Summary of Public Comments Received on the Government of Canada's Draft Screening Assessment Reports for Batch 1 Substances on the *Domestic Substances List*

The table below presents a summary of the comments received during the 60-day public comment period that took place from January 19, 2008, to March 19, 2008. Comments summarized below were received by one or more stakeholders.

Substances considered

- 2-Naphthalenecarboxamide, *N*-[4-(acetylamino)phenyl]-4-[[5-(aminocarbonyl)-2-chlorophenyl]azo]-3-hydroxy- (Pigment Orange 38), CAS RN 12236-64-5
- Benzenesulfonic acid, 4-[[3-[[2-hydroxy-3-[[(4-methoxyphenyl)amino]carbonyl]-1-naphthalenyl]azo]-4-methylbenzoyl]amino]-, calcium salt (2:1) (Pigment Red 187), CAS RN 43035-18-3
- 2-Naphthalenecarboxamide, 4-[[5-[[[4-(aminocarbonyl)phenyl]amino]carbonyl]-2-methoxyphenyl]azo]-*N*-(5-chloro-2,4-dimethoxyphenyl)-3-hydroxy- (Pigment Red 247:1), CAS RN 59487-23-9

No.	Comment	Response
Comments on solubility and toxicity		
1	... "The significant decrease of pigment solubility in octanol and water translates into changes for bioaccumulation and inherent toxicity data. It is unclear why there was such a shift in solubility data."...	Experimental values of good quality typically take precedence over modelled ones. Log K_{ow} is also often modelled using modelled water solubility, an approach that can compound errors in estimations. Experimental methods for determining K_{ow}, such as the shake flask method, generally exclude insoluble substances such as pigments. For this reason, industrial stakeholders have proposed to measure solubilities in water and octanol separately. The government has agreed that this approach is providing information that can be used in estimating the octanol/water partition coefficient. Detailed explanations to this effect are already provided in the Physical and Chemical Properties section of the screening assessment report (SARs).
2	..."Also, the modeled octanol/water partition coefficients were rejected as they indicated a higher octanol solubility for each of the three pigments. There were no explanations as to why the modeling coefficients were so inaccurate."...	
3	...."More scientific evidence should have been provided as to why the modeling coefficients were rejected."...	
4	... "For transparency reasons, the draft screening assessment documents should specify what certified standards were utilized for the new experimental solubility data and the original solubility data."...	There are no original solubility data. None of the experimental solubility studies reported having used reference chemicals of known solubilities. The evaluation of the key experimental solubility data was performed with the help of a robust study summary (RSS). These studies were considered to have a
5	"With respect to CAS RN 12236-64-5, 43035-18-3, and 59487-23-9, It is not clear from the assessment reports what	

	tests, if any, the government applied to validate the use of the experimental data for solubility in these assessments. Furthermore, it was also unclear from the assessments whether the experimental results followed the OECD Good Laboratory Practices to further validate the use of experimental data."	satisfactory degree of reliability, even though the criterion of testing a reference chemical was not met. The use of good laboratory practices is one of the considerations used in evaluating study quality.
6	"The results of the assessments on these three pigments would have been improved significantly if the survey applied during the industry challenge required the submission from industry of experimental data for developmental or other mammalian toxicity data on these substances. This type of data may have provided additional insight on how these substances are reacting in organisms exposed to these substances. The gaps in the assessment report on the use of analogues, combined with the absence of tests to validate the experimental data, raises some concern on the assessment conclusions for these substances."	The assessments would not have improved significantly with the submission of experimental data for developmental or other mammalian toxicity. Given the current release scenarios and quantities used in Canada, exposures through soils, suspended solids and sediment are not likely to be significant at this time, as indicated in the SAR. In these cases, because of the use of analogues, taken together with the exposure levels, the generation of new experimental data is not justified.
7	"With respect to on CAS RN 12236-64-5, 43035-18-3, and 59487-23-9, further investigation into the toxicity of these substances is warranted. It is premature to conclude that the three substances do not meet the criteria outlined under section 64 of CEPA."	Considering the current release scenarios, the quantities used in Canada and the low aquatic toxicities of these pigments, we have determined that further toxicological investigations are not needed at this time.
Comments on analogues		
8	..."The rationale for the inclusion of analogues for all three pigments was not identified in the draft screening documents. Apart from solubility parameters and possibility functionality (organic pigment – monoazo), other properties were not revealed as to how the analogues were chosen."...	Analogue data are frequently used to estimate toxicity and other chemical properties. Some important endpoints may be considered when determining an analogue for use in read-across and, in the present case, the crystalline nature of the pigments. Therefore, their solubilities in water and octanol are key ones.
9	..."The reasons and scientific guidelines used for the introduction of suitable analogues with similar solubility parameters should have been identified in the document."...	
10	"With respect to CAS Nos. 12236-64-5, 43035-18-3, and 59487-23-9, the	The analogue for a substance being evaluated has to belong to the same

	assessment reports provided insufficient information on what range of analogues were under consideration, how the analogues were selected, who supplied the information for the analogues (government or industry), and what features of the analogues determined suitability. Since the use of the analogues has significant implications for the determination of toxicity under CEPA for these three substances, we question why these analogues were not considered during the categorization phase, particularly in light of the fact that industry was given seven years to submit information to governments on these substances."	chemical category, and to provide a reliable experimental datum (or data) for use in read-across. Experimental data for analogues were primarily provided by the industry during the Challenge.
11	<u>Pigment Orange 38:</u> "For Pigment Orange 38 (i.e., CAS RN 12236-64-5), the analogue selected (Analog Pigment Red 2) was half the molecular weight of the substance. The assessment report should provide an adequate explanation of what impact this difference in molecular weight would have on the behaviour of the substance."	The analogue of PO 38 was Pigment Red 2 and the report did not indicate that it had a molecular weight lower than that of PO 38. In this case, solubility (not molecular weight) was a key element in read-across. Pigment Red 2 has a solubility in water of 5.4 µg L^{-1} and a solubility in octanol of 8.6 mg L^{-1}, this latter being roughly similar to that of PO 38.
12	..."In one case, the analogue for pigment orange 38 was identified as having a significantly lower molecular weight than pigment orange 38 but had comparable solubility parameters – depending on which one was chosen."...	
13	… "__Also, when an analogue with a significant difference in molecular weight is used, the rationale for such a choice should be readily available as molecular weight can influence the solubility of a substance."...	Molecular weight was not a key endpoint in the selection of analogues; solubility was.
Comment on bioaccumulation		
14	"It should also be noted that a study by Gobas et al. ((Kelly BC, Ikonomou G, Blair JD, Moriin A, and Gobas F A, 2007. Food web-specific biomagnification of persistent organic pollutants. Science. Vol 317: 236-238), noted that octanol-water partitioning cannot serve as a universal model for identifying bioaccumulative substances	Because of their very low vapour pressures and negligible Henry's Law constants, organic pigments are not expected to volatilize in receiving environments. Therefore, the air-to-lipid transfer pathway is not something to consider for these substances.

	in wildlife and humans, and that air to lipid transfer is an important consideration, particularly for low to moderately hydrophobic substances that bioaccumulate in food chains. It is unclear from the assessment reports whether this finding was taken into consideration when reviewing the experimental solubility data and the analogue data provided. If it has not already done so, the government ought to consider this factor in finalizing the adequacy of the data used, and therefore the use of analogues for bioaccumulation and inherent toxicity."	
15	The Draft SLRA for CAS No. 59487-23-9 (Pigment Red 187) states that this is an organic substance that is used in Canada and elsewhere primarily as a colour pigment in plastics, inks, paints and textiles, and is also used in the food and beverage sector. Its secondary use is as an inert ingredient in pesticides. Consideration of exposure to children, via food additives and personal care products, such as products applied to the skin, should be included in the use pattern questionnaire to industry and other stakeholders interested in this substance. It is unclear whether the Assessment addressed the migration of this pigment from food containers, or the fact that its possible use as a food additive may be another direct source of exposure to children. By way of example, three synthetic azo red-dyes used as food colour additives were examined, and because they induced colon DNA damage at a very low dose, starting at 10mg/kg the authors recommended that more extensive assessment of azo additives is warranted. (Tsuda S. et al. Toxicol Sci. 2001, May; 61(1): 92-9). A second study that investigated the effects of three azo dyes on mouse embryo culture cells pre-treated for 1 hr with S9-untreated azo dyes at concentrations of 0.3, 1.0, and 5 mM, found the cell growth was slightly reduced by 5 mM Ponceau 3R. All the S9-untreated azo dyes inhibited	Pigment Red 187 (CAS No. 59487-23-9) was categorized as a substance of high ecological concern and, therefore, the focus of the Challenge screening level risk assessment was on the potential ecological risks. The 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*. This substance remains subject to further assessment if information is identified that indicates that such evaluation is warranted.

	cell growth when added to the medium during cultivation (Okawa Y. et al. Shokuhin Eiseigaku Zasshi 1989; 30(6):496-500). The exposure routes and levels of exposure of children to these substances in consumer products should be required from industry and considered in these assessments.	