Summary of Public Comments Received on the Government of Canada's Draft Screening Assessment Report on Vinyl Acetate (CAS No. 108-05-4)

Formal comments made during the 60-day public comment period that took place from May 17, 2008 to June 16, 2008 on the draft screening assessment report on vinyl acetate monomer, a substance included in Batch 2 of substances to be addressed as part of the Chemicals Management Plan Challenge under the *Canadian Environmental Protection Act 1999* (CEPA 1999), were provide by the Vinyl Acetate and Emulsion Polymers Councils, Celanese Int. Inc., DOW, DuPont, Wacker Polymers, NACAN Products Ltd., Helmitin Inc., ASMAC, Home Hardware, Evalca, Halltech Inc., ASC, IfADo-Leibniz Research Centre, Lyondell, Roberts/ QEP Canada Ltd., Henkel Corporation, AVON, National Paint and Coating Association, Benjamin Moore, AkzoNobel, Ashland Canada Corp. Dural, Franklin International, SOCMA, MEDEC, Hexion, CEFIC, Reach for Unbleached, Canadian Environmental Law Association + Chemical Sensitivity Manitoba.

A summary of comments and responses is included below, organized by topic:

- Weight of evidence and precautionary principle
- International
- Human exposure and effects of human health
- Data collection
- Uses
- Food and consumer products
- Monitoring and research

TOPIC	COMMENT	RESPONSE
Weight of evidence and precautionary principle	Multiple public comments were received regarding the previous conclusion of the draft screening assessment that vinyl acetate be considered "toxic" under Section 64(c) of CEPA. While some submitters supported this approach, others argued that the draft screening assessment conclusion had been overly precautionary and did not consider the weight of evidence of new toxicology data. In particular, the submitters recommended that Health Canada consider a threshold mode of action for the carcinogenicity of vinyl acetate which has been recently proposed in the scientific literature and in risk assessments from Europe (e.g. EU RAR 2008).	Vinyl Acetate is part of the Challenge because as it was classified by the International Agency for Research on Cancer (IARC) as a "possible human carcinogen" (IARC 1995) and met the categorization criteria for greatest potential for human exposure. While preparing the draft screening assessment, the draft European Union Risk Assessment Report (EU RAR) for vinyl acetate was incomplete. External peer reviewers of the vinyl acetate draft screening assessment were asked if they considered the mode of action analysis, as presented in the unfinished draft EU RAR, to be sufficiently developed and the majority did not. Following the public comment period, the Government considered new toxicology data that corroborated the mode of action analysis in the draft EU RAR. This led the Government to conclude that the evidence supports a mode of action for vinyl acetate involving a

		threshold of exposure for induction of cancer via the inhalation route, the relevant route of exposure to humans. The use of precaution and weight of evidence in this decision was discussed with the Challenge Advisory Panel who supported the government approach. On this basis, the margin of exposure (MOE) between potential health effects and exposure to the general population from inhalation and from consumer products were considered to be adequately protective for Canadians. Therefore, the final screening assessment concluded that vinyl acetate was not "toxic" under Section 64(c) of CEPA.
International	Sections of the draft screening assessment with respect to health effects and exposure assessment were inconsistent with the draft European Union Risk Assessment Report (EU RAR 2008).	We acknowledge that there are differences between the EU draft RAR and the Canadian draft screening assessment. The Government of Canada is responsible for determining the health effects and exposures most relevant for consideration in a Canadian screening assessment. With respect to exposure, the differences are greater in the final screening assessment because data from a contemporary consumer products survey were used for determining Canadian exposures.
Human exposure and effects on human health	The Government should derive reference values (e.g. tolerable daily intake) for vinyl acetate.	Typically in the Challenge, derivation of reference values such as tolerable daily intake are beyond the scope of a screening level assessment. If necessary for risk management, they can be developed at a later date.
	It is recommended that LO(A)ECs (Lowest-Observed-[Adverse]-Effect Concentration) from a human respiratory irritation study by Smyth & Carpenter (1973) be used for calculation of MOEs (margins of exposure) from acute consumer exposure scenarios.	The consumer exposure MOE calculated in the draft screening assessment used an inhalation LO(A)EC of 528 mg/m3 from a 4 week study in mice (Owen 1979a) based on hunched posture and respiratory irritation. However, it is recognized that for comparisons against acute consumer exposures (i.e. minutes-hours) it may be more appropriate to use effect levels from acute toxicity studies. Also, whenever relevant studies in humans are available, this generally takes precedence over animal data. Therefore, the acute human irritation data from Smyth & Carpenter (1973) is used

		in the final screening assessment to calculate the MOE for acute inhalation exposure to consumer products.
	There are limitations in Health Canada's selection of a short-term inhalation (Lowest-Observed-[Adverse]-Effect Concentration) LO(A)EC of 528 mg/m3 (150 ppm) based on respiratory distress and hunched posture in mice following a 4-week inhalation exposure (Owen 1979a). An alternative short-term LO(A)EC of 2100 mg/m3 (600 ppm) based on nasal histopathological changes from a short-term study in rats (Bogdanffy et al. 1997) is recommended.	Health Canada recognizes the limitations submitted with regard to the selected short-term LO(A)EC of 528 mg/m3 (150 ppm) from the study by Owen (1979a). Specifically, it is noted that actual incidence data for the clinical effects of respiratory distress and hunched posture were not provided in this study and the results were only reported qualitatively. It is also noted that actual incidence data for these clinical effects were reported in a chronic (2-year) study by the same authors do not show any exposure related changes (Owen 1988, Bogdanffy et al. 1994a). However, the value of 150 ppm from Owen 1979a has been identified by the EU RAR (2008) as the LO(A)EC for this study based on local effects of the respiratory tract. Furthermore, the irritant properties of vinyl acetate have also been demonstrated following acute exposures in animals (Dudek et al. 1996) and in humans (Smyth & Carpenter 1973). On this basis, the value of 528 mg/m3 (150 ppm) has been maintained in the final screening assessment as a conservative lower end in a range of short-term inhalation LO(A)ECs. The upper end in this range is based on the value of 2110 mg/m3 (600 ppm) from the study by (Bogdanffy et al. 1997) as recommended in the public comments submitted. It should be noted that the comparison of this range of short-term inhalation LO(A)ECs with consumer products exposures gave MOEs (margins of exposure) of 3500 – 14000 which are considered to be adequately large to account for uncertainties in the exposure and effects databases. Additional limitations for the study by Owen (1979a) have been added to the final screening assessment.
	Public comments were received regarding the selection in the draft screening assessment of a chronic inhalation LO(A)EC of 10 mg/m3 (3 ppm) based on a study by Czajkowska et al. (1986). The public comments cited several limitations for this	The draft screening assessment previously identified the LO(A)EC from Czajkowska et al. (1986) as a lower end of the range of chronic inhalation LO(A)ECs based primarily upon the results as reported in the weight-of-evidence evaluation from IARC (1995) while several of the limitations for this study similar to those from

	study and recommended an alternative chronic LO(A)EC of 704 mg/m3 (200 ppm) based on a study in mice and rats (Bogdanffy et al. 1994a).	the public comments were also previously noted in the draft screening assessment. However, as an evaluation by SCOEL (2005) discounted the Czajkowska et al. study due to poor documentation, and since the study has not been cited in more recent assessments of vinyl acetate (EU RAR 2008, US EPA 2006b), this study is no longer considered in final screening assessment. The chronic inhalation LO(A)EC of 704 mg/m3 (200 ppm) based on the study by Bogdanffy et al. (1994a) was recommended in the public comments and was previously included in the draft screening assessment as an upper end in a range of chronic inhalation LO(A)ECs. For the final screening assessment, both the NO(A)EC (176 mg/m3, 50 ppm) and LO(A)EC (704 mg/m3, 200 ppm) from Bogdanffy et al. (1994a) have been used in the calculation of MOEs for general population chronic inhalation exposure from indoor air.
	An oral reproductive toxicity LO(A)EL (Lowest-Observed-[Adverse]-Effect Level) (700 mg/kg-bw/day, decreased mating performance, Mebus et al. 1995) is appropriate; however, the inhalation reproductive toxicity study cited in the draft screening assessment (Hurtt et al. 1995) was not designed to measure reproductive endpoints and should not be used in the draft screening assessment for selecting a reproductive toxicity NOAEC (No-Observed-[Adverse]-Effect Concentration).	In the study by Hurtt et al. (1995), pregnant rats were exposed to vinyl acetate by inhalation from gestational days (GD) 5-16 with sacrifice on GD20. This type of exposure period is designed to study developmental toxicity effects during the period of major embryo organogenesis (Hood 2006) and is not designed to measure reproductive toxicity even though results for several "reproductive parameters" are reported in Hurtt et al. (1995). Health Canada concurs with the public comment that Hurtt et al. (1995) should not be considered as a study of reproductive toxicity whereas Mebus et al. (1995) is sufficient for this purpose. For the purposes of the final screening assessment and in order to avoid any unnecessary confusion regarding terminology, the data from Mebus et al. (1995) and Hurtt et al. (1995) will be summarized together in the Appendix under a combined section for Reproductive & Developmental Toxicity.
	There are limitations in the selection of the lowest developmental inhalation LO(A)EC (Lowest-Observed-[Adverse]-Effect Concentration) cited in	The draft screening assessment identified a developmental inhalation LO(A)EC (Lowest-Observed-[Adverse]-Effect Concentration) of 3520 mg/m3 (1000 ppm) from the study by Hurtt

	the draft screening assessment. A different oral developmental LO(A)EL (Lowest-Observed-[Adverse]-Effect Level) should be used.	et al. (1995) based on decreased fetal weight and crown rump length as well as skeletal alterations. The public comment suggested that these effects were likely due to maternal toxicity and that the study did not demonstrate selective fetal toxicity. While the draft screening assessment noted the maternal toxicity observed at this exposure level, this LO(A)EC is consistent with the EU RAR (2008) who considered 1000 ppm as the low effect level for both dam and fetus from this study. Though interpretation of this study is limited due to the maternal toxicity, a conservative approach warrants maintaining a developmental LO(A)EC of 1000 ppm (3520 mg/m3). The public comment also noted the draft screening assessment incorrectly reported the dose conversion to be 704 mg/m3 rather than the correct 3520 mg/m3 and this has been corrected in the final screening assessment. The public comment also suggested an alternative oral developmental study in rats (Hurtt et al. 1995) to be more appropriate than that cited in the draft screening assessment (Mebus et al. 1995). The developmental LO(A)EL (Lowest-Observed-[Adverse]-Effect Level) cited in the draft screening assessment (decreased body weight of F1 rat pups at 5000 ppm or 700 mg/kg-bw/day, Mebus et al. 1995) is reported by the study authors and is supported by conclusions from IARC (1995) and the US EPA (1990). The alternative oral developmental study recommended in the public comment did not display any developmental effects at even the highest tested dose (NO(A)EL= 5000 ppm or 700 mg/kg-bw/day, Hurtt et al. 1995). Therefore the final screening assessment has maintained the LO(A)EL of 700 mg/kg-bw/day (5000 ppm) from Mebus et al. (1995) as it was the lowest developmental effect level identified and therefore the more conservative approach.
	There are limitations in selection of the lowest short-term oral LO(A)EL (Lowest-Observed-[Adverse]-Effect Level) cited in the draft screening assessment (200 mg/kg-bw/day or 1000 ppm, gastrointestinal colouration in mice, Gale 1979). No effects were	Several of the limitations highlighted in the public comment regarding the LO(A)EL (Lowest-Observed-[Adverse]-Effect Level) were cited in the draft screening assessment (200 mg/kg-bw/day or 1000 ppm, mice, Gale 1979) and concurs with additional limitations provided in the public comment. An alternative

	observed at the highest dose tested in this study and therefore a NO(A)EL (No-Observed-[Adverse]-Effect Level) of >5000 ppm should be reported by Health Canada in the screening assessment.	LO(A)EL in mice can be identified from this study (5000 ppm, reduced thymus weights) based on previous conclusions by EU RAR (2008) and ATSDR (1992) which is however contrary to the assertion from the public comment that 5000 ppm was the NO(A)EL (No-Observed-[Adverse]-Effect Level) for mice in this study. For the rats tested in the same study (Gale 1979) a lower LO(A)EL of 100 mg/kg-bw/day (1000 ppm) was identified by the EU RAR (2008) based on reduced body weights. Therefore, as this latter effect level of 1000 ppm in rats is lower than that reported for mice, 1000 ppm (100 mg/kg-bw/day) has been used as a more conservative short-term oral LO(A)EL in the final screening assessment.
	There are limitations in the selection of sub-chronic oral LO(A)EL cited in the draft screening assessment (38 mg/kg-bw/day or 200 ppm, spleen weight changes in mice, Gale 1980a). An alternative LO(A)EL of 2300 mg/kg-bw/day (10000 ppm) based on cell proliferation in the oral cavity of mice in a study by Valentine et al. (2002) should be used.	Several of the limitations highlighted in the public comments on the 3 month oral study by Gale (1980b) were previously noted in the draft screening assessment. However, the reporting of effects (reduction in spleen weight) and effect levels in the draft screening assessment for this study have primarily relied upon the results as reported in an evaluation by ATSDR (1992) and by consulting the original study. Despite limitations of the study, the results and effect levels presented in the draft screening assessment are consistent with those reported by ATSDR for this study. As cited in the public comment, we recognize that no gross or microscopic pathology in the spleen was noted in this study. However, ATSDR also reported that reductions in spleen weight were observed in other oral and inhalation studies of various duration. Overall, ATSDR considered the reductions in spleen weight "may be suggestive of an immunosuppressive action of vinyl acetate" though they note proper tests were not performed in this regard. Although there is lower confidence in this level, a conservative approach has been followed by maintaining the oral sub-chronic LO(A)EL of 38 mg/kg-bw/day in the final screening assessment. Additional limitations of this study submitted in the public comments will be added to the final screening assessment.
	There are limitations in the selection of chronic oral LO(A)EL (Lowest-Observed-[Adverse]-Effect	Several of the limitations highlighted in the public comment the study by Minardi et al. (2002) and related studies (Belpoggi et al.

	Level) cited in the draft screening assessment (140 mg/kg-bw/day or 1000 ppm, tumours & squamous cell dysplasia of GIT in rats, Minardi et al. 2002). An alternative LO(A)EL of 202 mg/kg-bw/day (5000 ppm) based on reduced body weights of female rats in a study by Bogdanffy et al. (1994b) should be used.	2002, Maltoni et al. 1997) were previously noted in the draft screening assessment. However, the tumours and squamous cell dysplasia reported in the upper gastro-intestinal tract (GIT) displayed a dose-dependant and statistically significant increase in exposed animals versus controls for both parental and F1 groups. While the incidence of these tumours were low in concurrent controls, information on historic control tumour incidence from the Minardi et al. laboratory were not readily available and therefore are not further discussed here. Nonetheless, the same type of tumour (squamous cell carcinoma) was also observed in the upper GIT for other are drinking water studies of vinyl acetate supporting that this was an was exposure-related effect (Maltoni et al. 1997, Belpoggi et al. 2002, Umeda et al. 2004). The identified LO(A)EL (Lowest-Observed-[Adverse]-Effect Level) of 1000 ppm for these effects is supported by the conclusion of EU RAR (2008) and is therefore maintained as a LO(A)EL for this study in the final screening assessment. This value is also within the range of chronic oral LO(A)ELs of 31 – 202 mg/kg-bw/day cited in the final screening assessment.
	The Cosmetic Ingredient Review assessment (2006) on the use of vinyl acetate based polymers in cosmetics endorsed a threshold determination (i.e., concentration below which there is no consequential risk of concern) regarding vinyl acetate's carcinogenic potential. The draft screening assessment relied on outdated information. The current studies show that there should be no health risks at exposures that might occur with the Canadian public. Copolymers based on vinyl acetate – crotonic acid – VeoVa 10 (t-Decanoic acid ethenyl ester) are used as binder for hair styling products (1 to 10 % copolymer as a binder (Johnson & Dekker 1997): hair spray 2-10%, styling mousse 1-5% and hair gel 2-5%. The Cosmetic Ingredient Review (2006) summarizes the historical use and use concentrations from 1976 to 2003 in the U.S. The	The final screening assessment considered this submission on the threshold modes of action for carcinogenicity. Modeling of exposures was modified based on the new residue data provided.

	use concentration of VP/VA copolymers in cosmetics ranged from 0.3% to 12% and were used in eye makeup, makeup, non-coloring hair care, hair coloring, nail care and skin care. The use of VP/VA copolymer is acceptable in these applications.	
Data collection	Accuracy and reliability of the Section 71 data was questioned. Reliance on section 71 submissions does not accurately portray residues of vinyl acetate monomer in Canadian consumer products.	The Government was in agreement with this comment and solicited industry to test consumer products in the North American marketplace for residues of vinyl acetate monomer. Since pre-publication in Canada Gazette Part I, new analytical vinyl acetate monomer residue data has been generated for consumer products thought to contain vinyl acetate. These new data are considered in the final screening assessment.
Uses	Styrene-butadiene rubber adhesives have largely replaced vinyl acetate based adhesives in the North American marketplace. In all analyses performed all-purpose flooring adhesives, there was no residual vinyl acetate monomer content above the 10 ppm detection level. While likely not used in carpet adhesives, vinyl acetate ethylene (VAE) copolymers are used in the manufacture of carpet. Manufactured carpet typically passes the CRI Green Label Plus standard which uses ASTM D5116-97 and requires <400 µg/m2/hour VOC levels. Differing carpet tile samples were analyzed and they showed no residual vinyl acetate monomer content upon testing.	Health Canada solicited industry for data on vinyl acetate and vinyl acetate copolymer usage within the North American carpet industry including some analyses. These new data are considered in the final screening assessment.
Food and consumer products	It should be noted that the UK Food Standards Agency 2004 study did not detect vinyl acetate in any of the foods analyzed. Tthe draft screening assessment correctly concludes that food is not likely to be a significant source of exposure to vinyl acetate. The Food Directive already regulates vinyl acetate copolymers that may be used in food applications.	This new information was considered in the final screening assessment.

	Some food packaging materials (e.g., bottle cap lids, drink dispenser tubes) were tested and results showed non-detectable levels of residual vinyl acetate (LOD: 10 ppm). In addition, testing was also conducted of food packaging materials including cereal boxes, tooth paste boxes, coffee cup insulators, snack packaging, and muffin and pie boxes. In all cases, the residual vinyl acetate level was non-detectable (LOD: 25 ppm7).	
Monitoring and research	There is a lack of environmental media monitoring data.	The Government of Canada agrees data are limited, and uses the data and information that is currently available.

References

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