to the evaluation of ecological risks.

Screening assessments focus on information critical to determining whether a substance meets the criteria 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.[†]

This draft screening assessment includes consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under the Challenge. Data relevant to the screening assessment of this substance were identified in original literature, review and assessment documents, stakeholder research reports and from recent literature searches, up to August 2010. Key studies were critically evaluated; modelling results may have been used to reach conclusions.

When available and relevant, information presented in hazard assessments from other jurisdictions was considered. The draft 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.

This draft 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 portion of this assessment has undergone external written peer review/consultation. Approaches used in the screening assessments under the Challenge have been reviewed by an independent Challenge Advisory Panel.

The critical information and considerations upon which the draft assessment is based are summarized below.

[1.] 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) Challenge Batches 1-12 is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the Controlled Products Regulations, which is part of regulatory framework for the Workplace Hazardous Materials Information System [WHMIS] 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.

Substance Identity

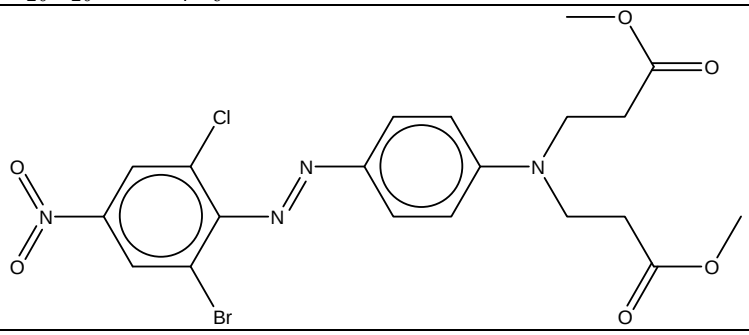
Substance Name

Disperse Yellow Brown, a trade name, is defined by the Colour Index (CII 2002−) as a combination of two CAS numbers, i.e., CAS RN 71872-49-6 and CAS RN 59709-38-5. For the purposes of the present report and the assessment of the substance, β-Alanine, N-[4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl]-N-(3-methoxy-3-oxopropyl)-, methyl ester will be referred to by its developed acronym, "ANMOM," derived from the DSL inventory name, refers exclusively to the CAS RN 59709-38-5.

It should be noted that the 2006 CEPA section 71 survey notice in Canada (Canada 2009b) indicated that the trade names commonly used for ANMOM such as "Disperse Yellow Brown" and "Dispersol Yellow Brown XF" could contain substances in addition to CAS RN 59709-38-5 whether alone, in a product, in a mixture or in a manufactured item in a quantity ≥ 100 kg, or used in a quantity ≥ 1000 kg at any concentration. Therefore, it is possible that the quantity and use information collected as a result of the 2006 section 71 notice may not be exclusive to CAS RN 59709-38-5.

Table 1. Substance identity for ANMOM

Chemical Abstracts Service Registry Number (CAS RN)	**59709-38-5**
DSL name	**β-Alanine, *N*-[4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl]-*N*-(3-methoxy-3-oxopropyl)-, methyl ester**
National Chemical Inventories (NCI) names[1]	*β-Alanine, N-[4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl]-N-(3-methoxy-3-oxopropyl)-, methyl ester* (AICS, ASIA-PAC, NZIoC) *β-Alanine, N-[4-[2-(2-bromo-6-chloro-4-nitrophenyl)diazenyl] phenyl]-N-(3-methoxy-3-oxopropyl)-, methyl ester* (TSCA) *Methyl N-[4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl]-N-(3-methoxy-3-oxopropyl)- β-alaninate* (EINECS) *N-[4-[(2-Bromo-6-chloro-4-nitrophenyl)azo]phenyl]-N-[2-(methoxycarbonyl)ethyl]- β-alanine methyl ester* (ENCS) *3,3'-[[4-[(2-Bromo-4-nitro-6-chlorophenyl)azo]phenyl]imino] bis[propanoic acid], dimethyl ester (*ECL)
Other names	*3,3'-[[4-[(2-Bromo-4-nitro-6-chlorophenyl)azo]phenyl]imino] bis[propanoic acid], dimethyl ester;* *N-{4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl}-N-(3-methoxy-3-oxopropyl)-β-alaninate de methyle;* *Dispersol Yellow Brown XF;* *Dianix Yellow Brown XF*
Chemical group (DSL Stream)	Discrete organics
Major chemical class or use	Disperse dye

Major chemical sub-class	Monoazo dyes – Nitroazobenzene
Chemical formula	$C_{20}H_{20}BrClN_4O_6$
Chemical structure	
SMILES[2]	O=C(OC)CCN(c(ccc(N=Nc(c(cc(N(=O)(=O))c1)Cl)c1Br)c2)c2)CCC(=O)OC
Molecular mass	527.75 g/mol

[1] National Chemical Inventories (NCI). 2007: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); NCS (Japanese Existing and New Chemical Substances); NZIoC (New Zealand Inventory of Chemicals) and TSCA (U.S. Toxic Substances Control Act Chemical Substance Inventory).

[2] Simplified Molecular Line Input Entry System.

Physical and Chemical Properties

ANMOM is a monoazo (nitroazobenzene) disperse dye. The azo bond (–N=N–) of this molecule is the functional group that contributes to the colour (Danish EPA 1999). In addition to chemical structure, dyes may be classified according to their industrial applications and the methods by which they are applied to the substrate of interest (ETAD 1995). This classification system tends to reflect groupings based on physical and chemical behaviour. A brief discussion of the uses of this dye can be found later in this document under the Uses section.

Some experimental data are available for ANMOM. At the Environment Canada-sponsored Quantitative Structure-Activity Relationship (QSAR) Workshop in 1999, invited modelling experts identified many structural classes of pigment and dyes as "difficult to model" using QSARs (Environment Canada 2000). The physical and chemical properties of many of the structural classes of dyes and pigments (including acid and disperse dyes) are not amenable to model prediction because they are considered to be "out of the model domain of applicability" (e.g., structural and/or property parameter domains). Therefore, the applicability of QSAR models to dyes and pigments is determined on a case-by-case basis. Environment Canada has considered that it is inappropriate to use QSAR models to predict the physical and chemical properties of ANMOM. Consequently, a number of analogues and a "read-across" approach and/or experimental values were identified, where available, to determine the approximate physical and chemical properties in Table 2. However, certain modelling results were deemed appropriate if adjusted with experimental data or based on the structural fragments. These results were subsequently used for further modelling in this assessment.

An analogue is a chemical that is structurally similar to the substance under assessment and is therefore expected to have similar physical and chemical properties, behavior in the environment and/or toxicity. Where there are experimental data for a given parameter for an analogue substance, these can be used directly or with adjustment as an estimate of that parameter value for the substance under assessment.

To find acceptable analogues, a review of data for several disperse azo dyes was performed (Anliker et al. 1981; Anliker and Moser 1987; Baughman and Perenich 1988; ETAD 1995; Brown 1992; Yen et al. 1989; Sijm et al. 1999). These compounds have structural similarities to ANMOM but also share other important attributes that contribute to their suitability as analogues. This includes properties affecting their fate in the environment such as high molecular weights, generally >300 g/mol; similar cross sectional diameters (1.3-2.2 nm); solid particulate structures; decomposition at greater than 120ºC; and "dispersibility" in water (i.e. not truly "soluble"). In addition, they have a negligible vapour pressure and are stable under environmental conditions, as they are designed to be so.

The modelling program ACD pKa/DB (2005) predicts that ANMOM ionizes in water as a base in one step by attracting a proton to the tertiary amine group. The primary base dissociation constant, pKb1 = 13.02, indicates that the protonation of the base form is negligible, such that the acid form has a negligible existence in water. In other words, ANMOM has minimal ionization in water and should, therefore, be considered as non-ionizing.

Table 2. Physical and chemical properties for neutral form of ANMOM and relevant analogues

Property	Type	Value[1]	Temperature (°C)	Reference
Melting point (ºC)	Experimental (ANMOM)	117*		Anliker and Moses 1987
	Analogue Disperse Blue 79:1	> 138-153		Sandoz Chemical 1989; Yen et al 1989
	Analogue Disperse Orange 30	157		PhysProp 2006
Boiling point (ºC)	Not applicable[2]			
Density (kg/m^3)	Not available			
Vapour pressure (Pa)	Analogue Disperse Blue 79	4.53×10^{-7}		Clariant 1996
Henry's Law constant ($Pa \cdot m^3/mol$)	Read-across (disperse dyes)[3]	10^{-8} to 10^{-1} (10^{-13} to 10^{-6} $atm.m^3/mol$)		Baughman and Perenich 1988
Log K_{ow} (Octanol-water partition coefficient) (dimensionless)	Modelled	5.12–5.35		Anliker and Moses 1987 (CLOGP 3.4)[4]
	Experimental (ANMOM)	4.1*		Anliker and Moses 1987
	Analogue Disperse Blue	4.1; 4.3		Clariant 1996; Brown 1992

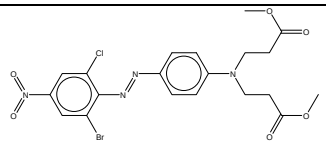
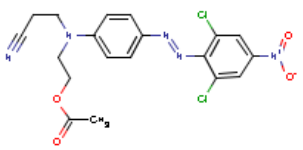
Property	Type	Value[1]	Temperature (°C)	Reference
	79			
	Analogue Disperse Blue 79:1	4.44, 4.8		Sijm et al 1999; Yen et al 1989
	Analogue Disperse Orange 30	4.2		Brown 1992
Log K_{oc} (Organic carbon-water partition coefficient) (dimensionless)	Modelled (estimated from First Order Molecular Connectivity Index)	3.9		KOCWIN 2008
	Read-across calculated (disperse dyes)[5]	3.4 to 4.2*		Baughman and Perenich 1988
Water solubility (mg/L)	Modelled (ANMOM)	2.8–9.2	20	Anliker and Moses 1987 (CLOGP 3.2)[4,6]
	Analogue Disperse Blue 79	0.0054, 0.02[6] 0.00094[6]	25 -- 15-25	Clariant 1996; Brown 1992; Baughman and Perenich 1988
	Analogue Disperse Blue 79:1	0.0052, 0.022	25	Baughman and Perenich 1988; Sijm et al 1999
	Disperse Orange 30	0.07[7]		Brown 1992
n-octanol solubility (mg/L)	Experimental (ANMOM)	1670*	20	Anliker and Moses 1987
	Analogue Disperse Orange 30	576		Anliker and Moses 1987
pK_b	Modelled	13.02		ACD/pK_aDB

Property	Type	Value[1]	Temperature (°C)	Reference
(Base dissociation constant) (dimensionless)	(ANMOM)	(base form)		2005

Abbreviations: K_{oc}, organic carbon-water partition coefficient; K_{ow}, octanol–water partition coefficient.
*Indicates selected value for modelling; primarily these values are empirical and specific to CAS RN 59709-38-5 (Appendix 2)
[1] Values in parentheses represent the original ones as reported by the authors or as estimated by the models
[2] Boiling point is generally not applicable to disperse dyes. For powder dyes, charring or decomposition occurs at high temperatures. For liquids and pastes, boiling will only occur for the solvent component while the un-evaporated solid will decompose or char (ETAD 1995)
[3] Solubilities of several disperse dyes at 25 and 80°C were used by Baughman and Perenich (1988) to calculate Henry'sLaw constants for these dyes. These values are presented here as a range to illustrate the expected Henry Law's constant for ANMOM
4Calculated by Pomona College Med. Chem. Project computer program (CLOGP)
[5] Log Koc values are based on calculations by Baughman and Perenich (1988) using a range of measured solubilities for commercial dyes and an assumed melting point of 200°C
[6] The study indicates that the Disperse Blue 79 used in the test had a purity (as organic materials) of 76% and a dispersion of 20% dye stuff.
[7] The study indicates that the Disperse Orange 30 used in the test had a purity (as organic materials) of 73% and a dispersion of 20% dye stuff.

Because of the paucity of empirical data for ANMOM and the error associated with model predictions for disperse dyes, selected empirical physical and chemical properties (Table 2), bioaccumulation data (Tables 5a,b) and toxicity data (Table 6) were used to support the weight of evidence and conclusions in this screening assessment. Specifically, data were obtained for three structurally similar monoazo dyes (Disperse Blue 79, Disperse Blue 79:1, and Disperse Orange 30). The substance identity information and the type of available empirical data for the selected analogues are presented in Table 3a. The molecular weights and cross sectional diameters for ANMOM and the selected analogues are presented in Table 3b.

Table 3a. Structural analogues for ANMOM

Common name (CAS RN)	DSL name	Structure	Major structural similarities and differences with ANMOM	Available empirical data
ANMOM (59709-38-5)	β-Alanine, *N*-[4-[(2-bromo-6-chloro-4-nitrophenyl)azo]phenyl]-*N*-(3-methoxy-3-oxopropyl)-, methyl ester		–	n-octanol solubility, log K_{ow}, melting point
Disperse Orange 30 (5261-31-4)	Propanenitrile, 3-[[2-(acetyloxy)ethyl][4-[(2,6-dichloro-4-nitrophenyl) azo]phenyl]amino]-		Similarity: Aromatic azo compound with two terminal nitro groups, one chlorine, one carboxylic functional group Differences: Disperse Orange 30 contains a nitrile	Melting point, log K_{ow}, solubility, aquatic toxicity, bioaccumulation data

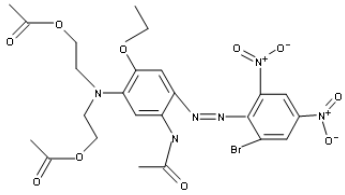
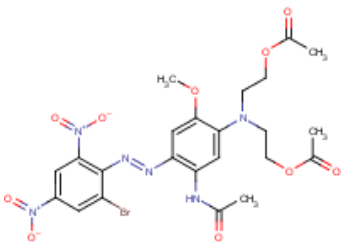
Common name (CAS RN)	DSL name	Structure	Major structural similarities and differences with ANMOM	Available empirical data
			group, a second chlorine and no bromine, and no aniline with two short carbon chains.	
Disperse Blue 79 (12239-34-8)	Acetamide, *N*-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[(2-bromo-4,6-dinitrophenyl)azo]-4-ethoxyphenyl]-		Similarity: Aromatic azo compound with a terminal nitro group, an aniline with two short carbon chains and a bromine moiety Differences: Disperse Blue 79 contains two carboxylic groups, an additional nitro functional group and no chlorine moiety.	Vapour pressure, log K_{ow}, solubility, toxicity data
Disperse Blue 79:1 (3618-72-2)	Acetamide, N-[5-[bis[2-(acetyloxy)ethyl]amino]-2-[(2-bromo-4,6-dinitrophenyl)azo]-4-methoxyphenyl]-		Similarity: Aromatic azo compound with a terminal nitro group, and aniline with two short carbon chains with one bromine moiety. Differences: Disperse Blue 79:1 contains two carboxylic groups, an additional nitro functional group, and aniline with two short carbon chains with no chlorine moiety.	Melting point, log K_{ow}, solubility, toxicity data

Table 3b. Comparison of the molecular mass and cross-sectional diameter for ANMOM and the monoazo disperse dye structural analogues

	CAS RN	Common name	Molecular mass (g/mol)	Minimum–maximum D_{max} (nm)[1]	Reference
ANMOM	59709-38-5	Not applicable	528	1.04	Anliker et al. 1988
ANMOM	59709-38-5	Not applicable	528	1.44	BBM 2008
Monoazo dye analogues	12239-34-8	Disperse Blue 79	639	1.69–2.05	BBM 2008
	3618-72-2	Disperse Blue 79:1	625	1.43–2.03	BBM 2008
	5261-31-4	Disperse Orange 30	450	1.75–1.98	BBM 2008
			Average Effective Diameter (angstroms)		
ANMOM	59709-38-5	Not applicable	11.00 (range from 9.31 to 12.79)		Dimitrov et al. 2005
Monoazo dye analogues	12239-34-8	Disperse Blue 79	12.29 (range from 11.07 to 13.39)		Dimitrov et al. 2005
	3618-72-2	Disperse Blue 79:1	11.97 (range from 10.77 to13.58)		Dimitrov et al. 2005
	5261-31-4	Disperse Orange 30	10.30 (range from 8.49 to 12.57)		Dimitrov et al. 2005

[1] Based on range of maximum diameters (D_{max}) for conformers calculated using CPOPs (2008)

It should be noted that there are several uncertainties associated with the use of physical and chemical, toxicological, and bioaccumulation data available for the substances. All these substances share the same chemical class—azo compounds. However, there are differences between these substances associated with their unique functional groups (see Table 3a) and some of their molecular sizes. In spite of the fact that some of these analogues have larger molecular weights than ANMOM, their comparable physical state, melting points, water solubilities, log K_{ow} values and cross-sectional diameters (Table 3b) provide a reasonable basis to conclude that the analogues will behave similarly to ANMOM in the environment and present an approximately equal bioavailability. Therefore, their use as analogues for ANMOM is judged to be an adequate basis for generating data using a read-across approach.

Sources and Uses

ANMOM is not naturally occurring in the environment.

For the 2005 calendar year, no manufacture of ANMOM was reported in response to a CEPA section 71 survey notice in Canada. However, one (1) company reported importing the substance in the 1001–100 000 kg range into Canada as a disperse dye in the finishing of textiles, fabrics and apparel in 2005 (Canada 2006). No companies identified themselves as having a stakeholder interest in the substance.

For the 2006 calendar year, no manufacture, use or import of ANMOM was reported in response to a CEPA section 71 survey notice in Canada. No companies identified themselves as having a stakeholder interest in the substance (Environment Canada 2009b).

It should be noted that the 2006 CEPA section 71 survey notice in Canada (Canada 2009b) indicated that the trade names commonly used for ANMOM such as "Disperse Yellow Brown" and "Dispersol Yellow Brown XF" could contain substances in addition to CAS RN 59709-38-5 whether alone, in a product, in a mixture or in a manufactured item in a quantity ≥ 100 kg, or used in a quantity ≥ 1000 kg at any concentration. Therefore, it is possible that the quantity and use information collected as a result of the 2006 section 71 notice may not be exclusive to CAS RN 59709-38-5.

During the DSL nomination (1984–1986), the DSL use codes for "Colourant - pigment/stain/dye/ink" and "pigment, dye and printing ink", were identified for ANMOM. The quantity reported was in the 1000–100 000 kg range (Environment Canada 1988).

ANMOM is not listed in the Drug Products Database (DPD 2010), the Therapeutic Products Directorate's internal Non-Medicinal Ingredients Database, the Natural Health Products Ingredients Database (NHPID 2010) or the Licensed Natural Health Products Database (LNHPD 2010) as a medicinal or non-medicinal ingredient present in pharmaceuticals or natural health products. This substance is not likely to be currently present in veterinary drugs in Canada (July 2010 personal communication from Therapeutic Products Directorate & Veterinary Drugs Directorate to Risk Management Bureau, Health Canada, unreferenced).

ANMOM is not listed on the Cosmetic Ingredient Hotlist, Health Canada's administrative list of ingredients that are intended to be prohibited or restricted for use in cosmetics in Canada (Health Canada 2009). In addition, no cosmetic and personal care products have been notified to Cosmetic Notification System (CNS) to contain ANMOM (CNS 2010).

This substance is not listed as an approved food additive under Division 16 of the *Food and Drug Regulations* (Canada. 1978) nor is it identified to be used/present in formulations of incidental additives or used in food packaging materials (July 9, 2010;

personal communication from Food Directorate to Risk Management Bureau, Health Canada; unreferenced).

This substance is not an active nor non-active ingredient in any registered pest control product in Canada (October 2010; personal communication from Pest Control Regulatory Agency to Risk Assessment Bureau, Health Canada; unreferenced).

In the U.S., between 10 000 and 500 000 pounds (4.54 to 22.7 tonnes) of ANMOM were manufactured and/or imported in 1994, 1998 and 2002 (US EPA 2006). ANMOM is an existing chemical in Europe and listed on the low production volume chemicals but not listed in a priority list (as foreseen under Council Regulation No 793/93 on the evaluation and control of the risks of existing substances lists (ESIS c1995-2009).

ANMOM was in use in Denmark and Sweden during 1999 to 2008 (SPIN 2010). The amounts and uses are confidential.

Releases to the Environment

There were no reports of use, import or manufacture of ANMOM in Canada in 2006 at or above the reporting thresholds specified in the CEPA section 71 notice (Environment Canada 2009b). Therefore, potential releases of this substance to the Canadian environment were estimated using 10 000 kg (i.e., the upper bound of the order-of-magnitude range into which the actual 2005 import quantity falls) throughout this screening assessment.

Environmental Fate

ANMOM, as indicated above, was not reported to be in commerce in Canada in 2006 above the reporting threshold of 100 kg. Nevertheless, the results of the site-specific exposure analysis and MegaFlush (see section Ecological Exposure Assessment section of this document), indicate that ANMOM is expected to be released to wastewater effluents during industrial processing and down-the-drain uses. The high experimental log K_{ow} value (4.1) and high read-across log K_{oc} (3.4 to 4.2) values (see Table 2) indicate that this substance may have affinity for solids. However, the log K_{oc} is a calculated value (see footnote 4 below Table 2) and the adsorption potential of disperse particulate dye structures is generally not well understood; therefore the degree to which this particular behaviour applies is uncertain.

According to aerobic biodegradation models, ANMOM is not expected to biodegrade quickly (see Table 4 below). Based on the modelled pKb of 13.02 (Table 2), this chemical behaves as a base and is negligibly ionized in water at the higher end of environmentally relevant pH (8–9). However, given the low water solubility of ANMOM (Table 2), ionization at elevated pH will likely have negligible impact on the partitioning or water solubility of this substance. Instead, when released into water, ANMOM is

expected to be mostly present as a particulate solid or adsorbed to suspended particles and eventually sink to surface bed sediments where they are expected to remain in a relatively biologically unavailable form. Razo-Flores et al. (1997) have stated that due to the recalcitrant nature of azo dyes in the aerobic environment, they eventually end up in anaerobic sediments, shallow aquifers and in groundwater.

The rate of volatilization from the surface of water is proportional to the Henry's Law constant (Baughman and Perenich 1988). The diffusivity in water and air also has an effect on the rate of volatilization. However, Baughman and Perenich (1988) also state that volatilization from aquatic systems will not be an important loss process for disperse dyes, which agrees with the low to negligible read-across Henry's Law constant values (10^{-8} to 10^{-1} Pa•m^3/mol; Table 2). Transport in air due to the loss of this substance from moist and dry soil surfaces is not likely to be important for this substance as indicated by very low analogue (Disperse Blue 79) vapour pressures (4.53×10^{-7}Pa; Table 2). These data are consistent with the physical state (solid particle) of the azo dyes which makes them unlikely candidates for volatilization.

Persistence and Bioaccumulation Potential

Environmental Persistence

No experimental or read-across degradation data for ANMOM or its analogues have been identified. No environmental monitoring data relating to the persistence of these dyes in the Canadian environment (air, water, soil, sediment) have been identified.

According to the Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers (ETAD), dyes are, with some exceptions, considered essentially non-biodegradable under aerobic conditions (ETAD 1995). Repeated evaluation of ready and inherent biodegradability using accepted screening tests (see OECD Guidelines for Testing Chemicals) have confirmed this assumption (Pagga and Brown 1986; ETAD 1992). Based on the chemical structure of ANMOM, there is no reason to expect that biodegradation will be other than described for dyes generally.

Some disperse azo dyes, including nitroazobenzenes, have been shown to undergo relatively rapid anaerobic degradation in sediment at depth where anoxic conditions prevail (Yen et al. 1991; Baughman and Weber 1994; Weber and Adams 1995). Disperse dyes enter the aquatic system mostly as a dispersion of fine suspended particles and eventually settle to the aerobic layers of surface sediment, where they will persist until sediment burial creates reducing conditions. The rate of sediment deposition and the extent of bioturbation vary from site to site and it is thus very difficult to ascertain the residence time of dyes in aerobic sediment layers. It is likely, however, that in many cases, this is greater than 365 days. Once under anaerobic or reducing conditions, azo dyes may undergo rapid degradation to substituted aromatic amine constituents, as demonstrated by Yen et al. (1991) who measured reduction half-life values of 1.9-2.0 days in compacted sediments at room temperature for nitroazobenzenes.

Given the hypothetical release of ANMOM as a dye into wastewater, persistence was primarily examined using predictive QSAR models for aerobic biodegradation in water. These models are considered acceptable for use in this situation as they are based on chemical fragments. The monoazo chemical fragments are represented in the training sets of all the BIOWIN models used, thereby increasing the reliability of the predictions (Environment Canada 2007). The following analysis applies primarily to the portion of this substance that is present in the environment in the dissolved form, recognizing that a significant proportion would also likely exist in dispersed form as solid particles. ANMOM and its analogues do not contain functional groups expected to undergo hydrolysis in aerobic environments (i.e., dyes are designed to be stable in aqueous conditions).

Table 4 summarizes the results for ANMOM of available QSAR models for biodegradation in water.

Table 4. Modelled data for degradation of ANMOM

Fate process	Model and model basis	Model result and prediction	Extrapolated half-life (days)
Primary biodegradation			
Biodegradation (aerobic)	BIOWIN 2008[1] Sub-model 4: Expert Survey (qualitative results)	2.78[3] "biodegrades slowly"	≥ 182
Ultimate biodegradation			
Biodegradation (aerobic)	BIOWIN 2008[1] Sub-model 3: Expert Survey (qualitative results)	1.25[3] "biodegrades slowly"	≥ 182
Biodegradation (aerobic)	BIOWIN 2008[1] Sub-model 5: MITI linear probability	-0.07[4] "biodegrades very slowly"	≥ 182
Biodegradation (aerobic)	BIOWIN 2008[1] Sub-model 6: MITI non-linear probability	0[4] "biodegrades very slowly"	≥ 182
Biodegradation (aerobic)	TOPKAT 2004[2] Probability	n/a	n/a
Biodegradation (aerobic)	CATABOL c2004-2008 % BOD (biological oxygen demand)	% BOD = 0.0268 "biodegrades very slowly"	≥ 182

[1] EPIsuite (2008)
[2] Model does not provide an estimate for this type of structure.
[3] Output is a numerical score from 0 to 5.
[4] Output is a probability score.

The results from Table 4 reveal that all ultimate biodegradation models (BIOWIN 3, 5, 6, and CATABOL) suggested that ANMOM biodegrades slowly. The TOPKAT model could not provide an estimate for this type of structure. Both BIOWIN 5 and 6 probability results are much less than 0.3 which is the cut-off suggested by Aronson et al. (2006) to identify substances as having a half-life > 60 days (based on the MITI probability models). Furthermore, the other ultimate degradation models, BIOWIN 3 and CATABOL, predict that ANMOM will be persistent in water.

When the results of the probability and the other ultimate degradation models are considered, there is model consensus suggesting that the ultimate biodegradation half-life in water is ≥ 182 days. This finding is consistent with what would be expected for these chemical structures (i.e., few degradable functional groups, solid sparingly soluble particle).

Using an extrapolation ratio of 1:1:4 for a water:soil:sediment biodegradation half-life (Boethling et al. 1995), the ultimate degradation half-life in aerobic soil is ≥ 182 days and the half-life in aerobic sediments is ≥ 365 days. This suggests that ANMOM is expected to be persistent in soil and sediment.

Based on modelled ultimate degradation data (Table 4) and expert judgment, ANMOM meets the persistence criteria in water, soil and sediment (half-lives in soil and water ≥ 182 days and half-life in sediment ≥ 365 days) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential for Bioaccumulation

Bioaccumulation models are known to predict poorly for pigments and dyes, and predictions from such models are considered unreliable for azo dyes. As a result, bioaccumulation modelling has not been used to evaluate the bioaccumulation potential of these substances.

Table 5a presents the empirical bioaccumulation factor (BAF) value in fish that indicates that this chemical has very low potential to bioaccumulate in biota.

In the absence of further experimental and modelled data, empirical bioconcentration (BCF) and BAF factors for structural analogues were used to estimate the bioaccumulation potential of ANMOM. To that end, a bioconcentration study submitted for a relatively close structural analogue, Disperse Orange 30, suggests that it is unlikely to accumulate in fish (Shen and Hu 2008). This test was performed according to OECD Guidelines (OECD 1996). The bioconcentration of Disperse Orange 30 in zebra fish (*Brachydanio rerio*) was determined in a 28-day semi-static test with renewal of the test medium every two days. An exposure test at a nominal concentration of 20 mg/L (mean measured concentrations ranged between 0.028 ~ 0.28 mg/L) was performed in accordance with the result of the fish acute toxicity test to check the bioconcentration potential of the test substance. Samples from both test solutions and test organisms were taken daily from day 26 to day 28 during the 28-day exposure test period. Samples were prepared by extracting the lipid component from the test fish. The measured concentration of test substance, fish lipid content and BCF calculation are reported in Table 5b.

Table 5a. Empirical data for bioaccumulation of ANMOM

Test organism	Endpoint	Value wet weight (L/kg)	Reference
Fish	BAF	5	Anliker et al. 1988

Table 5b. Measured concentrations, fish lipid content and BCF calculation for analogue Disperse Orange 30 (Shen and Hu 2008)

		Sampling time		
		Day 26	**Day 27**	**Day 28**
Treatments (20 mg/L)	Measured concentration of the test substance in extracted solutions (mg/L)	< 0.028	< 0.028	< 0.028
	Content of the test substance in the fish lipids (mg)	< 1.68	< 1.68	< 1.68
	Fish total weight (g)	2.07	2.13	2.53
	Concentration of the test substance in the fish C_f (mg/kg)	< 0.81	< 0.79	< 0.66
	Measured concentration of the test substance in the water C_w (mg/L)	0.028 ~ 0.28	0.028 ~ 0.28	0.028 ~ 0.28
	Fish lipid content (%)	0.81	0.57	1.25
	BCF	< 100	< 100	< 100
	Average BCF	< 100		

The Shen and Hu (2008) study was reviewed and considered acceptable (see Appendix 1). The very low level of detection in fish extracts (< 0.028 mg/L) suggests a limited solubility in lipids and/or limited potential to partition into fish tissue from aqueous systems. There is some uncertainty associated with limit-bounded values in any study because the actual value is not known. However, given the structure and likely behavior of disperse dyes in aqueous systems; a low BCF result is expected. Most disperse dyes, as their name suggests, exist as fine dispersible particles with limited truly soluble fractions. Solubility, however, can be increased by adding polar functional groups to the molecule.

While the above study serves as primary evidence to indicate the lack of bioaccumulation potential for ANMOM, other research corroborates this conclusion. Anliker et al. (1981) reported experimental fish bioaccumulation values for 18 monoazo disperse dyes, performed according to test methods specified by the Japanese Ministry of International Trade and Industry (MITI). Expressed on the basis of wet body weight of the fish, these log bioaccumulation factors ranged from 0.00 to 1.76 (Anliker et al. 1981). A lack of reporting of Chemical Abstract Service Registry Numbers (CAS RN) and chemical structures limited the utility of this study for read-across purposes to ANMOM. However, follow-up studies that provided the chemical structures for the disperse dyes tested, confirmed low bioaccumulation potential for 10 nitro-substituted azo dyes, with reported log bioaccumulation factors ranging from 0.3 to 1.76 (Anliker and Moser 1987; Anliker

et al. 1988). Studies available from MITI also support low bioaccumulation potential for disperse azo dyes. Reported BCFs for 3 disperse azo dyes (CAS RN 40690-89-9, CAS RN 61968-52-3 and CAS RN 71767-67-4) tested at a concentration of 0.01 mg/L were in the range of < 0.3 to 47 L/kg (MITI 1992). An accumulation study by Brown (1987) also showed that none of the twelve disperse dyes tested accumulated during an eight week study with carp.

A high log K_{ow} value for ANMOM and other related analogues (Table 2) is the only line of evidence that suggests ANMOM may have a high potential for bioaccumulation. Despite the high K_{ow} values for ANMOM and the other analogues, evidence for bioaccumulation of disperse azo dyes is lacking (Anliker et al. 1981; Anliker and Moser 1987; Anliker et al. 1988; MITI 1992). Authors who have measured high log K_{ow}s and concomitant low bioaccumulation factors for disperse azo dyes suggest that the low accumulation factors may be due to their low absolute lipid solubility (Brown 1987) or relatively high molecular weight, which may make transport across fish membranes difficult (Anliker et al. 1981; Anliker and Moser 1987). It is also likely that the lack of bioavailability and limited capacity to partition under BCF test conditions limits accumulation in fish lipids.

Recent 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 ~1.5 nm and much more so for molecules having a maximum diameter of greater than 1.7 nm. Sakuratani et al. (2008) have 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 (BCF < 5000) often have a D_{max} of > 2.0 nm and an effective diameter (D_{eff}) > 1.1 nm.

ANMOM and its closest analogues (similar monoazo dyes) have molecular weights ranging between 450 and 639 g/mol (see Table 3b) and their molecular structures are relatively uncomplicated. Both these characteristics indicate a bioaccumulation capability for these substances if molecular weight is used as the only indicator. In addition, Arnot et al. (2010) point out that there are no clear relationships for establishing strict molecular size cut-offs for assessing bioaccumulation potential. However, the report does not dispute the notion that a reduction in uptake rate can be associated with increasing cross-sectional diameter as demonstrated by Dimitrov et al. (2002, 2005). The maximum diameter of ANMOM, its closest analogues and their conformers ranges from 1.04 to 2.05 nm (BBM 2008; Anliker et al.1988; CPOPs 2008) suggesting that a potential for a significantly reduced uptake rate from water and reduced *in vivo* bioavailability exists for these dyes.

However, Arnot et al. (2010) noted that there are uncertainties associated with the thresholds proposed by Dimitrov et al. (2002, 2005) and Sakuratani et al. (2008) since the BCF studies used to derive them were not critically evaluated. Arnot et al. (2010) point

out that molecular size influences solubility, 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 in = slow out). 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. Consequently, when evaluating bioaccumulation potential, molecular size information should be considered with care and used together with other relevant lines of evidence in a weight-of-evidence approach.

Based on a lack of accumulation observed in bioconcentration tests with Disperse Orange 30 and other related disperse azo dyes, as well as data showing large cross-sectional diameters for ANMOM and its analogues that likely limit their partitioning behavior, ANMOM is expected to have a low potential for bioaccumulation. Therefore, considering the available evidence, ANMOM does not meet the bioaccumulation criteria (BCF or BAF $\geq$ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential to Cause Ecological Harm

Ecological Effects Assessment

A – In the Aquatic Compartment

There is modelled and experimental evidence that ANMOM does not cause harm to aquatic organisms following short-term (acute) and longer-term (chronic) exposure at relatively low concentrations.

An acute fish toxicity study was submitted for the analogue Disperse Blue 79 (BASF 1990). According to the study, Disperse Blue 79 has a 96-hour median lethal concentration (LC_{50}) of between 100 and 220 mg/L in golden orfe (Table 6). However, due to lack of details, this study was considered of uncertain reliability (Appendix 1).

A chronic study submitted for the analogue Disperse Blue 79:1 revealed its 122 day no-observed-effect concentration (NOEC) in rainbow trout to be greater than 0.0048 mg/L (Table 6). Reliability of this study was assessed as high (Appendix 1). However, this value was not used to calculate the predicted no-effect concentration because the value is an unbounded result (i.e., no certainty as to the threshold for effects).

A study submitted on behalf of ETAD provides acute ecotoxicity data in fish, invertebrates, algae and bacteria for 5 nitro-substituted azo disperse dyes (Brown 1992). Zebra fish, *Daphnia magna* and *Scenedesmus subspicatus* acute toxicity for the 2 analogues ranged from 340 to 710 mg/L, from 4.5 to 5.8 mg/L and from 6.7 to 9.5 mg/L, respectively (Table 6). In addition, all bacteria tests had a median inhibiting concentration

(IC_{50})exceeding 100 mg/L. The experimental details for the dyes tested were not provided, which greatly limited evaluation of these studies (Brown 1992). However, these data are considered usable and are included in this screening assessment as part of the weight of evidence.

When considering all structural analogue toxicity information in concert with the toxicity values for Disperse Blue 79, Disperse Blue 79:1 and Disperse Orange 30, these data suggest that ANMOM is not highly hazardous to aquatic organisms (i.e., acute LC_{50} values are > 1 mg/L).

Table 6. Empirical aquatic toxicity data for analogues of ANMOM

Common name or (CAS RN)	Test organism	Endpoint	Value (mg/L)	Reference
Disperse Blue 79[5] (12239-34-8)	Golden orfe (*Leuciscus idus*)	96-hr LC_{50}[1]	$100 < LC_{50} < 220$	BASF 1990
	Zebra fish (*Brachydanio rerio*)	LC_{50}	340	Brown 1992
	Daphnia magna	EC_{50}[2]	4.5	
	Scenedesmus subspicatus	EC_{50}	9.5	
	Bacteria	IC_{50}[3]	> 100	
Disperse Orange 30[6] (5261-31-4)	Zebra fish (*Brachydanio rerio*)	LC_{50}	710	
	Daphnia magna	EC_{50}	5.8	
	Algae (*Scenedesmus subspicatus*)	EC_{50}	6.7	
	Bacteria	IC_{50}	> 100	
Disperse Blue 79:1 (3618-72-2)	Rainbow trout (*Oncorhynchus mykiss*)	NOEC[4] (122 days)	> 0.0048	Cohle and Mihalik 1991

[1] LC_{50} – The concentration of a substance that is estimated to be lethal to 50% of the test organisms.
[2] EC_{50} – The concentration of a substance that is estimated to cause some toxic sublethal effect on 50% of the test organisms.
[3] IC_{50} – The inhibiting concentration for a specified percent effect. A point estimate of the concentration of a test substance that causes a 50% reduction in a quantitative biological measurement such as growth rate.
[4] NOEC – The no-observed-effect concentration is the highest concentration in a toxicity test not causing a statistically significant effect in comparison to the controls.
5 The study indicates that the Disperse Blue 79 used in the test had a purity (as organic materials) of 76% and a dispersion of 20% dye stuff.
[6] Disperse Orange 30 used in the test had a purity (as organic materials) of 73% and a dispersion of 20% dye stuff.

As with bioaccumulation, QSAR ecotoxicity predictions for disperse dyes were not considered reliable because of the potential error associated with input parameters and the unique nature of disperse dyes—specifically physical state, structural and/or physical and chemical properties which fall outside of the models' domain of applicability.

In general, due to their poor solubility (i.e., < 1 mg/L), disperse dyes are expected to have a low acute ecological impact (Hunger 2003). The results of empirical toxicity studies of the analogues of ANMOM are consistent with this expectation, indicating fish LC_{50} values in the 100–710 mg/L range, with *Daphnia* being the most sensitive organism

tested (EC_{50}s from 4.5 to 5.8 mg/L). Although interpretation of results from these tests is complicated by the fact that the reported effect values (i.e., EC_{50} and LC_{50}s) are likely to be much greater than the solubility of the substances tested and are likely the result of "indirect" toxic effects, the analogue data available do indicate that the toxicity of ANMOM is likely to be low. The available empirical ecotoxicity data for the analogues of ANMOM suggest that ANMOM is not likely to be highly hazardous to aquatic organisms.

The empirical analogue data for ANMOM indicates that this substance is not expected to cause acute harm to aquatic organisms at low concentrations (acute LC_{50}s are > 1.0 mg/L).

B – In Other Environmental Compartments

No suitable ecological effects studies were found for this compound in media other than water.

Ecological Exposure Assessment

No data concerning concentrations of this substance in water in Canada have been identified; therefore, environmental concentrations are estimated from available information, including estimated substance quantities, release rates, and size of receiving water bodies.

A site-specific exposure analysis was used to predict potential releases to water (sewers) from industrial use using quantities consistent with those reported in the past and Mega Flush (Environment Canada 2010) was used to predict releases to water (sewers) from consumer use of products containing this substance. It should be noted that the 2005 and 2006 CEPA section 71 notice in Canada (Canada 2006, 2009b) indicated that the trade names commonly used for ANMOM such as "Disperse Yellow Brown" and "Dispersol Yellow Brown XF" could contain substances in addition to CAS RN 59709-38-5 whether alone, in a product, in a mixture or in a manufactured item in a quantity ≥ 100 kg, or used in a quantity ≥ 1000 kg at any concentration. Therefore, it is possible that the quantity and use information collected as a result of the 2005 and 2006 section 71 notice may not be exclusive to CAS RN 59709-38-5. As a result, quantity of ANMOM may be over-predicted.

A – Industrial Release

The aquatic exposure of ANMOM is expected if the substance is released from industrial use to a wastewater treatment plant and the treatment plant discharges its effluent to a receiving water body. The concentration of the substance in the receiving water near the discharge point of the wastewater treatment plant is used as the predicted environmental concentration (PEC) in evaluating the aquatic risk of the substance. It can be calculated using the equation

$$C_{water-ind} = \frac{1000 \times Q \times L \times (1-R)}{N \times F \times D}$$

where

$C_{water-ind}$:	aquatic concentration resulting from industrial releases, mg/L
Q:	total substance quantity used annually at an industrial site, kg/yr
L:	loss to wastewater, fraction
R:	wastewater treatment plant removal rate, fraction
N:	number of annual release days, d/yr
F:	wastewater treatment plant effluent flow, m^3/d
D:	receiving water dilution factor, dimensionless

ANMOM was not reported to be manufactured, used or imported into Canada based on the CEPA section 71 notice for the year 2006 (Environment Canada 2009b). Therefore, potential releases of this substance to the Canadian environment were estimated using 10 000 kg (i.e., the use of the upper bound of the order-of-magnitude range into which the actual 2005 import quantity falls).Therefore, the hypothetical site-specific exposure scenarios described in this assessment are conservative.

A highly conservative site-specific exposure analysis is used to estimate releases to water and to estimate the aquatic concentration of the substance should ANMOM come into commerce in the future. This highly conservative scenario assumes that the quantity (i.e. 10 000 kg) is used at the facility that imports the substance and formulates it into products. The scenario also assumes that the loss to a local sewage treatment plant is high at 12% of the total quantity resulting from the cleaning of chemical containers and process equipment. Other input values are: a release period of 150 days per year, wastewater treatment plant (WWTP) removal at 54.8% as estimated by ASTreat (ASTreat 2006) for primary treatment systems and site specific conditions such as the WWTP effluent flow at 40 435 m^3/day and the 10-fold dilution of the receiving water. Based on the above assumptions, a total industrial use quantity of 10 000 kg/yr of ANMOM yields a PEC of 0.0089 mg/L near the point of the STP discharge.

B – Consumer Release

As ANMOM could potentially be found in consumer products and can be released to water, Mega Flush, Environment Canada's spreadsheet tool was employed to estimate the substance concentration in multiple water bodies receiving sewage treatment plant

effluents to which consumer products containing the substance may have been released (Environment Canada 2010). The spreadsheet tool provides these estimates for approximately 1000 release sites across Canada based on the following assumptions:

- loss to sewer at 10% which represents the losses of dye from household laundering manufactured articles
- sewage treatment plant removal rate estimated at 0% for no treatment, 55% for primary only treatment and 76% for primary-secondary combined treatment,
- number of annual release days at 365 days/year
- receiving water dilution factor in the range of 1 to 10.

The maximum predicted environmental concentration (PEC) of ANMOM in the receiving water bodies was estimated to be 6.4×10^{-4} mg/L. The estimate is based on a conservative total of 10 000 kg/year for the quantity of the substance used by consumers. The equation and inputs used to calculate the PEC are described in Environment Canada 2010.

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 highly conservative risk quotient calculation, as well as information on persistence, bioaccumulation, toxicity, sources and fate of the substance.

Based on read-across physical and chemical properties, ANMOM is predicted to degrade slowly in the aerobic environment and is expected to be persistent in water, soil and sediment. This substance is expected to have low bioaccumulation potential. Given that ANMON is currently not in commerce within Canada, the percentage of ANMOM that is expected to be released into sewers is negligible. In addition, the information on physical and chemical properties and uses indicates a low potential for overall releases into the Canadian environment. If released into the environment, this substance is expected to be discharged mainly to surface waters, although it is expected to ultimately be transferred to sediment. Through use of analogue data, ANMOM has also been demonstrated to have a relatively low potential for acute toxicity to aquatic organisms.

A risk quotient analysis, integrating a conservative cumulative PEC with a conservative estimate of the potential to cause adverse effects, or PNEC, was conducted for the aquatic environment and the resulting risk quotient (PEC/PNEC) is an important line of evidence in evaluating the potential risk to the environment.

A predicted no-effect concentration (PNEC) was estimated based on the 48-hour EC_{50} of 4.5 mg/L in *Daphnia magna* for analogue Disperse Blue 79 (Table 6). A factor of 100 was then applied to account for acute to chronic toxicity and lab to field extrapolations as well as the use of an analogue substance. The resulting PNEC is 0.045 mg/L.

When compared to the PEC calculated above for industrial releases to water through an STP (0.0089 mg/L), the resulting risk quotient (PEC/PNEC) is 0.0089/0.045 = 0.20. Therefore, potential releases of ANMOM resulting from industrial releases through a primary STP will likely not cause harm to aquatic organisms.

For exposure resulting from down-the-drain releases through consumer uses (conservative scenario), Mega Flush results estimate that the PEC for ANMOM will not exceed the PNEC at any sites (i.e., all risk quotients < 1). The maximum risk quotient calculated from the highest PEC (6.4×10^{-4} mg/L) divided by the PNEC (0.045 mg/L) is 0.014. This indicates that down-the-drain consumer releases of ANMOM are not expected to harm aquatic organisms.

In addition, ANMOM is currently not reported to be manufactured or used in Canada or imported into the country. In view of this, the total quantity of ANMOM (i.e., 10 000 kg) used in these highly conservative site-specific exposure scenarios is the upper bound of the order-of-magnitude range into which the actual 2005 import quantity falls. This quantity is also assumed to be used at one single industrial facility and with certain upper bounding assumptions. Thus, the PEC value obtained for these scenarios is considered highly conservative and likely overestimates the concentration of ANMOM in surface waters in Canada.

This information indicates that ANMOM does not have the potential to cause ecological harm in Canada from either industrial or consumer use.

Uncertainties in Evaluation of Ecological Risk

Uncertainties in this risk assessment exist due to a lack of experimental data on physical and chemical properties specific to ANMOM, notably their solubility in water, and carbon-water partition coefficient. However, read-across approaches, close analogue data, and modelled data were used to fill critical data gaps.

The evaluation of persistence is limited by the uncertainty about the rate of degradation in anaerobic sediments and the extent to which degradation occurs in these sediments and whether the degradation products (e.g. amines) would be biologically available. Nevertheless, it is clear that anaerobic degradation of the bioavailable portion of azo dyes in sediments to constitutive amines is much faster (half-lives in the order of days) than aerobic biodegradation. Although, the amine degradation products are not expected to be biologically available because they form only in relatively deep anoxic sediment and can be irreversibly bound to sediment through nucleophilic addition and oxidative radical coupling (Weber et al. 2001; Colon et al. 2002), this issue is a source of uncertainty in the toxicity assessment of ANMOM.

Uncertainties are also present due to the lack of information on environmental concentrations in Canada of ANMOM above reporting thresholds, however, the lack of

manufacturing, use and import quantity of ANMOM in Canada for the 2006 reporting year currently suggest low potential for releases into the Canadian environment.

The evaluation of bioaccumulation is limited by few bioaccumulation data specifically for ANMOM; therefore analogue data from Shen and Hu (2008) were used with the experimental results from Anliker et al.(1988). Although the experimental and analogue log K_{ow} (4.1–5.3) raises the possibility that ANMOM may have some bioaccumulation potential, factors such as large cross-sectional diameter, low lipid solubility and relatively high molecular weight are more relevant to the evaluation of bioaccumulation potential for disperse azo dyes such as ANMOM.

The experimental concentrations associated with toxicity to aquatic organisms have an additional source of uncertainty in that these concentrations exceed the solubility of ANMOM in water (either experimental or predicted). There is also some uncertainty related to the purity of the analogues used in the solubility and toxicity tests. Due to the low solubility of dyes, they are often mixed with water and a solubilizing agent to complete the test. This convention can produce solubilities that are artificially high and may affect the result of aquatic toxicity tests as well. However, efforts to make the dyes more soluble are likely to artificially increase bioavailability rather than decrease it. Despite this, the available data for the chemical analogues indicate that ANMOM is not highly hazardous to aquatic organisms in the water column. Also, regarding ecotoxicity, based on the predicted partitioning behaviour of these chemicals, the significance of soil and sediment as important media of exposure is not well addressed by the effects data available. Indeed, although the water column may not be the medium of primary long-term concern, the only effects data identified apply primarily to pelagic aquatic exposures. Nevertheless, based on the relatively low aquatic toxicity of these substances, potential for harm to soil-and sediment-dwelling organisms is also expected to be low.

Potential toxic by-products, from the degradation of ANMOM, may undergo reductive cleavage of the azo bond to form aromatic amines (Weber and Adams 1995). Bromodinitroaniline, a degradation product of Disperse Blue 79 has been detected in water and sediment downstream of a textile mill in Canada (Macguire and Tkaca 1991). Aromatic amines have greater aqueous solubility and could be released to the water column. One product of the degradation of ANMOM would be 2-bromo-6-chloro-4-nitroaniline however ortho-substituted anilines are generally less toxic than non-ortho-substituted anilines (Ramos et al. 2002); therefore, degradation products of ANMOM may not be as toxic. It seems unlikely that concentrations of substituted anilines resulting from the degradation of ANMOM in anoxic sediments could reach concentrations capable of causing toxicity to aquatic organisms.

Uncertainties are also associated with the fractions of the substances that are released during use and with the fraction that is removed in sewage treatment plants. These uncertainties were addressed by making conservative assumptions using best model estimates.

Given that ANMOM is used in other countries (SPIN 2010), it is possible that ANMOM is entering the Canadian market as a component of manufactured items and/or consumer products. However, information obtained from the section 71 Notice and other information sources did not indicate that ANMOM was present in these types of products in Canada. Available information is currently not sufficient to derive a quantitative estimate for these releases.

Potential to Cause Harm to Human Health

Exposure Assessment

Environmental media

Empirical data on concentrations of ANMOM in environmental media in Canada or elsewhere were not identified. ANMOM is not expected to be found in food or beverages. ChemCAN, a Canada-specific environmental exposure model, was used to estimate concentrations of ANMOM in various environmental media (ChemCAN 2003). This model is a level III fugacity model that is used to estimate average concentrations in various media to estimate general population exposure from the environment. ChemCAN differs from the point-source models used in the Ecological Assessment section of the document.

According to the section 71 notice information, the upper bound of the order-of-magnitude range into which the 2005 import quantity of ANMOM reported was 10 000 kg. Applying the loss percentages into a local sewage treatment plant at 12% and subsequent WWTP removal at 54.8% to this quantity (10 000 kg), the loss of ANMOM into surface water is calculated to be 542 kg. This estimate is considered to be an overestimate as explained in the Ecological Exposure Assessment section.

The environmental concentrations of ANMOM were estimated using ChemCAN based on 542 kg of ANMOM released to surface water (ChemCAN 2003). These estimated environmental concentrations of ANMOM were then used to derive conservative upper-bounding daily intakes of this substance by the general population in Canada. The estimated concentration in ambient air was used as a surrogate for indoor air data. In addition, the estimated concentration in surface water was used as a surrogate for drinking water data.

The upper-bound estimate of exposure from environmental media ranged from 0.001 µg/kg-bw (kilogram of body weight) per day for adults over 60 years old to 0.004 µg/kg-bw per day for children 6 months to 4 years old.

There is uncertainty in the exposure characterization because no empirical data on environmental concentrations of ANMOM were available. In addition, there is uncertainty due to assumptions used in the model. However; exposure estimates were

based on environmental concentrations derived from quantities in commerce in 2005, which is considered very conservative, and confidence is high that these estimates would be overestimates of actual exposure levels.

Consumer Products

Disperse dyes such as ANMOM are used in the textile industry to colour synthetic fabrics such as polyesters and polyamides. Disperse dyes derive their name from the dyeing process employed (Danish EPA 1998). Because of their low water solubility, the dye compounds are typically milled to produce a fine powder and applied as dispersion in water. The hydrophobic dye molecules adsorb to the hydrophobic textile, and heating induces uptake of the dye by the textile (Chudgar and Oakes 2003). Disperse dye does not form chemical bonds with the textile; therefore, migration is possible.

Although ANMOM was not imported manufactured or sold above the reporting threshold in Canada in 2006, and other information sources did not identify its presence in fabrics or textiles in Canada, given its importation in 2005 it is considered possible that it may be present in fabrics and textiles on the Canadian market.

Since ANMOM may be used as a dyeing agent for synthetic fibres for personal apparel and domestic textile uses, upper-bounding exposure estimates were derived for two likely scenarios for exposure: dermal exposure from wearing of apparel made of a fabric dyed with ANMOM and oral exposure via mouthing of the fabric by infants and young children. The upper-bounding dermal exposure to ANMOM was estimated to range from 0.1 to 3.73 µg/kg-bw per day by wearing new and unwashed apparel possessing good to poor colourfastness properties (ETAD 2004). For oral exposure via mouthing for infants and children, the estimated exposures were 0.031 µg/kg-bw (infants, 0 – 6 months old) and 0.015 µg/kg-bw (children, 6 months to 4 years old). A recent study found that the amount of a disperse dye that migrated to the skin of human volunteers was 300–600 times lower than that leached by sweat simulants (Meinke et al. 2009). This supports the conservative nature of the upper-bounding exposure estimates derived in this assessment. In addition, the loss of dyes in textiles is expected to occur primarily as a result of laundering, so any potential exposures would decline over time. Details of the assumptions used in these calculations are provided in Appendix 3 and Appendix 4.

There are uncertainties associated with the exposure assessment. Substance-specific information such as migration factors and solubility was not available and therefore not used in deriving exposure estimates. The sources of exposure have been broadly characterized as synthetic fabrics because no specific consumer products were identified. However, confidence is high in the conservative nature of the exposure estimates, because the migration factor used in the assessment corresponds to exposure to new, unwashed fabrics with poor colourfastness, while loss is expected to occur primarily during laundering. Additionally, there are empirical data demonstrating that the amount of a disperse dye in personal apparel that migrates to skin of human volunteers is substantially lower than that leaching into solution (Meinke et al. 2009).

Health Effects Assessment

No empirical health effects data were identified for ANMOM. Therefore, information on analogues and on potential azo cleavage products of ANMOM have been considered, along with consideration of (Quantitative) Structure Activity Relationship [(Q)SAR] models**.** Structures and a summary of the data available for each are available in Appendix 5.

ANMOM is a member of the family of azo colorants. It has been demonstrated that certain azo colorants can undergo reductive cleavage mediated by azoreductase enzymes found in mammalian tissues as well as bacteria of the intestine and skin (Platzek et al. 1999; Golka et al. 2004; Chen 2006; Stingley et al. 2010). 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), health effects information on potential azo cleavage products are considered relevant to the health effects characterization of the parent compound, as exposure to azo colourants may result in exposure to its corresponding azo cleavage products, typically aromatic amines (Danish EPA 1999; Hunger 2005). The carcinogenic potential of aromatic amines also varies considerably with molecular structure, with carcinogenic breakdown products being associated with moieties of benzidine, aniline, toluene or naphthalene for example (Danish EPA 1999, Hunger 2005). Water-soluble azo dyes as a class have demonstrated susceptibility to azo cleavage both *in vivo* and *in vitro* (Golka et al. 2004). The modelled and experimental data from ANMOM and its analogues indicate that the water solubility of ANMOM is low (see Table 2) which indicates that ANMOM would likely be less susceptible to cleavage compared to more soluble dyes. Although no chemical-specific information on azo reduction of ANMOM was identified, it was still considered appropriate to characterize the hazard of potential azo cleavage products. Accordingly, the potential azo cleavage products for ANMOM, namely 2-bromo-6-chloro-4-nitroaniline (CAS RN 99-29-6) and a second product (Cleavage Product 2; no CAS RN) are considered in this draft screening assessment (Appendix 5).

Genotoxicity and Carcinogenicity – ANMOM

The outputs of QSAR models for ANMOM were, overall, inconclusive for carcinogenicity (one positive prediction for carcinogenicity from DEREK[2010]) and reproductive and developmental toxicity (TOPKAT [2004], CASETOX [2008], and Model Applier [2009]). The outputs were positive for the Ames mutation assay in two models (Model Applier and DEREK) and positive for chromosomal aberrations *in vitro* in two models (Model Applier and CASETOX). Results were negative for micronuclei induction and DNA damage (Appendix 6).

Genotoxicity and Carcinogenicity –Potential Azo Cleavage Products

No empirical genotoxicity or carcinogenicity data were available for either potential azo cleavage products of ANMOM. The outputs of predictive QSAR models for carcinogenicity for 2-bromo-6-chloro-4-nitroaniline were mixed. Predictions for the other

potential azo cleavage product of ANMOM (Cleavage Product 2) were mainly negative. Predictions for genotoxicity were, overall, mixed for both potential cleavage products (see Appendix 6 for detailed results).

Genotoxicity and Carcinogenicity - Analogue Azo Dyes

Since no health effects information was available for ANMOM, relevant health effects data on analogue substances were also considered. Based on structural similarity, physical and chemical properties and availability of toxicity data (Appendix 5), five analogues were identified using a combination of ChemID (2010) and the OECD Toolbox ((Q)SARs Application Toolbox 2008): Disperse Blue 79:1 (CAS RN 3618-72-2), Disperse Blue 79 (CAS RN 12239-34-8), Disperse Orange 30 (CAS RN 5261-31-4), Disperse Red 54 (CAS RN 6657-37-0), and Disperse Orange 37 (CAS RN 13301-61-6). A summary of the available hazard data for analogues is presented below and with more detail in Appendix 5.

In genotoxicity studies, Disperse Blue 79:1 was positive for mutations in *in vitro* bacterial (*S. typhimurium* TA1537, TA1538, TA98, and TA100) strains, but inconclusive in mammalian cell systems (Clariant 1982, 1996; Foureman 1990; JCIETIC 1997) (Appendix 5). Disperse Blue 79:1 was negative for chromosomal aberrations in bone marrow of NMRI mice (male and female) by oral gavage of doses up to 5000 mg/kg-bw and for sex-linked recessive gene mutation in adult *Drosophila melanogaster* males exposed by injection to 50 ppm of Disperse Blue 79:1 (Foureman 1990; Clariant 1996).

Disperse Blue 79 was positive for mutations in *in vitro* bacterial (*S. typhimurium* TA1535, TA1537, TA1538, TA98 and TA100) strains without activation when administered in liquid form (Crompton & Knowles Corp 1987). Positive results were reported with and without activation in TA1538, TA98, and TA1537 strains and without activation in TA 1535 and TA100 strains when Disperse Blue 79 was administered in granular form (Life Science Research 1978) (Appendix 5).

In mutagenicity studies *in vitro*, Disperse Orange 30 was positive in *S. typhimurium* strains TA98, TA 100 and TA1537 with and without activation (RCC Group 1997a). An earlier study reported genotoxicity in strains TA98 and TA100 only with activation of S9 (no other information provided) (Ciba Geigy Corp 1986). It is noted that the Disperse Orange 30 product used in this study was of technical grade, not purified. Disperse Orange 30 was not clastogenic in bone marrow cells in mice *in vivo* (Baranski et al. 1992) (Appendix 5).

Disperse Red 54 was mutagenic for *S. typhimurium* TA97a, TA98 and TA100 both with and without activation (Baranski et al. 1992). A DNA repair assay in primary rat hepatocyte cultures *in vitro* showed that Disperse Red 54 induced a weak DNA repair synthesis (Palus et al. 1995). The authors suggested that the *in vivo* reduction of azo dyes is required for the genotoxicity. However, it was not clastogenic in bone marrow cells in mice *in vivo* (Baranski et al. 1992) (Appendix 5).

Disperse Orange 37 was positive in the *S. typhimurium* TA98 and YG1041 strains both with and without activation (Umbuzeiro et al. 2005) (Appendix 5).

Overall, empirical data from analogues showed positive mutagenicity and mixed results for other *in vitro* genotoxicity assays. However, the genotoxic potential in mammalian systems *in vivo* is less clear. The mainly negative results for *in vivo* genotoxicity assays, specifically the bone marrow assays, could be due to the low bioavailablity of the substance.

Non-cancer Effects – Potential Azo Cleavage Products

No empirical data were available to address non-cancer health effects associated with ANMOM. Limited empirical data was available for only one potential metabolite from azo cleavage. 2-bromo-6-chloro-4-nitroaniline was tested for acute oral dose toxicity, acute dermal toxicity, and acute inhalation toxicity. There were no deaths reported in any of these studies at the highest doses tested (50 m/kg-bw for oral; 200 mg/kg-bw for dermal; 2000 mg/m^3 for inhalation) (American Hoechst 1982a,b,c). However, the acute oral and dermal studies were not tested at the limit dose (2000 mg/kg-bw). In the oral toxicity study, isolated instances of chromorhinorrhea (coloured discharge from nose), were noted (no details provided) (American Hoechst 1982a). After acute dermal exposure to 2-bromo-6-chloro-4-nitroaniline, there were observations of bloated abdomen and adipsia in a few animals (no details provided) (American Hoechst 1982b). In the inhalation toxicity study, ptosis, piloerection and "yellow stained" bodies were noted in 5 or more out of 10 animals along with an isolated instance of chromorhinorrhea (American Hoechst 1982c). Results of QSAR predictions for developmental and reproductive endpoints were negative for 2-bromo-6-chloro-4-nitroaniline. For the other potential azo cleavage product of ANMOM (Cleavage Product 2), predictions for developmental toxicity were positive (Model Applier and CASETOX). Predictions for reproductive effects were negative for this substance (Appendix 6).

Non-cancer Effects - Analogue Azo Dyes

Empirical health effects data was available for two of the five analogues used in this assessment. Acute oral and dermal studies administered Disperse Blue 79 showed that LD_{50} values were greater than the limit dose of 2000 mg/kg-bw (See Appendix 5) (Crompton & Knowles 1987). Disperse Blue 79:1 was tested for acute, short-term, and subchronic toxicity using male and female Sprague Dawley rats (5 per group) via oral gavage at concentrations ranging from 0 to 2500 mg/kg (per day). In all three studies, no treatment-related differences in mortality, food consumption, body weights, ophthalmic examinations, clinical pathology, organ weights, final body weights, or histopathology were observed after acute, 14 and 90 days of exposure (Van Miller and Wagner 1991).

The effect of Disperse Blue 79:1 on development was examined in both rabbits and rats. Disperse Blue 79:1 was administered (0 to 600 mg/kg-bw per day, 16 per dose) by oral gavage to New Zealand white rabbits during gestation days 6 through to 18 (13 days), which resulted in maternal toxicity at 300 and 600 mg/kg-bw per day and a slight, but not

statistically significant, reduction in foetal body weight at 600 mg/kg-bw per day. The lowest-observed-adverse-effect level (LOAEL) for maternal toxicity was 300 mg/kg-bw based on a reduction in maternal weight gain during gestation (Tyl et al. 1991). A similar study using Sprague Dawley rats (dosed during days 6 to 15 of gestation) showed no maternal or foetal toxicity at similar and higher doses (Appendix 5) (Tyl et al. 1990).

Toxicokinetics

No data were identified on the toxicokinetics of ANMOM or its potential azo cleavage products.

A study using Disperse Blue 79:1 in rats (4 per sex per group) showed that the recovery of 85 to 91% of the administered single doses (0, 50 or 500 mg/kg-bw in corn oil) of Disperse Blue 79:1 in the faeces, indicates that it is not likely to be extensively absorbed in the gastrointestinal tract following oral ingestion. Excretion of radioactivity was virtually complete by 48 hours with less than 1% of the faecal radioactivity excreted between 48 and 96 hours. Small amounts were also found in urine (~5%), expired carbon dioxide (0.02–0.10%), tissues (0.03–0.14%), and in the carcass/pelt (0.00–1.40%) (Frantz et al. 1991).

Characterization of Risk to Human Health

In the absence of empirical health effects information on ANMOM, relevant health effects data on analogues and cleavage products were considered in the hazard characterization for human health. The selected analogues include Disperse Blue 79:1 (CAS RN 3618-72-2),Disperse Blue 79 (CAS RN 12239-34-8),Disperse Orange 30 (CAS RN 5261-31-4),Disperse Red 54 (CAS RN 6657-37-0), and Disperse Orange 37 (CAS RN 13301-61-6) (Appendix 5). The potential cleavage products identified were 2-bromo-6-chloro-4-nitroaniline (CAS RN 99-29-6) and a second product (Cleavage Product 2; no CAS RN).

Empirical data from analogues showed positive mutagenicity results for the five analogues and mixed results for other *in vitro* genotoxicity assays. Although no chemical-specific information on azo reduction of ANMOM was identified, it was still considered appropriate to characterize the hazard of potential azo cleavage products. No non-acute empirical health effects data were identified for ANMOM cleavage products. Mixed genotoxicity and carcinogenicity QSAR predictions were obtained for both potential cleavage products. Additionally, two QSAR models predicted positive results for developmental toxicity for Cleavage Product 2.

Therefore, although limited, the health effects data obtained for analogues and potential cleavage products of ANMOM indicate that there may be a potential hazard associated with this substance. However, the limited information available precludes selection of a critical effect level for use in risk characterization of ANMOM.

The potential for exposure of the general population to ANMOM from environmental media is expected to be low. The general population may be exposed to ANMOM from its potential use as a dye in textiles and fabrics; however, the estimated potential dermal and oral exposure is expected to be low.

Although ANMOM is recognized as having potentially hazardous properties based on the available health effects information on the analogues and potential metabolites of ANMOM, exposure for the general population of Canada to this substance is expected to be low, and consequently, the potential risk to human health is considered to be low at current levels of exposure.

Uncertainties in Evaluation of Risk to Human Health

The confidence in the health effects database for ANMOM is considered to be low. Due to the absence of empirical data on health effects related to ANMOM, the human health risk assessment is mainly based on limited health effects data on its analogues and potential cleavage products.

Uncertainty regarding the hazard potential of ANMOM is high due to lack of empirical health effects data for ANMOM; lack of data on the potential for ANMOM to undergo azo cleavage, limited health effects empirical data for the potential direct cleavage products of ANMOM; and inconclusive QSAR predictions.

There are uncertainties associated with the exposure assessment. The sources of exposure for ANMOM have been broadly characterized as synthetic fabrics and conservatively assumed to include clothing and fabrics available for mouthing by infants and toddlers. However, confidence is high that the modelled exposure values presented in this assessment overestimate actual exposure due to conservative nature of assumptions used.

Conclusion

Based on the information presented in this draft screening assessment, it is proposed that ANMOM is 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. Additionally, ANMOM meets the criteria for persistence but not for bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Based on the currently available information on its potential to cause harm to human health, it is proposed that ANMOM is 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 therefore proposed that ANMOM does not meet any of the criteria under section 64 of CEPA 1999.

Considerations for Follow-up

ANMOM belongs to a group of azo substances that may metabolize to aromatic amines, which as a chemical class are known to exhibit hazardous properties, including carcinogenicity. Therefore, additional activity (e.g. research, assessment, monitoring and surveillance) to characterize the risk to human health in Canada of this broader group of azo substances may be undertaken. A Notice of Intent outlining how Health Canada and Environment Canada will address this group of substances is available at the following Internet address: http://www.chemicalsubstanceschimiques.gc.ca/plan/approach-approche/azo_benzidine-eng.php

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Appendix 1 - Robust Study Summary

Robust Study Summaries Form: Aquatic B				
No.	**Item**	**Weight**	**Yes/No**	**Specify**
1	**Reference:** Shen G, Hu S. 2008. Bioconcentration test of C.I. Disperse Orange 30 in fish. Prepared by Environmental Testing Laboratory, Shanghai Academy of Environmental Sciences, Shanghai, China for Dystar in the name of Ecological and Toxicological Association of the Dyes and Organic Pigments Manufacturers (ETAD) Basel, Switzerland. Report No. S-070-2007. Submitted to Environment Canada in April 2008. Challenge Submission ID#8351			
2	Substance identity: CAS RN	n/a‡	Y	5261-31-4
3	Substance identity: chemical name(s)	n/a	Y	Propanenitrile, 3-[[2-(acetyloxy)ethyl][4-[(2,6-dichloro-4-nitrophenyl)azo]phenyl]amino]-
4	Chemical composition of the substance	2	N	
5	Chemical purity	1	N	
6	Persistence/stability of test substance in aquatic solution reported?	1	N	
7	If test material is radiolabelled, were precise position(s) of the labelled atom(s) and the percentage of radioactivity associated with impurities reported?	2	N	
	Method			
8	Reference	1	Y	OECD guidelines for the testing of chemicals No 305B-1996
9	OECD, EU, national or other standard method?	3	Y	OECD
10	Justification of the method/protocol if a nonstandard method was used	2		Not applicable
11	GLP (good laboratory practice)	3	N	
Test organism	***Test organism***			
12	Organism identity: name	n/a	*Y*	Zebra fish, *Brachydanio rerio*
13	Latin or both Latin and common names reported?	1	Y	Both
14	Life cycle age / stage of test organism	1	N	
15	Length and/or weight	1	Y	Mean body length 3.91+/-0.18 cm and mean body weight 0.32+/-0.06 g
16	Sex	1	N	
17	Number of organisms per replicate	1	Y	7
18	Organism loading rate	1	Y	20 mg/L
19	Food type and feeding periods during the acclimation period	1	Y	Fed a commercial fish diet until one day before start of test
	Test design / conditions			
20	Experiment type (laboratory or field)	n/a	Y	Laboratory
21	Exposure pathways (food, water, both)	n/a	Y	Water
22	Exposure duration	n/a	Y	28 days
23	Number of replicates (including controls)	1	Y	
24	Concentrations	1	Y	20 mg/L
25	Food type/composition and feeding periods during the test	1	Y	Fish were fed two hours before water renewal

‡ n/a = not applicable

26	If BCF/BAF derived as a ratio of chemical concentration in the organism and in water, was experiment duration equal to or longer than the time required for the chemical concentrations to reach steady state?	3	Y	28 days
27	If BCF/BAF derived as a ratio of chemical concentration in the organism and in water, were measured concentrations in both water and organism reported?	3	Y	
28	Were concentrations in the test water measured periodically?	1	Y	On three separate days
29	Were the exposure media conditions relevant to the particular chemical reported? (e.g., for metal toxicity - pH, DOC/TOC, water hardness, temperature)	3	Y	Yes, every second day
30	Photoperiod and light intensity	1	Y	12:12
31	Stock and test solution preparation	1	Y	
32	Analytical monitoring intervals	1	Y	Every second day for dissolved oxygen, pH and temperature
33	Statistical methods used	1	Y	
34	Was solubilizer/emulsifier used if the chemical was unstable or poorly soluble?	n/a	N	
	Information relevant to the data quality			
35	Was the test organism relevant to the Canadian environment?	3	Y	
36	Were the test conditions (pH, temperature, DO, etc.) typical for the test organism?	1	Y	
37	Does system type and design (static, semi-static, flow-through; sealed or open; etc.) correspond to the substance's properties and organism's nature/habits?	2	Y	Semi-static
38	Was pH of the test water within the range typical for the Canadian environment (6 to 9)?	1	Y	7.22–7.84
39	Was temperature of the test water within the range typical for the Canadian environment (5 to 27°C)?	1	Y	22–23
40	Was lipid content (or lipid-normalized BAF/BCF) reported?	2	Y	
41	Were measured concentrations of a chemical in the test water below the chemical's water solubility?	3	N	
42	If radiolabelled test substance was used, was BCF determination based on the parent compound (i.e., not on total radiolabelled residues)?	3	N	
	Results			
43	Endpoints (BAF, BCF) and values	n/a	n/a	BCF
44	BAF or BCF determined as: 1) the ratio of chemical concentration in the organism and in water, or 2) the ratio of the chemical uptake and elimination rate constants	n/a	n/a	1
45	Was BAF/BCF was derived from a 1) tissue sample or 2) whole organism?	n/a	n/a	2
46	Was 1) average or 2) maximum BAF/BCF used?	n/a	n/a	1
47	***Score*: .%**	***67.9***		
48	***EC reliability code*:**	***2***		
49	***Reliability category (high, satisfactory, low)*:**	***Satisfactory Confidence***		

50	***Comments***	*The present procedure is based on semi-static conditions (renewal of test solutions every 2 days). Therefore, test chemicals with very low water solubility like the disazo dyes can also be characterized as to their bioconcentration potential without adding solvents or other auxiliary substances that may affect the results.*

Robust Study Summaries Form: Aquatic iT				
No	**Item**	**Weight**	**Yes/No**	**Specify**
1	Reference: BASF. 1990. Bericht uber die Prufung der akuten Toxizitit an der Goldorfe (*Leuciscus idus L.,. Goldvariante*). Submitted by ETAD to Environment Canada, August 2008.			
2	Substance identity: CAS RN	n/a[§]		
3	Substance identity: chemical name(s)	n/a		
4	Chemical composition of the substance	2	N	
5	Chemical purity	1	N	
6	Persistence/stability of test substance in aquatic solution reported?	1	N	
Method				
7	Reference	1	N	
8	OECD, EU, national or other standard method?	3	N	
9	Justification of the method/protocol if a nonstandard method was used	2	N	
10	GLP (good laboratory practice)	3		
Test organism				
11	Organism identity: name	n/a	Y	Golden orfe
12	Latin or both Latin and common names reported?	1	Y	
13	Life cycle age / stage of test organism	1	N	
14	Length and/or weight	1	N	

[§] n/a = not applicable

15	Sex	1	N	
16	Number of organisms per replicate	1	N	
17	Organism loading rate	1	N	
18	Food type and feeding periods during the acclimation period	1	N	
Test design / conditions				
19	Test type (acute or chronic)	n/a	Y	Acute
20	Experiment type (laboratory or field)	n/a	N	
21	Exposure pathways (food, water, both)	n/a	N	
22	Exposure duration	n/a	Y	96 hr
23	Negative or positive controls (specify)	1	N	
24	Number of replicates (including controls)	1	N	
25	Nominal concentrations reported?	1	N	
26	Measured concentrations reported?	3	N	
27	Food type and feeding periods during the long-term tests	1		Not applicable
28	Were concentrations measured periodically (especially in the chronic test)?	1	N	
29	Were the exposure media conditions relevant to the particular chemical reported? (e.g., for metal toxicity - pH, DOC/TOC, water hardness, temperature)	3	N	
30	Photoperiod and light intensity	1	N	
31	Stock and test solution preparation	1	N	
32	Was solubilizer/emulsifier used if the chemical was poorly soluble or unstable?	1	N	
33	If solubilizer/emulsifier was used, was its concentration reported?	1	N	
34	If solubilizer/emulsifier was used, was its ecotoxicity reported?	1	N	
35	Analytical monitoring intervals	1	N	
36	Statistical methods used	1	N	
Information relevant to the data quality				
37	Was the endpoint directly caused by the chemical's toxicity, not by the organism's health (e.g., when mortality in the control > 10%) or physical effects (e.g., "shading effect")?	n/a	N	
38	Was the test organism relevant to the Canadian environment?	3	Y	
39	Were the test conditions (pH, temperature, DO, etc.) typical for the test organism?	1	N	

40	Does system type and design (static, semi-static, flow-through; sealed or open; etc.) correspond to the substance's properties and organism's nature/habits?	2	N	
41	Was pH of the test water within the range typical for the Canadian environment (6 to 9)?	1	N	
42	Was temperature of the test water within the range typical for the Canadian environment (5 to 27°C)?	1	N	
43	Was toxicity value below the chemical's water solubility?	3		
Results				
44	Toxicity values (specify endpoint and value)	n/a		LC_{50} = > 100 < 220 mg/L
45	Other endpoints reported - e.g., BCF/BAF, LOEC/NOEC (specify)?	n/a		NOEC = 100 mg/L
46	Other adverse effects (e.g., carcinogenicity, mutagenicity) reported?	n/a		
47	***Score*: %**			***9.5***
48	***EC reliability code*:**			***4***
49	***Reliability category (high, satisfactory, low)*:**			***Not Satisfactory***
50	***Comments***			***Not enough data submitted to properly assess the reliability of this study.***

Robust Study Summaries Form and Instructions: Aquatic iT				
No	**Item**	**Weight**	**Yes/No**	**Specify**
1	Reference: Cohle P and R Mihalik. 1991. Early life stage toxicity of C.I. Disperse Blue 79:1 purified presscake to rainbow trout (*Oncorhynchus mykiss*) in a flow-through system.			
2	Substance identity: CAS RN	n/a		
3	Substance identity: chemical name(s)	n/a		Disperse Blue 79:1
4	Chemical composition of the substance	2	Y	
5	Chemical purity	1	Y	96.61
6	Persistence/stability of test substance in aquatic solution reported?	1	N	
Method				
7	Reference	1	Y	
8	OECD, EU, national or other standard method?	3	Y	ASTM 1983

9	Justification of the method/protocol if a nonstandard method was used	2		Not applicable
10	GLP (good laboratory practice)	3	Y	
Test organism				
11	Organism identity: name	n/a		Rainbow trout
12	Latin or both Latin and common names reported?	1	Y	
13	Life cycle age / stage of test organism	1	Y	
14	Length and/or weight	1	Y	
15	Sex	1		Not applicable
16	Number of organisms per replicate	1	Y	20
17	Organism loading rate	1	Y	0.36 to 4.8µg/L
18	Food type and feeding periods during the acclimation period	1	Y	
Test design / conditions				
19	Test type (acute or chronic)	n/a	Y	Chronic
20	Experiment type (laboratory or field)	n/a	Y	Lab
21	Exposure pathways (food, water, both)	n/a	Y	Water
22	Exposure duration	n/a	Y	122 days
23	Negative or positive controls (specify)	1	Y	Control and carrier blank
24	Number of replicates (including controls)	1	Y	2
25	Nominal concentrations reported?	1	Y	5
26	Measured concentrations reported?	3	Y	
27	Food type and feeding periods during the long-term tests	1	Y	
28	Were concentrations measured periodically (especially in the chronic test)?	1	Y	
29	Were the exposure media conditions relevant to the particular chemical reported? (e.g., for metal toxicity - pH, DOC/TOC, water hardness, temperature)	3	Y	
30	Photoperiod and light intensity	1	Y	
31	Stock and test solution preparation	1	Y	

32	Was solubilizer/emulsifier used if the chemical was poorly soluble or unstable?	1	Y	
33	If solubilizer/emulsifier was used, was its concentration reported?	1	Y	
34	If solubilizer/emulsifier was used, was its ecotoxicity reported?	1	Y	No tox value but it was used as a control
35	Analytical monitoring intervals	1	Y	
36	Statistical methods used	1	Y	
Information relevant to the data quality				
37	Was the endpoint directly caused by the chemical's toxicity, not by the organism's health (e.g., when mortality in the control > 10%) or physical effects (e.g., "shading effect")?	n/a	Y	
38	Was the test organism relevant to the Canadian environment?	3	Y	
39	Were the test conditions (pH, temperature, DO, etc.) typical for the test organism?	1	Y	
40	Does system type and design (static, semi-static, flow-through; sealed or open; etc.) correspond to the substance's properties and organism's nature/habits?	2	Y	Flow-through
41	Was pH of the test water within the range typical for the Canadian environment (6 to 9)?	1	Y	
42	Was temperature of the test water within the range typical for the Canadian environment (5 to 27°C)?	1	Y	
43	Was toxicity value below the chemical's water solubility?	3		Cannot assess. Highest dose tested believed to be at limit of solubility.
Results				
44	Toxicity values (specify endpoint and value)	n/a	n/a	NOEC > 0.005 mg/L
45	Other endpoints reported - e.g., BCF/BAF, LOEC/NOEC (specify)?	n/a		
46	Other adverse effects (e.g., carcinogenicity, mutagenicity) reported?	n/a		
47	***Score*: %**	***97.7***		
48	***EC reliability code*:**	***1***		
49	***Reliability category (high, satisfactory, low)*:**	***High Confidence***		
50	***Comments***	***However, this value was not used to calculate the predicted no-effect concentration because the value is an unbounded result (i.e., no certainty as to the threshold for effects).***		

Appendix 2 – PBT Model Inputs Summary Table

	Phys-Chem/Fate
Model Input Parameters	EPIWIN Suite (all models, including: AOPWIN, KOCWIN, BCFWIN BIOWIN and ECOSAR)
SMILES Code	O=C(OC)CCN(c(ccc(N=Nc(c(cc(N(=O)(=O))c1)Cl)c1Br)c2)c2)CCC(=O)OC

Appendix 3. Upper-bound Estimates of Exposure to ANMOM in Textiles

Scenario	**Upper-bounding estimates of exposure as internal dose (µg/kg-bw per day) of ANMOM by various age groups.[1]**				
	0–6 months[2]	**0.5–4 years[3]**	**5–11 years[4]**	**12–19 years[5]**	**20+ years[6]**
wearing of textile (dermal exposure)	0.224 – 3.73	0.178 – 2.97	0.155 – 2.58	0.141 – 2.36	0.135 – 2.26
Child mouthing textile (oral exposure)	0.031	0.015	N/A	N/A	N/A

Abbreviations: N/A, not applicable.

[1] Refer to Appendix 4 for details of exposure derivations. Upper-bounding leachable fraction was estimated to range from 0.03% for colourfast textiles (ETAD 2004) to 0.5% for textiles with poor colourfastness (Kraetke and Platzek 2005).

[2] Assumed to weigh 7.5 kg, have body surface area (excluding head and hands) of 0.28 m^2 (Health Canada 1998) and spend 23 min/d mouthing (Norris and Smith 2002).

[3] Assumed to weigh 15.5 kg, have body surface area (excluding head and hands) of 0.46 m^2 (Health Canada 1998) and spend 29 min/d mouthing (Norris and Smith 2002).

[4] Assumed to weigh 31.0 kg and have body surface area (excluding head and hands) of 0.80 m^2 (Health Canada 1998).

[5] Assumed to weigh 59.4 kg and have body surface area (excluding head and hands) of 1.4 m^2 (Health Canada 1998).

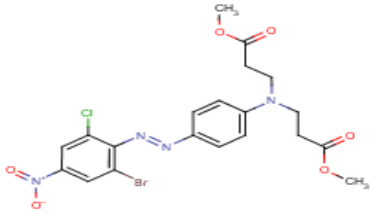
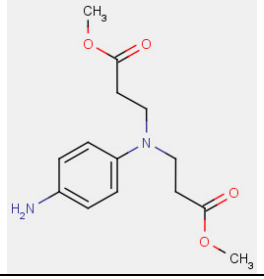
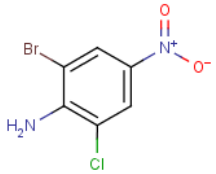
[6] Assumed to weigh 70.9 kg and have body surface area (excluding head and hands) of 1.6 m^2 (Health Canada 1998).

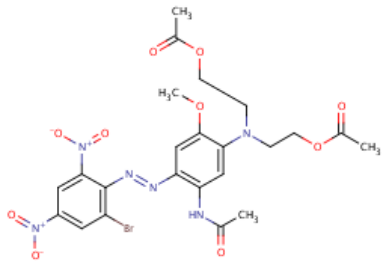
Appendix 4: Exposure Estimates from Dyed Textiles (example calculation for infants of age 0 to 6 months).

Consumer product scenario	Assumptions	Upper-bound estimate of exposure
Wearing of dyed clothing made from synthetic fabrics	Exposure scenario: ConsExpo 4.0, direct dermal contact with product: migration (RIVM 2005). Concentration: 1% by weight (Kraetke and Platzek 2005) Fabric density: 100 g/m^2 (Kraetke and Platzek 2005) **General assumptions** - Body weight: 7.5 kg (Health Canada 1998) - Body surface area excluding head, face and hands: 0.28 m^2 (Health Canada 1998) **Dermal route** - Exposed area: 1.6 m^2 (Health Canada 1998) - Leachable fraction: 0.5% (Kraetke and Platzek 2005) - Product amount[1]: 0.28 g - Skin contact factor: 1 (fraction) - Uptake fraction: 2% (Kraetke and Platzek 2005)	**Dermal chronic** Internal dose = 3.73 µg/kg-bw per day
Mouthing of dyed fabrics	The estimated daily intake for ingestion from mouthing: $= \frac{WS \times V_s \times CF \times FR \times AF_o \times EF}{BW}$ where; *WS* = modelled water solubility of ANMOM (Table 3) = 9.2 mg/L (Baughman and Perenich 1988) V_s = salivary flow rate = 0.22 mL/min (Environ 2003a, b) *CF* = Convert L to mL = 0.001 L/mL *FR* = Fractional extraction by saliva = 0.5% (ETAD 1983)[2] AF_o = Absorption factor by oral =1 *EF*= Exposure frequency of mouthing behaviour = 23 min/d (Norris and Smith 2002) *BW* = body weight = 7.5 kg (infants, age 0–6 months) (Health Canada 1998) The estimated daily intake for ingestion from mouthing = (9.2 mg/L × 0.22 mL/min × 0.001 L/mL × 0.005 × 1 × 23 min)/7.5 kg = 3.1x10^{-5} mg/kg-bw per day = 0.031 µg/kg-bw per day	**Oral chronic** Internal dose = 0.031 µg/kg-bw per day

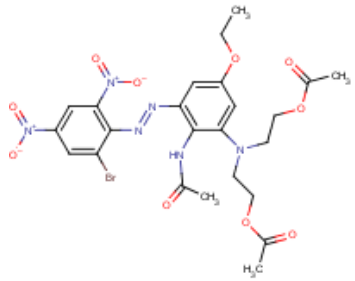
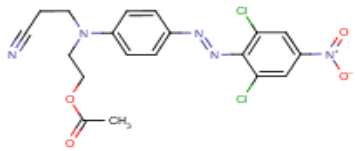
[1] Maximum amount of dye extracted by simulated saliva from child oriented synthetic textiles after 4 hours was 0.13%, 0.5% is used to represent an upper bound.

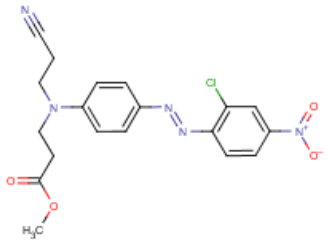
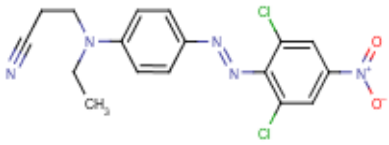
Appendix 5: Structures for ANMOM, its Analogues and Potential Cleavage Products and Data Considered in Characterization of Human Health Effects

CASN	Name	% Similarity	Structure	Data considered/available
59709-38-5	ANMOM [parent]	100%		QSAR (See Appendix 6).
Potential Cleavage Products				
No CAS number available		100%		QSAR (See Appendix 6).
99-29-6	2-bromo-6-chloro-4-nitroaniline	100%		**Acute Oral Toxicity (LD50, rats) >** 50 mg/kg (highest dose tested) in male Wis rats (10) where isolated instances of chromorhinorrhea were noted (no details provided) (American Hoechst 1982a). **Acute Dermal Toxicity (LD50, rats) >** 200 mg/kg (highest dose tested) in NZ v rabbits where there were observations of bloated abdomen and adipsia in a few animals (no details provided) (American Hoechst 1982b).

				Acute Inhalation Toxicity (LD50, rats) > 2000 mg/m^3 (highest dose tested) in Wistar rats (10) where ptosis, piloerection and "yellow stained" bodies were not 5 or more animals along with an isolated instance of chromorhinorrhea (no detai provided) (American Hoechst 1982c). QSAR (See Appendix 6).
Analogues				
3618-72-2	Disperse Blue 79:1 (DB 79:1)	71.5%		**Acute Oral Toxicity (LD50, rats) = >**2500 mg/kg (Van Miller & Wagner 1991) **Short Term Toxicity:** Oral NOEL = 2500 mg/kg. Male and female SD rats (5 p group) were administered DB 79:1 by oral gavage (0, 100, 500, 1000, or 2500 mg/kg-bw per day) 5 days/wk for 2 weeks. No treatment-related effects were observed (Van Miller & Wagner 1991). **Subchronic Toxicity:** Oral NOEL = 2500 mg/kg/day. Male and female SD rats per group) were administered the test substance by oral gavage (0, 100, 500, 100 2500 mg/kg-bw per day) 5 days/wk for 13 weeks. No treatment-related effects w observed (Van Miller & Wagner 1991). **Genotoxicity *in vitro:*** **Positive**: in *S. typhimurium* TA1537, TA1538, TA98, and TA100 strains with an without activation (Clariant 1982). **Negative** for mammalian cell gene mutation in Chinese Hamster Lung (CHL) Fibroblasts (V79) with and without metabolic activation (Clariant 1996). **Positive** in CHL cells for structural changes after 24hr and 48 hr treatment after incubation with 0.01 – 0.03 mg/ml application (JCIETIC 1997). **Genotoxicity *in vivo:*** **Negative** for chromosomal abberations (MN) in bone marrow of NMRI mice (m and female) by oral gavage of doses up to 5000 mg/kg (Clariant 1996). **Negative** in the *Drosophila* sp. SLRL test for sex-linked recessive gene mutation

				adult males exposed by injection to 50 ppm of DB 79:1 (Foureman 1990). **Developmental Toxicity:** Maternal LOAEL (oral) = 300 mg/kg-bw Developmental LOAEL (oral) = 600 mg/kg-bw DB 79:1 administered (0, 100, 300, 600 mg/kg-bw per day) to New Zealand Wh rabbits (16 per dose) by gavage during gestation days 6 to 18 (13 days) resulted i reduced maternal weight gain at 300 and 600 mg/kg-bw per day and a slight reduction in foetal body weight (males, but not females) at 600 mg/kg-bw per da (not statistically significant and unaccompanied by any other indications of developmental toxicity). There was no evidence of teratogenicity at any dose tes Gravid uterine and liver weights were unaffected by treatment. Food consumptio was equivalent across all doses except for a significant increase at 600 mg/kg/da days 6 through 9. Pre- and post-implantaton loss and foetal body weights per litt (gestational), were statistically equivalent across all groups (Tyl et al 1991). **Developmental and maternal NOEL (oral)** = 2000 mg/kg-bw per day DB 79:1 administered by gavage (0, 500, 1000, or 2000 mg/kg-bw per day in co oil) in SD rats (for 10 days; days 6 to 15 of gestation) resulted in no maternal or developmental toxicity at any dose tested (Tyl et al 1990).

12239-34-8	Disperse Blue 79	71%		**Acute Oral Toxicity (LD50, rats)** > 5000 mg/kg and 5000 ml/kg (Life Science Research 1978) **Acute Dermal Toxicity (LD50, rabbits)** > 2000 mg/kg (Crompton & Knowles 1987). **Genotoxicity *in vitro:*** **Positive**: in *S. typhimurium* TA1535, TA1537, TA1538, TA98, and TA10 strains with activation in liquid form and in TA 1535 and TA100 in granular for (Crompton & Knowles Corp 1987). **Positive** with and without activation in TA1 TA98, and TA1537 in granular form (Life Science Research 1978; Crompton & Knowles Corp 1987). **Eye/Skin Irritation and Sensitization:** Mild to no irritation to eye or skin of NZ white rabbits in liquid form, but slight irritation to the skin in granular form (Life Science Research 1978; Crompton & Knowles Corp 1987). Slight sensitization to skin of Guinea Pigs at 10% concentration in liquid form, b no sensitization in granular form (Life Science Research 1978).
5261-31-4	Disperse Orange 30	79.9%		**Genotoxicity**: **Positive:** in *S. typhimurium* strains TA98, TA1537, and TA100 both with and without S9 activation; TA1535 with S9 activation (RCC Group 1997a). **Positive:** in *S. typhimurium* TA98 and TA100 strains with activation of S9 (CIB Geigy Corp 1986). **Negative:** in *in vivo* mouse bone marrow micronucleus test (Baranski et al 1992) **Sensitization**: **Positive:** Maximization test in female albino Guinea Pigs (RCC Group 1997b). **Negative:** in Local lymph node assay with NMRI mice (Stahlmann et al. 2006).

6657-37-0	Disperse Red 54	82.6%		**Genotoxicity:** **Positive:** in *S. typhimurium* strains TA97a, TA98 and TA100 both with and with activation (Baranski et al. 1992).* **Positive (weak):** for DNA Repair in rat hepatocytes *in vitro* (Palus et al 1995). **Negative:** in *in vivo* mouse bone marrow micronucleus test (Baranski et al 1992) **Positive:** in *in vivo* Sister Chromatid Exchange assay in SFIS mice (Baranski et 1992).
13301-61-6	Disperse Orange 37	77.7%		**Genotoxicity**: **Positive:** in *S. typhimurium* strains TA98 (frameshift mutations) and YG1041 bo with and without activation (Umbuzeiro et al. 2005). **Sensitization**: **Positive:** Maximization test in female Dunkin-Hartley Guinea Pigs (Safepharm Laboratories 1994).

* Baranski et al. (1992) is in Polish; details obtained from Palus et al. (1995).

Appendix 6: Summary of QSAR Results for ANMOM (59709-38-5) and Potential Cleavage Products

Carcinogenicity

Name	CAS RN	Model Applier[1]				CASETOX[2]				TOPKAT[3]				DEREK[4]
		m-rat	f-rat	m-mice	f-mice	m-rat	f-rat	m-mice	f-mice	NTP m-rat	NTP f-rat	NTP m-mice	NTP f-mice	Mammalian species*
ANMOM	59709-38-5 (parent)	ND	ND	ND	ND	IC	IC	IC	IC	IC	IC	IC	IC	P
Potential Cleavage Product 1	99-29-6	N	N	P	N	N	N	N	N	P	IC	IC	IC	P
Potential Cleavage Product 2	N/A	N	N	N	N	N	N	N	N	P	IC	N	N	ND

CAS RN = Chemical Abstracts Registry Number.
ND – not in domain of model (model indicates query chemical to be outside of it's applicability domain); IC – inconclusive (unreliable prediction based on user-defined model specific criteria other than model's applicability domain); P – positive; N- negative; M – Marginal (0.4-0.6 probability as determined by the regression model of MA).
[1] Leadscope Model Applier [Prediction module]. 2009. Version 1.2.0-3. Columbus, OH: Leadscope, Inc. [cited 2010 Aug]. Available from: http://www.leadscope.com/all_products.php [restricted access].
[2] [CASETOX] [Prediction module]. 2010. Version 2.0. Beachwood (OH): MultiCASE. [cited 2010 Aug]. Available from: http://www.multicase.com/products/prod03.htm [restricted access].
[3] [TOPKAT] TOxicity Prediction by Komputer Assisted Technology [Internet]. 2004. Version 6.2. San Diego (CA): Accelrys Software Inc. [cited 2010 Aug]. Available from: http://www.accelrys.com/products/topkat/index.html
[4] [DEREK] - Deductive Estimation of Risk from Existing Knowledge [Prediction module on CD ROM]. 2008. Version 10.0.2. Cambridge (MA): Harvard University, LHASA Group. [cited 2010 Aug]. Available from: http://www.lhasalimited.org/index.php?cat=2&sub_cat=2# [restricted access].
* Dog, guinea pig, hamster, human, mammal, monkey, mouse, primate, rabbit, rat, rodent.

Genotoxicity

Name	CAS RN	Ames				Chromosome Aberration				Micronuclei Induction		Mouse Lymphoma mutation		DNA Damage
		MA[1]	CT[2]	TK[3]	DK[4]	MA		CT	DK	MA	CT	MA	CT	MA
						in vitro	*in vivo*							
ANMOM	59709-38-5 (parent)	P	IC	IC	P	P	ND	P	IC	N	IC	ND	IC	N
Potential Cleavage Product 1	99-29-6	P	N	P	P	P	N	N	IC	N	N	M	N	N
Potential Cleavage Product 2	N/A	N	IC	ND	ND	P	ND	P	P	N	N	ND	P	ND

CAS RN = Chemical Abstracts Registry Number,
ND – not in domain of model; IC – inconclusive; P – positive; N- negative.

1. MA = Model Applier
2. CT = CASETOX
3. TK = TOPKAT
4. DK = DEREK

Name	CAS RN	Developmental			MA only
		TOPKAT	Model Applier	CASETOX	
ANMOM	59709-38-5 (parent)	IC	ND	IC	ND
Potential Cleavage Product 1	99-29-6	N	N	N	N
Potential Cleavage Product 2	N/A	ND	P (visceral organs)	P (rats)	N (male sperm)

Reproductive and Developmental

CAS RN = Chemical Abstracts Registry Number,
ND – not in domain of model; IC – inconclusive; P – positive; N- negative.
*Positive prediction (0.984) for effects on rat sperm.