March 31, 1987

# 820K87121

## ACRYLAMIDE

Health Advisory
Office of Drinking Water
U.S. Environmental Protection Agency

## I. INTRODUCTION

The Health Advisory (HA) Program, sponsored by the Office of Drinking Water (ODW), provides information on the health effects, analytical methodology and treatment technology that would be useful in dealing with the contamination of drinking water. Health Advisories describe nonregulatory concentrations of drinking water contaminants at which adverse health effects would not be anticipated to occur over specific exposure durations. Health Advisories contain a margin of safety to protect sensitive members of the population.

Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as new information becomes available.

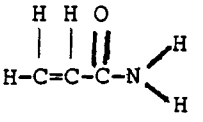
Health Advisories are developed for One-day, Ten-day, Longer-term (approximately 7 years, or 10% of an individual's lifetime) and Lifetime exposures based on data describing noncarcinogenic end points of toxicity. Health Advisories do not quantitatively incorporate any potential carcinogenic risk from such exposure. For those substances that are known or probable human carcinogens, according to the Agency classification scheme (Group A or B), Lifetime HAs are not recommended. The chemical concentration values for Group A or B carcinogens are correlated with carcinogenic risk estimates by employing a cancer potency (unit risk) value together with assumptions for lifetime exposure and the consumption of drinking water. The cancer unit risk is usually derived from the linear multistage model with 95% upper confidence limits. This provides a low-dose estimate of cancer risk to humans that is considered unlikely to pose a carcinogenic risk in excess of the stated values. Excess cancer risk estimates may also be calculated using the One-hit, Weibull, Logit or Probit models. There is no current understanding of the biological mechanisms involved in cancer to suggest that any one of these models is able to predict risk more accurately than another. Because each model is based on differing assumptions, the estimates that are derived can differ by several orders of magnitude.

This HA is based on information presented in the Office of Drinking Water's draft Health Effects Criteria Document (CD) for Acrylamide (U.S. EPA, 1985a). The HA and CD formats are similar for easy reference. Individuals desiring further information on the toxicological data base or rationale for risk characterization should consult the CD. The CD is available for review at each EPA Regional Office of Drinking Water counterpart (e.g., Water Supply Branch or Drinking Water Branch), or for a fee from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Rd., Springfield, VA 22161, PB # 86-117744/AS. The toll-free number is (800) 336-4700; in the Washington, D.C. area: (703) 487-4650.

## II. GENERAL INFORMATION AND PROPERTIES

CAS No. 79-06-1

Chemical Structure



Synonyms:

- 2-Propenamide, acrylic amide, acrylic acid amide, akrylamid, ethylene carboxamide and propinoic acid amide.

Uses:

- As the monomer, in:
  - Grouts
  - Soil stabilizers
- As the polyacrylamide, in:
  - Flocculant production - drinking water and wastewater treatment plants
  - Additive for enhanced oil recovery
  - Fog dissipator
  - Soil stabilizer
  - Paper and paperboard strengthener
  - Adhesive/binder component
  - Metal coating
  - Food packaging
  - Photography applications
  - Chromatography gel
  - Electrophoresis gel
  - Dye applications

Properties (Windholz, 1976; Verschueren, 1983)

| | |
|---|---|
| Chemical Formula | $C_3H_5NO$ |
| Molecular Weight | 71.08 |
| Physical State (room temp.) | white crystals |
| Boiling Point (at 25 mmHg) | 125 °C |
| Melting Point | 84.5 °C |
| Vapor Pressure (25°C) | 0.007 mmHg |

| | |
|---|---|
| Specific Gravity (30°C) | 1.122 g/mL |
| Water Solubility (30°C) | 2155 g/L |
| Chloroform Solubility (30°C) | 26.6 g/L |
| Benzene Solubility (30°C) | 3.46 g/L |
| Octanol/Water Partition Coefficient | -- |
| Taste Threshold (water) | -- |
| Odor Threshold (water) | -- |
| Odor Threshold (air) | |
| Conversion Factor | 1 $mg/m^3$ = 0.34 ppm |
| Conversion Factor | 1 ppm = 2.95 $mg/m^3$ |

Occurrence

- The production of acrylamide in 1982 was estimated to be 86 million pounds (U.S. ITC, 1984). Acrylamide is used primarily in the production of polyacrylamide polymers and co-polymers. It is also used as a grouting agent, and approximately 1 million pounds is used for this purpose (U.S. EPA, 1984).

- Acrylamide monomer occurs as a contaminant in polyacrylamide. The monomer may be released to the environment during its production, its use in manufacturing polymers and during the use of polyacrylamides. However, the major source of release occurs as a result of its use as a grout. No information on production and manufacture releases is available. Due to the low vapor pressure of acrylamide, no releases to air are expected (U.S. EPA, 1984).

- Acrylamide has been shown to biodegrade in surface waters within a few days (Brown and Rhead, 1979). Waters which routinely receive acrylamide releases will degrade it even more readily. Hydrolysis of acrylamide to acrylic acid has been reported to occur, but is likely to be a relatively slow reaction (Brown and Rhead 1979; Brown et al. 1980b).

- Acrylamide has not been surveyed for in U.S. food and drinking water. Based upon standards recommended by EPA for polymers used in drinking water, the levels of acrylamide monomer in drinking water have been reported to occur up to 0.5 ug/L (U.S. EPA, 1980). One study in England has reported tap water levels of acrylamide in the low ug/L range (Brown and Rhead, 1979). No information has been identified on the occurrence of acrylamide in food. Low levels of acrylamide also may occur in some foods from the use of polyacrylamides in the manufacture of those foods (U.S. EPA, 1984).

## III. PHARMACOKINETICS

### Absorption

- When acrylamide (10 mg/kg) was administered to rats *per os*, it was absorbed rapidly and completely from the gastrointestinal tract (Miller et al., 1982).

- By comparing the blood levels of acrylamide after iv or dermal administration, it was calculated that approximately 25% of either applied dose (2 or 50 mg/kg) was absorbed through the skin (Ramsey et al., 1984).

- Recently, it was reported that 26% of a 0.5% solution of acrylamide was absorbed through the skin of rats in 24 hours. An additional 35% was present in the skin and, potentially, available for absorption. Using excised skin preparations, they found that 67% (54% absorbed and 13% present in skin after washing) of the acrylamide was either absorbed or available for absorption (Frantz et al., 1985).

Distribution

- After acrylamide was administered to rats by gavage, the highest concentrations were found in red blood cells, with lower amounts found in all other tissues examined (Ramsey et al., 1984).

- Results reported by Hashimoto and Aldridge (1970) indicate that acrylamide is bound covalently to proteins or other cellular macromolecules.

- Acrylamide freely crosses the placenta in pregnant female rats, rabbits, dogs and pigs (Edwards, 1976; Ikeda et al., 1983) and is uniformly distributed throughout dog and pig fetal tissue (Ikeda et al., 1983).

- Autoradiographic studies revealed that, after oral administration of 120 mg/kg, acrylamide was widely distributed in male and female mice. The fetuses of pregnant mice were uniformly labeled, except that there was a concentration of acrylamide in fetal skin (Marlowe et al., 1986).

Metabolism

- In rats, acrylamide is metabolized primarily by conjugation with cellular glutathione (Miller et al., 1982).

- The major metabolite (greater than 50%) of acrylamide is the mercapturic acid, N-acetyl-S-(3-amino-3-oxypropyl) cysteine (detected in the urine of rats given acrylamide orally or intravenously (Miller et al., 1982; Ramsey et al., 1984).

- Another metabolite resembling cysteine-S-propionamide has been tentatively identified (Dixit et al., 1982).

Excretion

- In rats, excretion of acrylamide and its metabolic products occurs primarily via the urine (Miller et al., 1982; Ramsey et al., 1984).

- Over 60% of a dose of acrylamide, administered either orally or iv, appeared in the urine of rats within 24 to 72 hours (Miller et al., 1982; Ramsey et al., 1984).

- Minor routes (less than 6%) of acrylamide elimination in rats include fecal excretion (Miller et al., 1982) and release of the amide carbon as $CO_2$ following oxidation (Hashimoto and Aldridge, 1970; Ramsey et al., 1984).

## IV. HEALTH EFFECTS

### Humans

- Acrylamide intoxication has been reported in five individuals (three adults and two children) exposed via ingestion of drinking water contaminated with 400 ppm acrylamide (Igisu et al., 1975). All three adults exhibited symptoms of widespread central and peripheral nervous system dysfunction. The children apparently consumed less water than the adults and were less severely affected.

- Additional reports on human exposure to acrylamide deal primarily with dermal or inhalation exposure of workers. The predominant effects included dysfunction of the central and/or peripheral nervous systems. Quantitative data on dose and duration of exposure generally were not available in these reports (Auld and Bedwell, 1967; Garland and Patterson, 1967; Fullerton, 1969; Davenport et al., 1976; Kesson et al., 1977).

### Animals

- Evaluation of the toxicological data base for acrylamide indicates that this chemical is a cumulative poison. It has been shown that when the total dose of acrylamide administered over either short or longer periods of time reaches 100 to 150 mg/kg, signs of neuropathology begin to appear in many species tested (U.S. EPA, 1985a).

### Short-term Exposure

- Reported acute oral $LD_{50}$ values for rats, guinea pigs and rabbits range from 150 to 180 mg/kg (McCollister et al., 1964). Acute oral $LD_{50}$ values for mice have been reported to range from 107 to 170 mg/kg (NIOSH, 1976; Hashimoto et al., 1981).

- An acute oral $LD_{50}$ for acrylamide in male F-344 rats was reported to be 202.5 (range of 188.9 to 217.3) mg/kg (Pryor et al., 1983).

- Single doses of acrylamide, administered at levels as low as 25 mg/kg, have been shown to significantly increase binding of the neurotransmitter $^3$H-spiroperidol in rat brains (Agrawal et al., 1981).

- Single doses of acrylamide (1 to 100 mg/kg), administered via ip injection, were shown to cause significant inhibition of retrogade axonal transport in rats at doses of 25 mg/kg or greater. Doses of 1, 5, or 15 mg/kg caused no inhibition of transport (Miller et al., 1983).

- Cats given acrylamide in the diet at levels of 20 mg/kg/day for 2 or 3 weeks developed hind limb weakness and general unsteadiness of the posterior half of the body which usually progressed to hind limb paralysis (Leswing and Ribelin, 1969). Microscopically, the affected nerves exhibited degeneration of myelin and axons.

- Dogs that were given acrylamide orally at levels of 5 mg/kg/day developed ataxia and muscular weakness by day 21 of treatment; de-myelination of nerves was evident after 60 days (Thomann et al., 1974).

- Rats administered acrylamide in their drinking water displayed hind limb splaying after 14 days of treatment at a dose of 30 mg/kg/day. Microscopic changes in peripheral nerves were observed in animals dosed at 10 and 30 mg/kg/day. A NOAEL of 3 mg/kg/day was identified (Gorzinski et al., 1979).

- Monkeys treated with an average dose of 7.1 mg/kg/day (administered orally in fruit juice) developed signs of visual impairment after 28 days; ataxia and motor impairment occurred after 46 to 65 days of exposure (Merigan et al., 1982).

Long-term Exposure

- Most adverse health effects of acrylamide appear to be the result of damage to central or peripheral nerve tissue. The most characteristic effects are weakness and ataxia in hind limbs, progressing to paralysis with continued exposure (Pryor et al., 1983; Thomann et al., 1974; McCollister et al., 1964).

- The subacute (5 days/wk for 4 wks) and subchronic (5 days/wk for 15 wks) $LD_{50}$s for acrylamide are 32.0 (25.8 to 38.2) and 17.0 (15.3 to 18.7) mg/kg, respectively (Pryor et al., 1983).

- Acrylamide administered in drinking water to rats at levels of 1 mg/kg/day for 90 days caused no external signs of toxicity, but histologic evidence of neuropathy was noted (axolemmal invaginations) (Burek et al., 1980). The NOAEL in this study was determined to be 0.2 mg/kg/day.

- Cats receiving oral doses of 1 mg/kg/day for 125 days developed ataxia (Kuperman, 1958).

- Cats fed 0.7 mg/kg/day for 240 days developed hind limb weakness; a NOAEL of 0.2 mg/kg/day was identified in this study (McCollister et al., 1964).

Reproductive Effects

- Mice, dosed orally with acrylamide at 10.1 mg/kg/day for 8 to 10 weeks, displayed testicular atrophy and significant reduction in testes weight with degeneration of the epithelial cells of the seminiferous tubules (Hashimoto et al., 1981).

Developmental Effects

- Acrylamide, administered by gavage at 20 mg/kg/day to pregnant rats on days 7 through 16 of gestation, significantly reduced $^{3}$H-spiroperidol binding in the striatal tissue of 2-week-old pups (Agrawal and Squibb, 1981).

Mutagenicity

- Acrylamide did not elicit mutagenic activity in the Salmonella Ames test in strains TA 98, TA 100, TA 1535 and TA 1537 with or without microsomal activation (Bull et al., 1984a).

- In the hepatocyte primary culture DNA repair test, acrylamide did not exert mutagenic effects (Miller and McQueen, 1986).

- Acrylamide induced chromosome breaks and aberrations in spermatogonia of mice exposed to 75 mg/kg/day in the diet for two or three weeks (Shiraishi, 1978).

- In a dominant lethal study, male rats received acrylamide at 0, 15, 30 or 60 mg/L for 80 days in their drinking water (0, 1.5, 2.8 or 5.8 mg/kg/day; Smith et al., 1986). The males were mated to untreated females which were killed on day 14 of gestation. A significant increase in preimplantation loss was noted in females mated to males treated at 60 mg/L. Significant post-implantation loss was observed in females mated to the mid- and high-dose males (30 and 60 mg/L). The authors concluded that acrylamide produces dominant lethality in the male rat. This effect was noted at dose levels at which no hindlimb splaying was evident or significant histopathological lesions of the sciatic nerve occurred as determined by light microscopy.

Carcinogenicity

- Groups of male and female Fischer 344 rats received drinking water containing acrylamide monomer at 0, 0.01, 0.1, 0.5 or 2.0 mg/kg/day for 2 years (Johnson et al., 1986). After a year, significant depression of body weight was observed in the highest dose males. Distal neuropathy was observed in the peripheral nerves of animals in this group. Tumor incidence was not increased significantly in the groups receiving 0.01 or 0.1 mg/kg/day. Male rats receiving 0.5 mg/kg/day had significantly increased incidences of scrotal mesothelioma. Statistically significant increased incidences of tumors in the following tissues were determined in rats treated at 2.0 mg/kg: Females -- mammary gland (benign and malignant), central nervous system (malignant), thyroid gland follicular epithelium (benign and malignant), mouth (benign), uterus (malignant) and clitoral gland (benign); males -- scrotal mesothelioma (malignant) and thyroid gland follicular epithelium (benign).

- Female Swiss-ICR mice, administered acrylamide orally at doses of 5.4, 10.7 or 21.4 mg/kg/day for 2 weeks had a dose-dependent increase of tumors induced by the phorbal ester TPA (2.5 ug/mouse, 3 times per week for 20 weeks; Bull et al., 1984b).

° Male and female mice that received acrylamide orally or intraperitoneally at average daily doses of 2.7, 5.4 or 10.7 mg/kg/for eight weeks showed statistically significant increases in the incidence of lung adenomas (Bull et al., 1984a). Acrylamide was more potent by gavage than by systemic routes.

## V. QUANTIFICATION OF TOXICOLOGICAL EFFECTS

Health Advisories (HAs) are generally determined for One-day, Ten-day, Longer-term (approximately 7 years) and Lifetime exposures if adequate data are available that identify a sensitive noncarcinogenic end point of toxicity. The HAs for noncarcinogenic toxicants are derived using the following formula:

$$HA = \frac{(NOAEL \text{ or } LOAEL) \times (BW)}{(UF) \times (\_\_\_ \text{ L/day})} = \_\_\_ \text{ mg/L } (\_\_\_ \text{ ug/L})$$

where:

NOAEL or LOAEL = No- or Lowest-Observed-Adverse-Effect-Level in mg/kg bw/day.

BW = assumed body weight of a child (10 kg) or an adult (70 kg).

UF = uncertainty factor (10, 100 or 1,000), in accordance with NAS/ODW guidelines.

___ L/day = assumed daily water consumption of a child (1 L/day) or an adult (2 L/day).

No adequate dose-response data representing the oral route of exposure are available from which to develop short term risk assessments. However, in view of substantial chemical disposition evidence showing that acrylamide is absorbed rapidly and completely by virtually any route of exposure, it is considered acceptable to use data generated following exposure via other routes.

### One-day Health Advisory

The results of Miller et al. (1983) are considered appropriate for use in calculating the One-day HA. In this study, male Sprague-Dawley rats (five animals per dose) were injected intraperitoneally with a single dose of acrylamide (1 to 100 mg/kg) and the rate of retrograde axonal transport of iodinated nerve growth factor was measured. The authors determined that significant inhibition of transport occurred at or above doses of 25 mg/kg, while no significant changes were seen at or below 15 mg/kg. A NOAEL of 15 mg/kg was identified.

The One-day HA for the 10 kg child is calculated as follows:

$$\text{One-day HA} = \frac{(15 \text{ mg/kg/day})(10 \text{ kg})}{(100)\ (1 \text{ L/day})} = 1.5 \text{ mg/L } (1500 \text{ ug/L})$$

where:

15 mg/kg/day = NOAEL, based on absence of neurotransport inhibition in rats.

10 kg = assumed body weight of a child.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

1 L/day = assumed daily water consumption of a child.

Ten-day Health Advisory

The results of Gorzinski et al. (1979) are considered appropriate for use in calculating the Ten-day HA. In this study, acrylamide was administered at levels of 0, 1, 3, 10 or 30 mg/kg/day in drinking water to male and female CDF Fischer 344 rats for 21 consecutive days. Based upon histological examination of peripheral nerves using both light and electron microscopy, it was determined that axon degeneration and demylenization occurred at the 10 and 30 mg/kg/day dose levels while no significant changes were apparent at the 0, 1 or 3 mg/kg/day dose levels. A NOAEL of 3 mg/kg/day was identified.

The Ten-day HA for the 10 kg child is calculated as follows:

$$\text{Ten-day HA} = \frac{(3 \text{ mg/kg/day})(10 \text{ kg})}{(100)(1 \text{ L/day})} = 0.3 \text{ mg/L } (300 \text{ ug/L})$$

where:

3 mg/kg/day = NOAEL, based on absence of neuropathy in rats.

10 kg = assumed body weight of a child.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

1 L/day = assumed daily water consumption of a child.

Longer-term Health Advisory

The results of Burek et al. (1980) are considered appropriate for use in deriving the Longer-term HA. In this study, acrylamide was administered in drinking water for 90 days to male and female CDF rats at dose levels of 0, 0.05, 0.2, 1, 5 or 20 mg/kg/day. Electron microscopy revealed that animals dosed at 1 mg/kg/day exhibited axolemmal invaginations of peripheral nerves. No significant alterations were observed at the 0, 0.05 and 0.2 mg/kg/day dose levels. Thus, based on the most sensitive measure of toxicity employed in these studies (ultrastructural examination of peripheral motor nerves), it was concluded that 0.2 mg/kg was the NOAEL.

The Longer-term HA for the 10 kg child is calculated as follows:

$$\text{Longer-term HA} = \frac{(0.2 \text{ mg/kg/day})\ (10 \text{ kg})}{(100)\ (1 \text{ L/day})} = 0.02 \text{ mg/L } (20 \text{ ug/L})$$

where:

0.2 mg/kg/day = NOAEL, based on absence of neuropathy in rats.

10 kg = assumed body weight of a child.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

1 L/day = assumed daily water consumption of a child.

The Longer-term HA for the 70 kg adult is calculated as follows:

$$\text{Longer-term HA} = \frac{(0.2 \text{ mg/kg/day})\ (70 \text{ kg})}{(100)\ (2 \text{ L/day})} = 0.07 \text{ mg/L } (70 \text{ ug/L})$$

where:

0.2 mg/kg/day = NOAEL, based on absence of neuropathy in rats.

70 kg = assumed body weight of an adult.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

2 L/day = assumed daily water consumption of an adult.

Lifetime Health Advisory

The Lifetime HA represents that portion of an individual's total exposure that is attributed to drinking water and is considered protective of noncarcinogenic adverse health effects over a lifetime exposure. The Lifetime HA is derived in a three step process. Step 1 determines the Reference Dose (RfD), formerly called the Acceptable Daily Intake (ADI). The RfD is an estimate of a daily exposure to the human population that is likely to be without appreciable risk of deleterious effects over a lifetime, and is derived from the NOAEL (or LOAEL), identified from a chronic (or subchronic) study, divided by an uncertainty factor(s). From the RfD, a Drinking Water Equivalent Level (DWEL) can be determined (Step 2). A DWEL is a medium-specific (i.e., drinking water) lifetime exposure level, assuming 100% exposure from that medium, at which adverse, noncarcinogenic health effects would not be expected to occur. The DWEL is derived from the multiplication of the RfD by the assumed body weight of an adult and divided by the assumed daily water consumption of an adult. The Lifetime HA is determined in Step 3 by factoring in other sources of exposure, the relative source contribution (RSC). The RSC from drinking water is based on actual exposure data or, if data are not available, a value of 20% is assumed for synthetic organic chemicals and a value of 10% is assumed for inorganic chemicals. If the contaminant is classified as a Group A or B carcinogen, according to the Agency's classification scheme of carcinogenic potential (U.S. EPA, 1986), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical.

The study by Burek et al. (1980) is the most appropriate from which to derive the DWEL. The experimental details are described in the Longer-term Health Advisory section. An additional uncertainty factor of 10 is included in order to accommodate for use of a less-than-lifetime study. From the results of the study, a NOAEL of 0.2 mg/kg was identified.

The RfD and DWEL are calculated as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(0.2 \text{ mg/kg/day})}{(1{,}000)} = 0.0002 \text{ mg/kg/day}$$

where:

0.2 mg/kg/day = NOAEL.

1,000 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study of less-than-lifetime duration.

Step 2: Determination of the Drinking Water Equivalent Level (DWEL)

$$DWEL = \frac{(0.002 \text{ mg/kg/day})(70 \text{ kg})}{(2 \text{ L/day})} = 0.007 \text{ mg/L (7 ug/L)}$$

where:

70 kg = assumed body weight of an adult.

2 L/day = assumed daily consumption of water of an adult.

Step 3: Determination of the Lifetime Health Advisory

Acrylamide may be classified in group B2: Probable Human Carcinogen. Therefore, a Lifetime HA is not recommended for acrylamide.

The estimated excess cancer risk associated with lifetime exposure to drinking water containing acrylamide at 7 ug/L is approximately $7 \times 10^{-4}$. This estimate represents the upper 95% confidence limit from extrapolations prepared by EPA's Carcinogen Assessment Group using the linearized, multistage model. The actual risk is unlikely to exceed this value, but there is considerable uncertainty as to the accuracy of risks calculated by this methodology.

Evaluation of Carcinogenic Potential

- The data from the Bull et al. (1984a,b) and the Johnson et al. (1986) studies in mice and rats show that acrylamide has significant carcinogenic potential.

- On the basis of the results observed in the rat drinking water study (Johnson et al., 1986), EPA's Carcinogen Assessment Group (CAG) has prepared a draft quantitative risk assessment of acrylamide exposure (U.S. EPA, 1985c). In this draft assessment, CAG derived several

carcinogenic potency factors from different sets of dose-response data. CAG recommended, however, that the human potency factor ($q_1^*$) of 3.7 $(mg/kg/day)^{-1}$ derived from the combination of tumor incidence data on mammary gland, thyroid and uterus in the females be used for estimating the increased lifetime risk of human exposure to acrylamide. Assuming that a 70 kg adult ingests 2 L of water per day over a 70-year lifetime, the estimated excess cancer risk at $10^{-4}$, $10^{-5}$ and $10^{-6}$ would be 1 ug/L, 0.1 ug/L and 0.01 ug/L, respectively. (These estimates were made by the Office of Drinking Water). While recognized as statistically alternative approaches, the range of risks described by using any of these modelling approaches has little biological significance unless data can be used to support the selection of one model over another. In the interest of consistency of approach and in providing an upper bound on the potential cancer risk, the Agency has recommended use of the linearized multistage approach.

° Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986), acrylamide is classified in Group B2: Probable human carcinogen. Group B2 contains substances with sufficient evidence of carcinogencity in animals and inadequate evidence from human studies.

## VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

° Polyacrylamide products used as coagulant aids in the treatment of drinking water should not have a residual monomer content greater than 0.5 ug/L (U.S. EPA, 1980).

## VII. ANALYTICAL METHODS

° There is no standardized method for the determination of acrylamide in drinking water. An analytical procedure for the determination of acrylamide has been reported in the literature (Brown and Rhead, 1979). This procedure consists of bromination, extraction of the brominated product from water with ethyl acetate and quantification using high performance liquid chromatography (HPLC) with an ultraviolet detector. The concentration of the ethyl acetate to dryness and dissolution in a small volume of distilled water prior to HPLC analysis allows the detection of acrylamide at concentrations of 0.2 ug/L.

## VIII. TREATMENT

° Croll et al. (1974) conducted laboratory experiments to determine the effectiveness of conventional treatments such as coagulation and rapid gravity sand filtration for removal of acrylamide. Several 400 ml samples of Thames River water (pH 7.5) containing 25 mg/L kaolin were coagulated by adding 32 mg/L alum and 2 mg/L of an acrylamide-based polymer with a residual acylamide monomer content of 0.19%. Only about 5% of the residual monomer was removed by this method, suggesting that full-scale water plants using conventional treatment techniques would not be successful in removing acrylamide from drinking water.

- The removal of acrylamide from water by adsorption was studied by Brown et al. (1980a) using various adsorbants including granular activated carbon (GAC) and synthetic resins. The data indicated that GAC may be an effective treatment process. GAC removed 94 to 96% of the acrylamide from a sample containing 0.5 mg/L and 68 to 70% from a sample containing 10 mg/L. The adsorption of acrylamide was not affected significantly by changes in pH. No significant adsorption was achieved by any of the resins tested, including the XAD-2 resin.

- In a laboratory experiment conducted by Croll et al. (1974), water containing 6 ug/L acrylamide (at pH 5.0) was dosed with 8 mg/L powdered activated carbon (PAC) and mixed for 30 minutes. Only 13% of the acrylamide was removed. These data indicate that PAC may not be effective for acrylamide removal from drinking water under conditions used generally in water treatment plants.

- No data were found on the removal of acrylamide by aeration. Since its Henry's Law Constant is $4.38 \times 10^{-3}$ atm (at 20°C), aeration probably would not be very effective.

- Croll et al. (1974) evaluated the effects of some chemical oxidative treatments on removal of acrylamide. Potassium permanganate and ozone were found to be highly effective in removing the substance. Additional data to optimize these processes are needed. Oxidative degradation products also should be identified and evaluated for toxicity and reactivity.

- Selection of individual or combinations of technologies to achieve acrylamide reduction must be based on a case-by-case technical evaluation and an assessment of the economics involved.

## IX. REFERENCES

Agrawal, A.K., P.K. Seth, R.E. Squibb, H.A. Tilson, L.L. Uphouse and S.C. Bondy. 1981. Neurotransmitter receptors in brain regions of acrylamide-treated rats. I: Effects of a single exposure to acrylamide. Pharmacol. Biochem. Behav. 14:527-531.

Agrawal, A.K., and R.E. Squibb. 1981. Effects of acrylamide given during gestation on dopamine receptor binding in rat pups. Toxicol. Lett. 7:233-238.

Auld, R.B., and S.F. Bedwell. 1967. Peripheral neuropathy with sympathetic overactivity from industrial contact with acrylamide. Can. Med. Assoc. J. 96:652-654.

Brown, L., and M. Rhead. 1979. Liquid chromatographic determination of acrylamide monomer in natural and polluted aqueous environment. Analyst. 104:391-399.

Brown, L., K.C.C. Brancroft and M.M. Rhead. 1980a. Laboratory studies on the adsorption of acrylamide monomer by sludge, sediments, clays, peat, and synthetic resins. Water Res. 14:779-781.

Brown, L., M.M. Rhead, K.C.C. Bancroft and N. Allen. 1980b. Model studies of the degradation of acrylamide monomer. Water Res. 14:775-779.

Bull, R.J., M. Robinson, R.D. Laurie, G.D. Stoner, E. Greisiger, J.R. Meier and J. Stober. 1984a. Carcinogenic effects of acrylamide in SENCAR and A/J mice. Cancer Res. 44:107-111.

Bull, R.J., M. Robinson and J.A. Stober. 1984b. Carcinogenic activity of acrylamide in the skin and lung of Swiss-ICR mice. Canc. Lett. 24:209-212.

Burek, J.D., R.R. Albee, J.E. Beyer, T.J. Bell, R.M. Carreon, D.C. Morden, C.E. Wade, E.A. Hermann and S.J. Gorzinski. 1980. Subchronic toxicity of acrylamide administered to rats in the drinking water followed by up to 144 days of recovery. J. Environ. Pathol. Toxicol. 4:157-182.

Croll, B.T., G.M. Arkell and R.P.J. Hodge. 1974. Residues of acrylamide in water. Water Res. 8:989-993.

Davenport, J.G., D.F. Farrell and S.M. Sumi. 1976. Giant axonal neuropathy caused by industrial chemicals. Neurology. 26:919-923.

Dixit, R., P.K. Seth and H. Mukhtar. 1982. Metabolism of acrylamide into urinary mercapturic acid and cysteine conjugates in rats. Drug Metab. Disp. 10:196-197.

Edwards, P.M. 1976. The insensitivity of the developing rat foetus to the toxic effects of acrylamide. Chem.-Biol. Interact. 12:13-18.

Frantz, S.W., M.D. Dryzga, N.L. Freshoar and P.G. Watanabe. 1985. In vivo/ in vitro determination of cutaneous penetration of residual monomer from polyacrylamides. Toxicologist. 5:39. (Abst.)

Fullerton, P.M. 1969. Electrophysiological and histological observations on peripheral nerves in acrylamide poisoning in man. J. Neurol. Neurosurg. Psychiat. 32:186-192.

Garland, T.O., and M.W.H. Patterson. 1967. Six cases of acrylamide poisoning. Brit. Med. J. 4:134-138.

Gorzinski, S.J., D. C. Morden, R.R. Albee, C.E. Wade, R.M. Carreon, E.A. Hermann, J.E. Beyer and J.D. Burek. 1979. Results of palatability (12-day) and tolerance (21-day) studies on acrylamide monomer administered in the drinking water to rats.

Hashimoto, K., and W.N. Aldridge. 1970. Biochemical studies on acrylamide, a neurotoxic agent. Biochem. Pharmacol. 19:2591-2064.

Hashimoto, K., J. Sakamoto and H. Tanii. 1981. Neurotoxicity of acrylamide and related compounds and their effects on male gonads in mice. Arch. Toxicol. 47:179-189.

Igisu, H., I. Goto, Y. Kawamura, M. Kato, K. Izumi and Y. Kuroiwa. 1975. Acrylamide encephaloneuropathy due to well water pollution. J. Neurol. Neurosurg. Psychiat. 38:581-584.

Ikeda, G.J., E. Miller, P.P. Sapienza, T.C. Michel, M.T. King, V.A. Turner, H. Blumenthal, W.E. Jackson, III and S. Levin. 1983. Distribution of $^{14}C$-labeled acrylamide and betaine in foetuses of rats, rabbits, beagle dogs and miniature pigs. Food Chem. Toxicol. 21:49-58.

Johnson, K.A., S.J. Gorzinski, K.M. Brodner, R.A. Campbell, C.H. Wolf, M.A. Friedman and R.W. Mast. 1986. Chronic toxicity and oncogenicity study on acrylamide incorporated in the drinking water of Fischer 344 rats. Toxicol. Appl. Pharmacol. 85:154-168.

Kesson, C.M., A.W. Baird and D.H. Lawson. 1977. Acrylamide poisoning. Postgrad. Med. J. 53:16-17.

Kuperman, A.S. 1958. Effects of acrylamide on the central nervous system of the cat. J. Pharmacol. Exp. Ther. 123:180-192.

Leswing, R.J., and W.E. Ribelin. 1969. Physiologic and pathologic changes in acrylamide neuropathy. Arch. Environ. Hlth. 18:22-29.

Marlowe, C., M.J. Clark, R.W. Mast, M.A. Friedman and W.J. Waddell. 1986. The distribution of [$^{14}C$]acrylamide in male and female Swiss-Webster mice studied by whole body autoradiography. Toxicol. Appl. Pharmacol. 86:457-465.

McCollister, D.D., F. Oyen, and V.K. Rowe. 1964. Toxicology of acrylamide. Toxicol. Appl. Pharmacol. 6:172-181.

Merigan, W.H., E. Barkdoll and J.P.J. Maurissen. 1982. Acrylamide-induced visual impairment in primates. Toxicol. Appl. Pharmacol. 62:342-345.

Miller, M.J., D.E. Carter and I.G. Sipes. 1982. Pharmacokinetics of acrylamide in Fischer-344 rats. Toxicol. Appl. Pharmacol. 63:36-44.

Miller, M.J., and C.A. McQueen. 1986. The effect of acrylamide on hepatocellular DNA repair. Environ. Mutagen. 8:99-108.

Miller, M.S., M.J. Miller, T.F. Burks and I.G. Sipes. 1983. Altered retrograde axonal transport of nerve growth factor after single and repeated doses of acrylamide in the rat. Toxicol. Appl. Pharmacol. 69:96-101.

Miller, M.S., and P.S. Spencer. 1984. Single doses of acrylamide reduce retrograde transport velocity. J. Neurochem. 43:1401-1408.

NIOSH. 1976. National Institute for Occupational Safety and Health. Criteria for a recommended standard...occupational exposure to acrylamide. U.S. Dept. of Health, Education and Welfare, Public Health, Center for Disease Control.

Pryor, G.T., E.T. Uyeno, H.A. Tilson and C.L. Mitchell. 1983. Assessment of chemicals using a battery of neurobehavioral tests: A comparative study. Neurobehavioral. Toxicol. Teratol. 5:91-117.

Ramsey, J.C., J.D. Young and S.J. Gorzinski. 1984. Acrylamide: Toxicodynamics in rats. Unpublished report. Dow Chemical Co., Midland, MI.

Shiraishi, Y. 1978. Chromosome aberrations induced by monomeric acrylamide in bone marrow and germ cells of mice. Mutation. Res. 57:313-324.

Smith, M.K., H. Zenick, R. Preston, E.L. George and R.E. Long. 1986. Dominant lethal effects of subchronic acrylamide administration in the male Long-Evans rat. Mutat. Res. 173:273-278.

Thomann, P., W.P. Koella, G. Krinke, H. Petermann, F. Zak and R. Hess. 1974. The assessment of peripheral neurotoxicity in dogs: Comparative studies with acrylamide and clioquinol. Agts. Act. 4:47-53.

U.S. EPA. 1980. U.S. Environmental Protection Agency. Coagulant aids in the treatment of drinking water. Office of Drinking Water.

U.S. EPA. 1984. U.S. Environmental Protection Agency. Miscellaneous synthetic organic chemicals. Occurrence in drinking water, food, and air. Office of Drinking Water.

U.S. EPA. 1985a. U.S. Environmental Protection Agency. Draft health effects criteria document for acrylamide. Criteria and Standards Division. Office of Drinking Water.

U.S. EPA. 1985b. U.S. Environmental Protection Agency. Draft technologies and costs for the removal of synthetic organic chemicals from potable water supplies. Science and Technology Branch. Criteria and Standards Division. Office of Drinking Water.

U.S. EPA. 1985c. U.S. Environmental Protection Agency. Assessment of carcinogenic risk of exposure to acrylamide. (Draft). A staff paper prepared by W.C. Pepelko and J. Cagliano for the Office of Health and Environmental Assessment, Office of Research and Development.

U.S. EPA. 1986. U.S. Environmental Protection Agency. Guidelines for carcinogen risk assessment. Federal Register. 51(185):33992-34003. September 24.

U.S. ITC. 1984. United States International Trade Commission. Synthetic organic chemicals. U.S. production and sales - 1983. U.S. ITC Publication No. 1588, Washington, D.C., pp. 255 and 268.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals. 2nd Edition. Van Nostrand Reinhold Co., New York.

Windholz, M., ed. 1976. The Merck Index. 10th Edition. Merck and Co., Inc. Rahway, NJ.