PUBLIC COMMENTS ON AND RESPONSES TO PUBLIC COMMENTS ON THE DRAFT SCREENING HEALTH ASSESSMENT ON PFOS, ITS SALTS AND ITS PRECURSORS

Comments on the *Canadian Environmental Protection Act, 1999* (CEPA 1999) Screening Health Assessment on Perfluorooctane Sulfonate (PFOS), Its Salts and Its Precursors were provided by:

- Fe de Leon (Canadian Environmental Law Association) and Rich Purdy (independent toxicologist);

- A group representing:
  - The Allergy and Environmental Illness Group (PE);
  - Canadian Association of Physicians for the Environment (ON);
  - Canadian Environmental Law Association (ON);
  - Canadian Institute for Environmental Law and Policy (ON);
  - Citizens' Network on Waste Management (ON);
  - Edmonton Friends of the North Environmental Society (AB);
  - Georgia Strait Alliance (BC);
  - Great Lakes United (QC);
  - Nature Saskatchewan (SK);
  - Ontario Toxic Waste Research Coalition (ON);
  - STORM Coalition (ON);
  - Saint John Citizens Coalition for Clean Air (NB);
  - Sierra Club of Canada (ON);
  - Toxics Watch Society (AB);

- Margaret Grenier (Le Comité de la Protection de la Santé et de l'Environnement de Gaspé Inc. in association with the Canadian Environmental Law Association);

- B. McElgunn (Learning Disabilities Association of Canada);

- P. Hjertass and D. Hjertass (Canadian Environmental Law Association); and

- M. McGrath and J. Butenhoff (3M Company Canada and 3M , respectively).

As part of its mandate under CEPA 1999, Health Canada strives to ensure the transparency and robustness of its screening health assessments through a transparent process that includes several stages of internal and external peer review. To ensure the integrity of this process and its timely completion, there is a cut-off date for inclusion of information in the database relevant to the assessment. Health Canada actively encourages early submission of relevant data to ensure their consideration in the assessment. Data submitted following the cut-off date are considered primarily to inform decisions regarding risk management, strategic options or priority of the need for updating of the assessment at later stage.

Comments for which responses have been provided in the following table are those related to the basis for the conclusions of the screening health assessment on PFOS, its salts and its precursors.

Comments on the Basis for Conclusions in the Draft Screening Health Assessment on PFOS, Its Salts and Its Precursors

Comment	Response
An opinion was expressed of agreement with the overall conclusion of the screening health assessment.	No response required.
An opinion was expressed supporting the use of internal dose metrics for estimating exposure to PFOS, its salts and its precursors.	No response required.
An opinion was expressed that the choice of the critical effects and effect levels used in decision-making "*overstate the already low potential risk*."	The approach adopted for the screening health assessment of existing substances (including PFOS) relies on identifying the lowest effect level, as well as upper-bound (95th percentile) measurements/estimates of human exposures, for use in decision-making (see http://www.hc-sc.gc.ca/ewh-semt/contaminants/existsub/screen-eval-prealable/screen-sub_e.html). Margins are interpreted in the context of their inherent degree of conservatism and associated uncertainties, consistent with principles adopted for the health assessment of Priority Substances under CEPA 1999.
An opinion was expressed supporting use of a weight of evidence approach and use of both mean and 95th percentile exposure values in the margin of exposure approach comparison.	No response required.
An opinion was expressed that the estimates of human intake should be deleted from the supporting documentation.	Estimates of human intake retained in supporting working document.
An opinion was expressed that selection by Health Canada of hepatocellular hypertrophy in the chronic rat study as a critical endpoint was inappropriate, since it was not of toxicological consequence (it was suggested that this was only an adaptive response and not an adverse effect), and that, therefore, a higher effect	The protective approach adopted for the screening health assessment of existing substances (including PFOS) relies on identifying the lowest effect level for use in decision-making (see http://www.hc-sc.gc.ca/ewh-semt/contaminants/existsub/screen-eval-prealable/screen-sub_e.html). As such, it is appropriate to use the observation of microscopic

Comment	Response
level from this study should have been used.	changes in the liver as a critical endpoint for decision-making within a screening context.
An opinion was expressed that in the chronic rat study, the liver and serum values of PFOS observed after only 14 weeks on study should be used, instead of those determined after two years, as noted in the screening health assessment.	Serum values observed after two years were most relevant, since this was the time point at which the critical effects were evaluated.
An opinion was expressed that it was inappropriate to use an effect level of 0.03 mg/kg bw per day (from a toxicity study in monkeys) in decision-making, apparently conflicting with conclusions of veterinary pathologists who conducted and reviewed this study for the study sponsor. A no-observed-adverse-effect level five times higher than the value used by Health Canada was suggested as being more appropriate for decision-making.	The protective approach adopted for the screening health assessment of existing substances (including PFOS) relies on identifying the lowest effect level but interpreting margins of exposure in the context of their inherent degree of conservatism and uncertainties in decision-making (see http://www.hc-sc.gc.ca/ewh-semt/contaminants/existsub/screen-eval-prealable/screen-sub_e.html). This approach, coupled with the observation that, at this and higher doses, an increased incidence of effects (thyroid) was observed in these animals, supports use of this as the critical endpoint in decision-making within a screening assessment context.
An opinion was expressed that the critical effect level for decision-making should be a PFOS blood level of 36 mg/L in the dams (associated with changes in pup weight) from a two-generation rat reproduction study.	The protective approach adopted for the screening health assessment of existing substances (including PFOS) relies on identifying the lowest effect level for use in decision-making (see http://www.hc-sc.gc.ca/ewh-semt/contaminants/existsub/screen-eval-prealable/screen-sub_e.html). Therefore, it is appropriate to use the critical effect levels for PFOS in blood of 13.9 and 14.5 µg/L (in rats and monkeys, respectively) in decision-making within a screening assessment context.
An opinion was expressed that the phrase "*evidence of carcinogenicity*" should be replaced with "evidence of tumorigenicity."	Basis for recommendation unclear, and phrase not changed.
An opinion was expressed that since the primary manufacturer of these substances phased out production in May 2000, data on importation/uses from a survey covering the years 1997–2000 should be changed.	Information was not changed, since it was accurate for the time period that the survey covered, as noted in screening health assessment documentation.

Comment	Response
An opinion was expressed that text presented on page 4 of the screening health assessment ("*Moreover, based upon the data identified, health-related effects associated with exposure to these substances would appear to be somewhat less severe and/or are observed at higher exposures (doses) than those associated with exposure to PFOS itself*") was more accurate than text presented on page 3 of the screening health assessment ("*The toxicity profile of those PFOS precursors examined here (see table below) appears to be generally similar to that of PFOS itself. Available data indicate that effects associated with the PFOS precursors occur at exposures that are similar to or slightly higher than those for PFOS*").	Basis for reviewers' opinion is unclear. Upon review, these texts were not considered to be significantly inconsistent, and no changes were made.
An opinion was expressed that information presented in the supporting documentation to the screening health assessment concerning a toxicological study involving intraperitoneal injection should be deleted, since this route of administration is not relevant to human health risk assessment.	Supporting documentation is intended to provide a summary of toxicological hazards based on as complete a review of available data as possible. Information on this study was therefore retained therein.
It was noted that the assessment (and supporting documentation) noted an increased incidence of bladder cancer in a group of workers, but that new information would be released.	Information cited in the report was accurate to the cut-off date for the literature citation.
Reference to the bioaccumulation of PFOS on page 5 of the supporting documentation should be changed based upon comments on this subject provided to Environment Canada.	Text has been revised based upon material presented in the ecological screening assessment report.
An opinion was expressed that there was sufficient evidence to conclude that PFOS, its salts and its precursors should be found "toxic" under Paragraph 64(c) of CEPA 1999.	Specific technical basis for suggestion of reviewers was not provided. All relevant data on exposure and effects were carefully reviewed and considered by Health Canada using an approach protective of human health, the basis for conclusions was well documented and the assessment was peer reviewed by external

Comment	Response
	scientific experts.
The opinion was expressed that PFOS should be found toxic under Paragraph 64(c) owing to the number of exposure data available.	Specific technical basis (i.e., magnitude as opposed to number of data available on exposure) for suggestion of reviewer was not provided. All relevant data on exposure and effects were carefully reviewed and considered by Health Canada using an approach protective of human health, the basis for conclusions was well documented and the assessment was peer reviewed by external scientific experts.
An opinion was expressed that it was not clear that the margins of exposure noted in this assessment are adequate to protect human health.	The basis for the conclusion that the margins of exposure were considered to be protective for human health was presented in detail in the screening health assessment. This is based on the degree of conservatism of the margins of exposure and associated uncertainties.
The opinion was expressed that uncertainty factors should have been used.	The basis for the conclusion that the margins of exposure were considered to be protective for human health was presented in detail in the screening health assessment. The margin of exposure approach is more protective within a screening context than is reliance on a no-observed-effect level from a single study (and uncertainty factors). Adequacy of the margins of exposure is determined taking into account the same considerations on which uncertainty factors are based.
The opinion was expressed that a no-observed-effect level should have been used.	Margins of exposure are more appropriately based on lowest-observed-effect levels (LOELs), since they provide more information on the critical dose–response relationship. Use of a LOEL improves comparability across margins of exposure, since it avoids variation due to differences in dose spacing in critical studies.
An opinion was expressed that use of the 95th percentile of exposure in the margin of exposure analysis is not a conservative enough approach (and does not take into account data uncertainties or differences in impact from animals to humans) and that the worst-case scenario should be used.	The selection of exposure values is not related to considering differences in effects between animals and humans. The 95th percentile for exposure estimation represents a reasonable upper-bound estimate of exposure of the general population of Canada. The margin of exposure approach is more protective within a screening context than is reliance on a no-observed-effect level from a single study (and uncertainty factors). Adequacy

Comment	Response
	of the margins of exposure is determined taking into account the same considerations on which uncertainty factors are based.
A margin of exposure is not equated with a margin of safety.	The basis for the conclusion that the margins of exposure were considered to be protective for human health was presented in detail in the screening health assessment. The margin of exposure approach is more protective within a screening context than is reliance on a no-observed-effect level from a single study (and uncertainty factors). Adequacy of the margins of exposure is determined taking into account the same considerations on which uncertainty factors are based.
An opinion was expressed that the data used to make conclusions on the impacts of PFOS may be outdated. More recent data may provide information on trends in human exposure.	Information cited in the report was accurate to the cut-off date for literature citation. Any newer information published since then has been considered in preliminary fashion for any possible impact on the proposed conclusion and noted within the document.
An opinion was expressed that data do not adequately reflect the impact of PFOS on vulnerable populations that depend on consumption of wildlife.	Information cited in the report was accurate to the cut-off date for literature citation. Recent data (Tittlemier, 2004, personal communication) have indicated that the levels of PFOS in the blood of northern populations may be only very slightly higher than those collected from other North Americans living in lower latitudes. This will be noted in the revised screening health assessment.
An opinion was expressed that in the rat study, effects may have been observed at doses lower than the lowest effect level noted in the study, since the thymus was not examined.	The thymus was examined microscopically in the 0, 5 and 20 ppm dose groups in this study. Based upon the data presented in this report, the lowest effect value was considered to be 2 ppm PFOS, based upon changes in the liver, which was examined microscopically at all doses.
An opinion was expressed that the screening health assessment did not take into account the different effects of exposure on males and females.	The average serum levels of PFOS in males and females in the critical study used for decision-making were 28.3 and 29.7 ng/mL, respectively. Use of the 95th percentile for the total study population obviates the need to use different values for each sex.
An opinion was expressed that unique exposure pathways for children were not	The consideration of blood levels of PFOS in children within this screening assessment takes

Comment	Response
considered.	into account their exposure to this substance from all sources and all routes.
An opinion was expressed that data from the monkey study do not include a no-observed-effect level (NOEL) and that the assessment does not mention use of an uncertainty factor with the NOEL.	The critical effect level used for decision-making in this study was based upon the lowest dose of PFOS administered to these animals (i.e., there was no NOEL). In addition, margins of exposure are more appropriately based on lowest-observed-effect levels (LOELs), since they provide more information on the critical dose–response relationship. The basis for the conclusion that the margins of exposure were considered to be protective for human health was also presented in detail in the screening health assessment. Adequacy of the margins of exposure is determined taking into account the same considerations on which uncertainty factors are based. This includes consideration of the nature of effects at the LOEL, which are generally not considered to be adverse, as is the case for the lowest-observed-adverse-effect level (LOAEL), to which additional uncertainty factors are applied.
An opinion was expressed that there was no mention of uncertainty factors in extrapolating toxicity responses from animals to humans.	A margin of exposure approach has been adopted for the decision-making in screening health assessments. This approach has been documented in a fact sheet prepared by the Existing Substances Division (see http://www.hc-sc.gc.ca/ewh-semt/contaminants/existsub/screen-eval-prealable/screen-sub_e.html).
An opinion was expressed that the assessment failed to take into account a finding of higher cancer rates among people living in the vicinity of manufacturing facilities making and using perfluorinated compounds.	A weight of evidence approach taking into account documented criteria for causality was used to evaluate the carcinogenic potential of PFOS in humans.