SNARL for Tetrachloroethylene
Office of Drinking Water
U.S. Environmental Protection Agency
Washington, D.C. 20460

THE OFFICE OF DRINKING WATER "SNARLS" PROGRAM

The Office of Drinking Water provides advice on health
effects upon request, concerning unregulated contaminants
found in drinking water supplies. This information suggests
the level of a contaminant in drinking water at which adverse
health effects would not be anticipated with a margin of
safety; it is called a SNARL (suggested no adverse response
level). Normally values are provided for one-day, 10-day
and longer-term exposure periods where available data exists.
A SNARL does not condone the presence of a contaminant in
drinking water, but rather provides useful information to
assist in the setting of control priorities in cases when
they have been found.

In the absence of a formal drinking water standard for
tetrachloroethylene, the Office of Drinking Water has estimated
a suggested no adverse response level (SNARL) following the
state-of-the-art concepts in toxicology for non-carcinogenic
risk for short and long term exposures. For carcinogenic
risk, a range of risk estimates is provided for life-time
exposures using a model and computations from the NAS Report
(1979) entitled "Toxicity of selected drinking water contami-
nants." However, SNARLS are given on a case-by-case basis
in emergency situations such as spills and accidents. The
SNARL calculations for short-term and chronic exposures
ignore the possible carcinogenic risk that may result from
those exposures. In addition, SNARLS usually do not consider
the health risk resulting from possible synergistic effect
of other chemicals in drinking water, food and air.

SNARLs are not legally enforceable standards; they are not
issued as an official regulation, and they may or may not
lead ultimately to the issuance of a national standard or
Maximum Contamination Level (MCL). The latter must take
into account occurrence, relative source contribution factors,
treatment technology, monitoring capability, and costs, in
addition to health effects. It is quite conceivable that
the concentration set for SNARL purposes might differ from
an eventual MCL. The SNARLs may also change as additional
information becomes available. In short SNARLs are offered
as advice to assist those that are dealing with specific
contamination situations to protect public health.

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General Information and Health Effects

Substantial quantities of tetrachloroethylene are being produced (700 million pounds in the U.S. in 1973). Tetrachloroethylene (perchloroethylene) is used as a dry cleaning and degreasing solvent, heat-transfer medium, and in the manufacture of fluorocarbons. This chemical is slightly soluble in water (0.01% by volume).

Little work has been done to delineate the uptake, distribution, metabolism and excretion patterns following oral exposures to tetrachloroethylene. For our purposes, an assumption is being made that 30% is absorbed via respiration and almost 100% via the gastrointestinal tract, as has been shown for trichloroethylene. Only a small fraction of tetrachloroethylene is metabolized to trichloroacetic acid and/or trichloroethanol. The urinary half-life of tetrachloroethylene is markedly longer (144 hours) than that of trichloroethylene indicating some level of bioaccumulation.

Tetrachloroethylene, like other halogenated hydrocarbons at high doses, has been reported to produce liver and kidney damage and central nervous system disturbances in mammals, including humans. In addition, tetrachloroethylene has been demonstrated to lower the DNA and RNA content of several organ systems of rats. High concentrations of this chemical result in growth inhibition and mortality as demonstrated in animal inhalation studies.

Investigations of chronic toxicity of tetrachloroethylene in animals have all involved inhalation exposure, with the exception of an assessment of carcinogenesis which involved oral dosing (NCI, 1977). The National Cancer Institute has reported tetrachloroethylene-induced hepatocellular carcinoma in male and female mice, but not in male or female rats.

Schwetz et al. (1975) reported that tetrachloroethylene was not teratogenic to rats and Swiss Webster mice after inhalation exposures of 300 ppm for seven hours per day on days six-15 of gestation. Careful examination of their data, however, indicate that there were a number of modest but statistically significant deviations of adverse health effect parameters from control animals, including increased body maternal weights, decreased body weight of mouse fetuses increased fetal resorptions and increased incidence of split

sternebrae, subcutaneous edema and delayed ossification of skull bones in mouse fetuses. Shumacher et al. (1962) exposed three week old mice for eight hours/day, three days each to 200, 400, 800 and 1600 ppm perchloroethylene. The exposures produced significant mortality and growth inhibitio in survivors.

Tetrachloroethylene SNARL

Tetrachloroethylene is a carcinogen in mice, and also causes non-carcinogenic bioeffects at high doses. One-day, 10-day and chronic SNARL values based on non-carcinogenic bioeffects are computed incorporating appropriate factors of safety. Estimates of concentrations projected to increase the lifetim cancer risk by one in 100,000 and one in a 1,000,000 are also provided using the NAS model. The non-carcinogenic SNARL recommendations are made considering the child and other sensitive members of the population.

A one-day SNARL of 2.3 mg/l can be calculated using a study by Kylin (1963). In this study mice were exposed to 200 ppm tetrachloroethylene in air for a period of four hours. Histological examinations of the liver demonstrated fatty infiltration but not cellular necrosis. Even though the exposure levels ranged from 200 to 1600 ppm tetrachloro-ethylene, the no-adverse-effect level was not established.

Using the method by Olsen and Gehring (1976) whereby the lung/whole body ratios for humans and animals are assumed to be roughly equivalent, the total exposure of 200 ppm (1358 mg/m^3) for four hours via inhalation, could be used to determine the one-day SNARL:

$$\frac{(1358 \text{ mg/m}^3)(4 \text{ m}^3/\text{day})(0.30) \quad (1)}{(1 \text{ l/day})(100 \text{ uncertainty factor})(7)} = 2.3 \text{ mg/l}$$

Where:
- 1/7 = child/adult body weight ratio
- 0.30 = absorption factor
- 1 l/day = child's daily water consumption
- 100 uncertainty factor because of animal experimen
- 1358 mg/m^3 = (200 ppm)(6.79 conversion factor)
- 4m^3 = according to Olsen and Gehring whereby the lung-whole body ratios for humans (adults) and rats (adults) are assigned to be roughly equivalent

An uncertainty factor of 100 was chosen rather than 1,000 even though the SNARL is based upon an animal experiment in which the no-observed-effect level was not identified. It

was felt that the index of toxicity, namely fatty infil-
tration of the liver, is a delicate disorder in itself which
is reversible and not life-threatening after a short exposure,
therefore an additional margin of safety was not warranted.

The National Academy of Sciences (NAS, 1979) has computed a
one-day SNARL of 172 mg/l and 24.5 mg/l for the seven-day
SNARL. Calculations used by the NAS to determine a one-day
SNARL were based on hepatotoxicity at a dose level of 490
mg/kg body weight given intraperitoneally to the animals.
The calculations were made for a 70 kg man and the drinking
water was considered to be the sole source of exposure. The
seven-day NAS SNARL was calculated by dividing the one-day
SNARL value by the appropriate number of days.

The NAS chose to work with data in animals given intra-
peritoneal injections. The Office of Drinking Water selected
an inhalation study in animals for extrapolation of its
SNARL and calculated the SNARL for the 10 kg child. Animal
studies and a human case history suggest that, in this case,
children appear to be a sensitive population which needs to
be protected from the adverse health effects.

The Office of Drinking Water 10-day SNARL was calculated
using an inhalation study by Savolainen, et al. (1977) in
which inhalation exposures of adult male rats to 200 ppm of
tetrachloroethylene six hours daily for five days caused
diminished brain RNA content. The 10-day SNARL of 175 ug/l
was thus determined:

$$\frac{(1358 \text{ mg/m}^3)(6 \text{ m}^3)(0.30)(1)(1)}{(1 \text{ l/day})(1000)\qquad(7)(2)} = 175 \text{ ug/l}$$

Where: 1358 ug/m^3 = (200 ppm)(6.79 conversion factor)
         6 m^3 = according to Olsen and Gehring whereby the
             lung-whole body ratio for humans (adults) and
         rats
             (adults) are assumed to be roughly equivalent
         0.30 = absorption factor
         1 l/day = Child's daily consumption of drinking
             water
         1000 = uncertainty factor due to animal experi-
             ment where the no-observed-effect level was not ide
         1/7 = child/adult body weight ratio
         1/2 = factor to provide for equivalent toxicity on
             day 10 as noted on day five

As a matter of interest "Medical World News" contained a
report of a six week old baby with jaundice and an enlarged
liver; the baby was breast fed by a mother who was frequently

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exposed to tetrachloroethylene in a dry cleaning establishme[nt] (Anonymous, 1978). The mother's milk contained perchloroeth[ylene] levels up to one mg %. The child's symptoms vanished when breast feeding was discontinued.

Longer-Term SNARL:

A longer-term SNARL of 20 ug/l (rounded from the computation) can be estimated from a study by Navrotskii et al. (1971). The authors reported increased urinary urobilinogen and pathological changes in the parenchyma of the liver and kidneys of rabbits after inhalation exposure to 100 mg/m[^3] perchloroethylene for three to four hours/day for seven to 11 months. The calculations for a longer-term SNARL are:

$$\frac{(100 \text{ mg/m}^3)(4 \text{ m}^3/\text{day})(0.30)}{(1 \text{ l/day})(1000 \text{ uncertainty factor})(7)} \quad (1) \quad = \quad 0.017 \text{ mg/l}$$

Where: 100 mg/m^3 = observed effect level
4m^3 = according to Olsen and Gehring whereby the lung-whole body ratio for humans (adults) and rats (adults) are assumed to be roughly equ[al]
0.30 = absorption factor
1 l/day = child's consumption of drinking water
$1/7$ = child/adult body weight ratio.
1000 = uncertainty factor due to animal study where health effect was observed

Since tetrachloroethylene is considered a carcinogen, at least for mice, and using the risk etimates generated by th[e] National Academy of Sciences (NAS), it is possible to ident[ify] that range of tetrachloroethylene concentrations that would increase the risk of one excess cancer per 10^6 or 10^5 peopl[e] exposed over a lifetime. From the NAS model it is estimate[d] that consuming 2 l/day over a lifetime having a tetrachlor[o] concentration of 3.5 ug/l or 35 ug/l would increase the ris[k] by one excess cancer/million exposed or one excess cancer/[?] exposed, respectively. This is the range of risks where many EPA regulatory values for other carcinogens have been.

These risk extrapolations were based on an assumption that there is no threshold effect level for carcinogens. The state-of-the-art at the present time is such that no exper[imental] tools can accurately define the absolute numbers of excess cancer deaths attributable to tetrachloroethylene in drink[ing] water. Due to biological variability and the number of assumptions required, each of the risk estimating procedur[es] leads to a different value. There is wide variation betwe[en] these estimates and also in their interpretation. For thi[s]

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reason we report the results of the NAS risk computations, which is a conservative approach, as a range of values from one in 100,000 to one in 1,000,000 incremental risk (risk above background) for a carcinogen. The NAS risk estimates are based on the multistage model concept. "At low dose, the multistage model is often mathematically equivalent to the linear or single hit model. Therefore, its use for extrapolation is consistent with the conservative linear risk estimation. If the precise mechanism of carcinogenesis is represented by a threshold or log-normal dose response relationship, the multistage model may considerably over estimate the risk at low dose levels. However, this possibility cannot be reasonably quantified" (NAS-1979).

In summary, the one-day, ten-day and longer-term SNARL values for tetrachloroethylene are 2300 ug/l, 175 ug/l and 20 ug/l, respectively, if drinking water is the only source of exposure. The concentrations resulting in a lifetime risk of 10^{-6} and 10^{-5} are 3.5 ug/l and 35 ug/l, respectively, if the contaminated drinking water was consumed over a lifetime. The longer-term SNARL of 20 ug/l tetrachloroethylene in drinking water may result in excess cancer risk of approximately six in one million, if the exposure was for a lifetime (70 years).

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