Summary of Public Comments Received on the Government of Canada's Draft Screening Assessment Report on TDIs
(Mixed isomers of toluene diisocyanate, CAS RN 26471-62-5; 2,4-diisocyanato-1-methyl-benzene (2,4-toluene diisocyanate = 2,4-TDI), CAS RN 584-84-9; and 2,6-diisocyanato-1-methyl-benzene (2,6 toluene diisocyanate = 2,6-TDI) CAS RN 91-08-7))

Comments on the draft screening level assessment report on TDIs, substances included in Batch 1 of substances to be addressed as part of the Chemical Management Plan Challenge under the *Canadian Environmental Protection Act 1999* (CEPA 1999), were provided by the American Chemistry Council, Bayer Inc., the Canadian Council of Grocery Distributors, Chemical Sensitivities Manitoba, Dow Chemical Canada Inc., Johnson Controls LP, the Learning Disabilities Association of Canada, and Woodbridge Foam Corporation during the 60-day public comment period that took place from January 19, 2008 to March 19, 2008. A summary of the comments that relate specifically to the draft assessment of TDIs, along with responses, is presented in the table below. Comments related to subsequent risk management of the substance are addressed separately.

Comment	Response
Two commenters agreed that TDI isomers be considered toxic under Section 64 of CEPA and one commenter stated that the draft screening assessment was thorough and did include a careful calculation, based on the limited data available, of potential exposure to children.	Comment noted.
A concern was expressed regarding the lack of detail in the documentation regarding the nature of the peer review undertaken	Information concerning the nature of external peer review of the sections relevant to assessment of risk to human health will be included in the revised draft.
Relying on other international agencies without understanding the context and/or the regulatory implication of these decisions is not an adequate weight of evidence process for a screening assessment.	Information on health hazards is based principally on the weight of evidence based assessments of other agencies.
One commenter suggested that the risk assessment instead apply the "precautionary principle" rationale with respect to the known human health effects associated with working with isocyanates (TDI's) and that the precautionary principle is already enshrined within a regulation under Ontario provincial law, which in the commenter's opinion, is considered to be the most stringent piece of legislation that addresses the known human health hazards associated with isocyanates, in the world.	Occupational exposures are largely a provincial mandate and therefore beyond the scope of assessments under CEPA 1999.
The opinion was expressed that carcinogenicity studies in rats and mice with inhalation exposure to TDI did not reveal a carcinogenic potential when tested up to the maximum tolerated dose and that the carcinogenicity findings of these chronic oral	Considering principally weight of evidence-based assessments by several international and national agencies (the World Health Organization International Agency for Research on Cancer (IARC), the European Union (EU), and the

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gavage studies in rats and mice were not considered relevant to human health risks.	National Toxicology Program of the United States Department of Health and Human Services (U.S. NTP)), as well as an independent published review (Bolognesi et al. 2001), it was determined that the available human epidemiological data and the experimental inhalation animal data are equivocal and thus inadequate to determine the carcinogenic risk of inhalation exposure to TDI in humans. Even though there was a lack of carcinogenic effects in inhalation studies in experimental animals, there was evidence of carcinogenicity at multiple sites in orally dosed animals. Therefore, applying precaution, the government considers TDI to be carcinogenic. A similar approach was taken in the assessment by the California Environmental Protection Agency (California EPA), which extrapolated that oral rat carcinogenicity study data to calculate a TDI inhalation cancer unit risk factor (California EPA 1999). Therefore, the carcinogenicity findings of the chronic oral gavage studies are considered relevant to human health risks. Bolognesi C, Baur X, Marczynski B, Norppa H, Sepai O, Sabbioni G. 2001. Carcinogenic risk of toluene diisocyanate and 4,4'-methylenediphenyl diisocyanate: epidemiological and experimental evidence. Crit Rev Toxicol 31: 737-772.
The opinion was expressed that there is enough knowledge about the mode of action mechanism and that the weight of evidence suggests there is no evidence to suggest that TDI is a non-threshold carcinogen. One commenter also disagreed with using the EU Category 3 list for carcinogens and mutagens to determine that a substance is a non-threshold cancer agent.	Based principally on weight of evidence based assessments by several international and national agencies (IARC, EU and US NTP), as well as an independent published review (Bolognesi et al. 2001), the available human epidemiological data and the experimental inhalation animal data are equivocal and thus inadequate to determine the carcinogenic risk of inhalation exposure to TDI in humans. The independent published review by Bolognesi et al (2001) observed that “the possible carcinogenic mechanism of TDI ……is not clear.” In the absence of a fully elucidated mode of action, it cannot be precluded that tumours observed in experimental animals resulted from direct interaction with genotoxic material. Therefore, applying precaution, TDI is considered to be carcinogenic.
The opinion was expressed that the results of the chronic oral gavage studies were compromised by deficiencies in test substance handling that led to the administration of unidentified breakdown and reaction products of TDI and that these studies were unreliable for hazard evaluation as well as risk assessment. It was also stated that the introduction of TDI directly into the acidic milieu of the stomach leads to significant formation of	These studies have been included in the weight of evidence assessments by several international and national agencies (IARC, EU and US NTP). Also, an independent published review of the same experimental animal as well as human epidemiological data (Bolognesi et al 2001) observed that “the possible carcinogenic mechanism of TDI ……is not clear.”. As stated in the screening assessment, “…it is recognized that

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toluenediamine (TDA), a known animal carcinogen with genotoxic properties, and that the hydrolysis of TDI to TDA is the most plausible explanation for the observed tumours following oral administration of TDI.	there may be differences between the nature of TDI when administered orally versus by inhalation. The differential formation of TDA via the two routes of exposure may contribute to the mechanism by which TDI was carcinogenic in mice and rats by oral but not inhalation exposure." However, it will be clarified in the screening assessment that there is still uncertainty whether maximum tolerated doses were attained in inhalation studies.
The opinion was expressed that the weight of evidence suggest that the carcinogenic risk associated with TDI depends greatly on the amount of TDA formed in vivo and that route dependent differences in TDI metabolism are likely explanations for the differences seen in the outcome of the gavage and inhalation carcinogenicity studies conducted on TDI. It was also stated that data from several studies indicate that this conversion of TDI to TDA does not occur in the relatively neutral pH environment of the lung following the deposition of inhaled TDI, the primary exposure pathway for humans and that this interpretation is further supported by the available animal data that revealed negative results after chronic inhalation exposure up to the maximum tolerated dose.	Considering principally weight of evidence-based assessments by several international and national agencies (IARC, EU and US NTP), as well as an independent published review (Bolognesi et al. 2001), it was determined that the available human epidemiological data and the experimental inhalation animal data are equivocal and thus inadequate to determine the carcinogenic risk of inhalation exposure to TDI in humans. As stated in the screening assessment, "…it is recognized that there may be differences between the nature of TDI when administered orally versus by inhalation. The differential formation of TDA via the two routes of exposure may contribute to the mechanism by which TDI was carcinogenic in mice and rats by oral but not inhalation exposure." However, it will be clarified in the screening assessment that there is still uncertainty whether maximum tolerated doses were attained in inhalation studies.
The opinion was expressed that overall, the in vitro and in vivo studies do not support the conclusion that TDI is a genotoxin. It was stated that the positive results of some in vitro tests were flawed due to the use of solvents that resulted in the formation of TDA, that in vivo genotoxicity tests with TDI have been negative, and that the absence of genotoxicity following in vivo exposures to TDI is likely due to the ability of the isocyanate group to react with cellular macromolecules in vivo, thereby preventing its hydrolysis to the genotoxic TDA. It was also stated that considering that inhalation is the relevant route of human exposure, the body of evidence indicates that TDI does not have a mutagenic or genotoxic potential and that oral intake of TDI is not expected to lead to the formation of TDA since the reaction of TDI with macromolecules in the buccal cavity and esophagus reduces the amount of unreacted TDI reaching the stomach.	As stated in the screening assessment, "Mixed results have been obtained for TDI in in vivo and in vitro genotoxicity assays (Appendix 3)." As stated in an independent published review (Bolognesi et al. 2001), the positive in vitro tests suggest potential genotoxicity of TDI but in all studies, the stability of the applied diisocyanate was not studied, and that the reacting species may not be the same between the in vitro and in vivo studies. The conclusion of Bolognesi et al. (2001) was that TDI was "probably genotoxic". Also, the screening assessment includes recent information on both positive and negative genotoxicity results in human subjects (Bilban 2004; Marczynski et al. 2003, 2005). Thus, based on mixed genotoxicity results in both humans and in vitro studies, the potential genotoxicity of TDI is maintained. Also, an independent published review of the same experimental animal as well as human epidemiological data (Bolognesi et al 2001) observed that "the possible carcinogenic mechanism of TDI ……is not clear." In the absence of a fully elucidated mode of action, it

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	cannot be precluded that tumours observed in experimental animals resulted from direct interaction with genotoxic material. Bilban M. 2004. Mutagenic testing of workers exposed to toluene-diisocyanates during plastics production process. Am J Ind Med 45(5):468-474. Marczynski B, Merget R, Teschner B, Korn M, Rabstein S Bruning T. 2003. Changes in low molecular weight DNA fragmentation in white blood cells after diisocyanate exposure of workers. Archs Toxicol 77: 470-476. Marczynski B, Merget R, Mensing T, Rabstein S, Kappler M, Bracht A, Haufs MG, Kafferlein HU, Bruning T. 2005. DNA strand breaks in the lymphocytes of workers exposed to diisocyanates: indications of individual differences in susceptibility after low-dose and short-term exposure. Archs Toxicol 79:355-362.
The opinion was expressed that an independent recent weight of evidence report (Zeiger and Woolhiser 2007) indicated that there is no reliable evidence that TDI is genotoxic to humans.	Zeiger and Woolhiser (2007) is an abstract in the journal, Toxicologist. As the full weight of evidence assessment has not been published, it cannot be considered.
The opinion was expressed that epidemiological studies do not support the Government's tentative conclusion that TDI is a human carcinogen and that more recent follow-up of mortality and cancer morbidity of the same studies mentioned in the screening assessment report confirm conclusions that exposure to TDI is not associated with cancer.	The recent epidemiological studies mentioned by the commenter are already cited in appendix 3 of the screening assessment. The commenter's suggestion that these more recent data do not support a correlation between TDI exposure and cancer has not yet been subject to international assessment and in depth weight of evidence analyses of the overall epidemiological data are not practicable within the context of this screening assessment. The statement pertaining to epidemiological studies in the screening assessment, "These studies may be of limited value due to the small sample sizes, relatively short follow-up, young cohorts and lack of consideration of smoking.", will be maintained as it is cited from one of the most recent international reviews on carcinogenic risk of TDI (Bolognesi et al 2001).
One commenter stated that the results of the NTP study in rats and mice must be at least compared with other studies such as a NIOSH human mortality study conducted in 1995, and a study conducted by Swensson & Andersson in 1985. It was stated that both studies did not yield any data to support a linkage of cancer cases in humans associated with exposure to TDI, and that both NIOSH and IARC have stated that there is no hard evidence to support the genotoxic label, and have	The commenter's suggestion that these specific studies do not support a correlation between TDI exposure and cancer has not been addressed in international assessments and in depth weight of evidence analyses of the overall epidemiological data are not practicable within the context of this screening assessment. However, based principally on weight of evidence based assessments by several international and national agencies (IARC, EU and US NTP), as well as an

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opted instead for the risk phrase "**potential** for TDI-induced cancer in humans".	independent published review (Bolognesi et al. 2001), the available human epidemiological data and the experimental inhalation animal data are equivocal and thus inadequate to determine the carcinogenic risk of inhalation exposure to TDI in humans. Also, based on mixed genotoxicity results in both humans and in vitro studies, the potential genotoxicity of TDI is maintained. In the absence of a fully elucidated mode of action, it cannot be precluded that tumours observed in experimental animals resulted from direct interaction with genotoxic material. Therefore, applying precaution, TDI is considered to be carcinogenic. This is consistent with the risk phrase "potential for TDI-induced cancer in humans."
The opinion was expressed that elicitation of an asthmatic response in previously sensitized individuals is an inappropriate non-cancer endpoint and that the elicitation of an asthmatic response in an individual with existing occupational diisocyanate asthma should not be used to determine the critical effect level for short term, non-neoplastic effects via inhalation because proven cases of diisocyanate sensitization appear to occur exclusively in the workplace. It was stated that a more appropriate level would be concentrations found to elicit a response in the general populations, including sensitive individuals such as general asthmatics with mild to severe bronchial hyperresponsiveness.	There is evidence for diisocyanate sensitization occurring outside the workplace in the reviews of Ott et al (2003) and Krone and Klingner (2005). Thus, elicitation of an asthmatic response in an individual with existing occupational diisocyanate asthma is considered to be appropriate to determine the critical effect level for shortterm, non-neoplastic effects via inhalation. It is considered appropriate to derive margins of exposure for both general and sensitive populations. Ott MG, Diller WF, Jolly AT. 2003, Respiratory effects of toluene diisocyanate in the workplace: A discussion of exposure-response relationships. Critical Reviews in Toxicology 33:1–59. Krone CA, Klingner T. 2005. Isocyanates, polyurethane and childhood asthma (review article). Pediatr Allergy Immunol 16: 368-379.
The opinion was expressed that data provided in another review (Ott et al. 2003) suggest that measurements of responsiveness, even in asthmatic individuals sensitized to TDI, can be quite variable and that this variability stems from inconsistent responsiveness due to the degree of bronchial hyprerresponsiveness, as well as methodology limitations. It was also stated that an understanding of the mechanisms that underlie the degree of hypersensitivity and responsiveness remains elusive.	As stated in the screening assessment, "Exact exposure conditions and concentrations leading to sensitization have not been determined.", which agrees with the commenter's statement that "An understanding of the mechanisms that underlie the degree of hypersensitivity and responsiveness remains elusive...". The variability in sensitization responses to TDI will be addressed by considering the review by Ott et al (2003), as well as information in a review article not cited by the commenter (Krone and Klingner 2005).
The opinion was expressed that data provided in another review (Ott et al. 2003), concluded that short-term exposure to TDI concentrations up to 20 ppb should be without adverse effects in healthy	The review by Ott et al. (2003) discusses both occupational and non-occupational exposures However, Ott et al (2003) also shows data agreeing with the data of Lemiere et al (2002)

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subjects and that those with severe bronchial hyperresponsiveness, which defines general asthmatics, may experience symptoms at short-term TDI concentrations in the range of 10 to 20 ppb	already cited in the screening assessment, i.e. that 1 ppb (0.007 mg/m^3) caused a sensitization reaction in previously sensitized individuals (persons diagnosed with TDI-induced asthma reacted with bronchoconstriction to concentrations as low as 1 ppb for 30 min). The commenter did not cite another review article which showed evidence for diisocyanate sensitization occurring outside the workplace (Krone and Klingner 2005). Lemière C, Romeo P, Chaboillez S, Tremblay C, Malo JL 2002. Airway inflammation and functional changes after exposure to different concentrations of isocyanates. J Allergy Clin Immunol. 110(4):641-646.
The concern was expressed that the state of science does not support the Government's assertion that "dermal" exposure can lead to respiratory hypersensitivity or isocyanate asthma, and requested removal of "dermal" in the sentence referring to isocyanate asthma. It was argued that that there is still no animal model that can reliably model for respiratory allergy in humans, and that the role of dermal sensitization as it relates to respiratory allergy.	The review of Bello et al (2007) concluded that multiple lines of evidence from animal, human, and biomarker studies indicate that in certain exposure settings, human skin is likely an important route of isocyanate exposure and can contribute to the development of isocyanate asthma. However, in the case of TDI, only studies using animal models provided evidence of skin exposure followed by inhalation exposure resulted in respiratory sensitization. As a result, the sentence in question will be modified to remove "isocyanate asthma". However, Bello et al's (2007) conclusion regarding the link between isocyanate skin exposure and isocyanate asthma will be added to the screening assessment. Bello D, Herrick CA, Smith TH, Woskie SR, Streichner RP, Cullen MR, Liu YL, Redlich CA. 2006. Skin exposure to isocyanates: Reasons for concern. Environmental Health Perspectives 115: 328-335.
One commenter stated that there is very limited evidence to establish a reliable NOAEC for respiratory and skin sensitization outside the workplace, thus the baseline to compare potential exposure.	In the screening context, focus is directly on the conservative effect level (LO(A)ECs or LO(A)ELs) to establish the baseline to compare potential exposure, not the determination of no effect levels (NO(A)ECs or NO(A)ELs) which requires in depth weight of evidence evaluation. Based on published studies reviewed by Krone and Klingner (2005), elicitation of a sensitization response in an individual with existing occupational diisocyanate asthma is considered to be appropriate to determine the critical effect level for shortterm, non-neoplastic effects via inhalation. It is considered appropriate to derive margins of exposure for both general and sensitive

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	populations. The review article from Ott et al. (2003) will also be noted as it discusses both occupational and non-occupational exposures.
One commenter stated that the developmental study did show a structural effect, which would in some cases trigger a neurodevelopmental study.	A neurodevelopmental study was not identified. As stated in the screening assessment, the LOEC of 0.5 ppm (3.57 mg/m^3) in the developmental study was based on a single skeletal variation, which was noted to be a common variation. This type of effect is not considered to be a criterion for the requirement of a neurodevelopmental study.
The opinion was expressed that the overwhelming evidence of TDI isomers being strong human sensitizers should be included in the evidence for scheduling as CEPA-toxic.	In the draft assessment, reference was made to the numerous studies in humans and animals indicating the dermal and respiratory sensitization potential of TDI. However, two review articles discussing TDI and respiratory sensitization will also be included. A review by Ott et al. (2003) on respiratory effects of TDI in the workplace also included a discussion of non-occupational exposures. Also, a review article by Krone and Klinger (2005) on isocyanates provided examples of respiratory sensitization to TDI outside the workplace.
The opinion was expressed that "vulnerable populations" (those with allergies and sensitivities, lung disorders, babies, children and pregnant women) should have been considered in the draft screening.	Sensitive populations were already addressed in the draft assessment in the discussion of margins of exposure (e.g. critical effect level in sensitized humans utilized for short-term effects; margin of exposure based on chronic effects, as documented, accounts for the potential exposure to children). There is evidence for diisocyanate sensitization occurring outside the workplace in the reviews of Ott et al (2003) and Krone and Klingner (2005). Thus, it is considered appropriate to derive margins of exposure for both general and sensitive populations.
The concern was expressed that NPRI data not be considered until their accuracy have been verified. An example was provided that a Canadian plant accounted for 60 % of the total TDI (mixed isomers) emissions to air during 2005, as stated in the screening assessment report, but that this plant is currently implementing a more aggressive and accurate accounting system for its emissions. It was requested that the Government recognize that NPRI values are likely inflated and do not represent actual mixed isomer releases.	The emissions of mixed isomers of TDI from the plant in question reported to the NPRI for 2006 are 1400 kg and for 2005 they were 846 kg. This is a 65% increase. The 2006 NPRI data had not been validated at the time of the draft screening assessment, but have now been validated. An alternate estimate of the concentration of TDI outside the plant boundaries using a different model was made. This estimate could not be used because of confidentiality reasons. Information to refine the estimate of TDI concentration at plant boundaries was not submitted during the comment period.
Comments were directed at the application of a model used in Europe, the EUSES (European Union System for the Evaluation of Substances) to generate an exposure estimate, raising the following questions:	The model is a mathematical description of emissions and its application is equally valid in Europe and Canada. In the assessment report, the following statement

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• is the model valid in Canada? A number of the inputs were questioned • the extrapolation assumed was linear; is this valid given the model and its mathematics?	appears: "It is expected that short-term air concentrations will vary from this average because of production cycles, plant stack height, wind, local topography and other factors." From Tury et al (2003): "The predictions (of average atmospheric concentrations) are linearly proportional to the emissions rates." A separate estimate of the concentration of TDI outside the plant boundaries using a different model was made by Environment Canada which incorporated Confidential Business Information data. As such , this information could not be presented in the assessment, but it was considered in preparing the assessment. Tury B, Pemberton D, Bailey RE. 2003. Fate and potential environmental effects of methylenediphenyl diisocyanate and toluene diisocyanate released into the atmosphere. J Air Waste Manage Assoc 53:61-66.
An objection was raised to the assumption that the concentration of TDI in indoor air is the same as in ambient air. It was stated that other impacts would have significantly reduced the concentration before becoming indoor air.	In the absence of monitoring data, for individuals living in the vicinity of the point source, it is reasonable to assume that the indoor air concentration will be the same as the ambient air concentration.
The opinion was expressed that the use of a solvent to simulate real-life extraction conditions is complicated in the case of polyurethane foam by the fact that there can be low levels of oligomeric, non-polyurethane TDI derivatives in the foam that can be decomposed by an organic solvent medium. A further concern was expressed that studies currently underway (unpublished) indicate that TDI generation by solvent contact contributes to the level of “free TDI in foam.”	The use of organic solvents to extract TDI from polyurethane foam serves to establish that TDI or TDI precursors such as the biurets and allophanates from which TDI may be derived are present in the polyurethane foam. The discussion in the screening assessment of the release of TDI from polyurethane foam covers both positive and negative findings. It does not mean that TDI is readily extracted by body fluids or during conditions of normal use in the same amount as obtained by organic solvents.
The observation was made that in the Krone et al (2003) article, instructions for a commercially-available, colourimetric indicating pad called for mineral oil as the extraction medium but the authors used acetone instead because it would solubilize the colourimetric indicator and allow it to penetrate the foam matrix to react with “bound isocyanate groups” in the foam. It was stated that such “bound isocyanate groups” have no bearing on ”free TDI” and potential real-life exposures.	Krone et al (2003) reported positive results for isocyanate presence by using a colourimetric detecting pad and then extraction of polyurethane foam by solvent and analysis by HPLC. TDI was detected in the solvent used to extract isocyanates from polyurethane foam. At issue is whether TDI is produced by the action of a solvent such as acetone on chemical species in polyurethane foam which then release TDI or whether TDI remains present in the foam after

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	aging.
Several commenters agreed with the Government's assessment that TDI does not volatilize from polyurethane foam in measurable quantities after an initial curing period, and stated that the same conclusion was reached by Hugo et al. (2000) where airborne TDI measurements were taken from air passed through polyurethane foam three days after production and after spiking the foam with known quantities of TDI.	The work reported by Hugo et al (2000) has been correctly summarized in the comment. There is contradictory experimental evidence which is discussed in the section entitled "Consumer Products" in the screening assessment report. Hugo JM, Spence MW, Lickly TD. 2000. The Determination of the Ability of Polyurethane Foam to Release Toluene Diisocyanate into Air. Appl. Occ Env Hygiene 15(6): 512-519.
The concern was stated that the Katsuyama et al (2003) study mentioned in the draft assessment shows that there were no emissions of TDI above the detection limits from the urethane adhesive, paint, and varnish systems tested and that the acetone concentration mentioned in this study was far in excess of indoor air values reported elsewhere. Katsuyama Y, Shinohara N, Kumagai K, Fujii M, Yanagisawa Y. 2003. Emission of diisocyanates in indoor air. Proceedings of ISIAQ 7th International Conference, December 2003.	In the screening assessment report, the paragraph in which the work by Katsuyama et al (2003) is discussed concludes with the following sentence: "Rigid polyurethane foam slab is not a building material typically used in Canadian residential construction and the concentration of acetone in air used in the experiment does not represent normal residential conditions; therefore, the exposure is not considered pertinent."
The observation was made that all data on the release of free TDI from consumer products including mattresses and furniture stuffing, TDI–based paints, adhesives and sealants and the industrial versions of the latter three products are not consistent. It is quite possible that the industrial products have higher TDI content in their formulations.	The available literature on emissions of TDI from consumer products was reviewed for the screening assessment. No laboratory studies of the release of TDI from consumer products apart from those reported in the screening assessment were located. Some coating adhesive and sealant products are formulated for use by professionals only and the concentration of TDI in these products may be higher than in similar products for use by Do-It-Yourself consumers. Uncertainties are discussed in the screening assessment report.
One commenter requested that there should be some data disclosure on TDI release versus time to better understand the extent of TDI exposure from household products, and also wondered whether TDI could be released in household products where solvents are not used.	TDI can be extracted by solvent from aged polyurethane foam and it has been measured in the air of test chambers where a TDI-based coating was applied. Both these findings are presented in the screening assessment.
A concern was expressed that most products (e.g., paints and coatings) containing TDI are designed for and sold only to licensed individuals and that	The Government has sought information on surface coatings and other consumer products available to retail consumers containing

Comment	Response
the industry takes significant effort to ensure that these products do not end up in the hands of the general public or consumer markets. It was also stated that contracts with distributors contain strong language that the contract with the jobber is subject to termination if the jobber is detected diverting any of these coatings into non-approved markets.	measurable quantities of TDI. It was determined that the deck sealer product modelled in the screening assessment based on work by Jarand et al.(2002) is sold in Canada and it contains up to 3% TDI. It could not be determined that the product tested in Kelly et al. (1999) was sold in Canada Jarand CW, Akapo SO, Swenson LJ, Kelman BJ. 2002. Diisocyanate emission from a paint product: a preliminary analysis. Appl Occup Environ Hyg 17(7):491-494. Kelly TJ, Myers JD, Holdren MW. 1999. Testing of household products and materials for emission of toluene diisocyanate. Indoor Air 9:117–124.
Two commenters expressed the concern that the experimental conditions used in the Kelly et al (1996) study did not simulate normal use of the product, and that it should not be used as a basis for exposure scenario modeling.	Agreed that the method of application was not typical of product use.
The observation was made that modeling based on the Jarand et al (2002) study was more appropriate in the draft assessment ('Concrete Sealer Version 1) and the commenter provided additional information.	The scenario using the Jarand et al (2002) data was modified by the commenter to include ventilation and wall effects. The net result is a three-fold decrease in the estimated average concentration during painting.
One commenter agreed with the Government that its elaboration of a scenario for infant exposure to TDI through mouthing polyurethane foam from pillows or other objects greatly overestimates TDI intake for a number of reasons, but the commenters specified,that the estimated intake level does not account for the protective barrier due to the reactivity of TDI with saliva, that it is likely that only TDI at the surface of the foam would be available for translocation instead of 5% of the total unreacted TDI in the foam piece, that any foam present will likely be covered by other material, and that direct comparison of the estimates indicates that the mouthing estimate is only 0.12% of the ambient air estimate.	The comparison of the estimated exposure to TDI through mouthing polyurethane foam to the estimated intake from air is included to demonstrate the relative contribution of inhalation and ingestion arising from mouthing polyurethane foam as routes of exposure to TDI. For populations exposed to the emissions reported by the highest emitting facility in Canada, inhalation is the more important route of exposure. This child mouthing foam scenario was intended to examine a maximum plausible exposure scenario and that scenario was found to present a negligible contribution to total exposure for a child who is exposed in the vicinity of a polyurethane foam plant. Reaction of TDI with saliva is mentioned in the draft SAR but was not quantified.
A question was raised regarding the use of TDI in the food industry, if the inks and adhesives applied to food packaging are checked for residual TDI isomers. Also, 'restricted use as a food contact material' from the assessment document lacks details.	This is a conclusion based on the knowledge of the use conditions of these chemicals and their chemical and physical properties, not on any experimental determination of TDI in foods. The use of TDI-based products as food contact materials has been restricted to use conditions

Comment	Response
	where migration to food is not expected.
The opinion was expressed that Information on the use of TDI in the food industry could have been expanded so that the general public could have a better understanding of the rationale for using TDI-based products in this industry.	Further consultation within Health Canada has resulted in clarification of information.
An objection was raised that the assessment report notes that no reports of measurement of toluene diisocyanate in food or beverages were located. Reports of the migration of toluene diisocyanate from food packaging were located, but they are not indicative of the concentration of TDI in food and beverages, which begs the question why are they not, and if not – what do the concentrations in food and beverages indicate?	Toluene diisocyanates were detected in packaging materials. No data were located on the concentration of TDI in any food. Health Canada is planning to conduct limited testing of TDI levels in specified foods to validate the current assumptions regarding the presence of TDI in foods.
An objection was raised regarding a statement in the screening assessment that the use of TDI is packaging precludes the occurrence of detectable TDI levels in the food with which they are in contact, further arguing that if this is an assumption then it should be reviewed, or supported by research.	This is a conclusion based on a weight of the evidence from submissions to Health Canada as well as knowledge of the use conditions of these chemicals and their chemical and physical properties. Recognizing the need to validate these conclusions, Health Canada is planning to conduct limited testing for TDI in specified foods.
A concern was raised about application of the precautionary principle, or development of new regulatory requirements, as they pertain to food products. It was recommended that further analysis of the likelihood of TDI transfer and likely concentration levels (in food) be undertaken.	Health Canada is planning to conduct limited testing of TDI levels in specified foods to validate the current assumptions regarding the presence of TDI in foods.
One commenter stated that TDI was taken off the Appendix A List of toxic chemicals of the Chemical Facility Anti-Terrorism Standards in the U.S.A.	The removal of TDI from Appendix A (Chemical Facility Anti-Terrorism Standards) list in the U.S.A. is not relevant to screening assessments under Canada's Challenge program.

Summary of Public Comments Received on the Government of Canada's Risk Management Scope Document for Batch one substances toluene diisocyanates (TDI) [CAS 91-08-7, 584-84-9 and 26471-62-5] 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 of the stakeholders listed.

Comments on this publication were provided by:

1. Dow Chemical Canada Inc.
2. Learning Disabilities Association
3. Reach for Unbleached
4. Canadian Environmental Law Association
5. Woodbridge Foam Corporation
6. Chemical Sensitivities Manitoba

Comment	Response
Potential sources in food should be included in the scope of risk management The use of TDI in food packaging should be prohibited.	The potential use of TDI in food packaging and the legislation related to food packaging was noted in the risk management scope document under Sections 1.4, 2.1 and 2.2. Based on the draft assessment, food was not indicated to be a major source of exposure to Canadians for TDI and thus was not a primary focus of the risk management scope document. However, Health Canada is continuing to investigate food packaging as a potential source of exposure. In addition, future submissions for the use of TDI in food packaging materials will be scrutinised by Health Canada so that residual levels in finished materials are as low as possible or there is a functional barrier between the packaging material and food to prevent the contact and therefore potential migration into food will be negligible. Health Canada is also planning to conduct limited testing of TDI levels in specified foods.
Options for risk management should focus on the potential for releases of TDI from consumer products containing polyurethane and other foam.	Based on the draft assessment, the estimate of potential oral exposure to TDI from consumer products containing foam was less than 1% of the estimate of exposure to TDI from air in the vicinity of a foam plant. The assessment also noted experimental evidence that TDI in polyurethane foam is not volatilized in measurable quantities after an initial curing period of several days. Based on the assessment, products containing foam were not indicated as a major source of exposure to Canadians to TDI and thus were not a primary focus of the risk management scope.

Comment	Response
The risk management approach should also examine the potential for release and exposure during recycling of paper products and disposal of paper recycling sludge.	Based on the draft assessment, recycling of paper products and disposal of paper recycling sludge was not indicated as a major source of exposure to Canadians to TDI and thus was not a primary focus of the risk management scope. It is unlikely that the public is exposed to TDI through the disposal of paper recycling sludge because any residual TDI in paper coatings will rapidly react with the large volume of water used in the deinking and pulping processes. Releases of TDI to the environment from pulp and paper recycling would not be a significant source of exposure to TDI for Canadians.
The government should develop an action plan to reduce and eliminate TDI in industrial applications and consumer products. The plan should be based on a pollution prevention strategy and may include a process to identify safer alternatives, a call for a reduction of use of TDI by facilities, and monitoring of the potential release of TDI into dust as well as from polyurethane household furniture.	The risk management approach will consider the releases of TDI from industry applications and non- foam consumer products as indicated in the risk management scope document. Alternatives, pollution prevention and monitoring will be considered in the risk management process.
The government should ensure that possible disposal methods for products containing TDI do not include incineration as an option. Expanded data is needed on the incineration by-products of some TDI containing products.	Releases to air from incineration of TDI containing products would not be a significant exposure source to Canadians, therefore, the risk management approach does not propose any risk management actions for waste disposal
The government is urged to develop a CEPA Guideline for consumer products identifying conditions for which consumer products are not allowed.	As indicated in the risk management approach document, non-foam consumer products will be further investigated.
It is suggested that the government prioritize and act in areas where “real risks” are identified, with “real risks” being defined as cases where the margin of exposure is less than 1.	The screening assessment conclusion for TDI was based upon the carcinogenicity of TDI, for which there may be a possibility of harm at any level of exposure, as well as the potential inadequacy of the margins of exposure for non-cancer effects. The Government’s goal for non-threshold carcinogens/toxicants is to reduce exposure to the extent practicable.

Comment	Response
Where alternative substances exist for the manufacture of some products, the use of TDI isomers should be prohibited for import, export and domestic use, for those products. The opinion was expressed that lacking in the risk management documents is a sense of how active the isocyanate industry is in moving towards a chemistry that is safer for the workplace and the consumer.	Regulations, instruments and / or tools, as well as alternative substances will be considered as part of the risk management process.
Industry must provide all the necessary documentation as to the safety of any alternatives to TDI isomers.	Information on alternatives was requested of industry through the voluntary Questionnaire survey
The concern was expressed that, where there is the possibility of formulating with excess diisocyanate in TDI-based formulations, industry should review this practice if utilized, and reconsider the health repercussions of such a decision.	Information on current practices was considered in the risk management process.
The opinion was expressed that the genotoxic label could threaten a significant number of industries.	The determination of “toxic” under Section 64 of CEPA 1999 is a scientific process bases upon protection of human health and the environment. The development of risk management actions will take into account socioeconomic and other considerations.