6560-50-P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 372

[EPA-HQ-TRI-2006-0319; FRL–9787-1]

RIN 2025-AA19

Acetonitrile; Community Right-to-Know Toxic Chemical Release Reporting

AGENCY: Environmental Protection Agency (EPA).

ACTION: Denial of Petition.

SUMMARY: EPA is denying a petition to remove acetonitrile from the list of chemicals subject to reporting requirements under section 313 of the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) and section 6607 of the Pollution Prevention Act of 1990 (PPA). EPA has reviewed the available data on this chemical and has determined that acetonitrile does not meet the deletion criterion of EPCRA section 313(d)(3). Specifically, EPA is denying this petition because EPA's review of the petition and available information resulted in the conclusion that acetonitrile meets the listing criterion of EPCRA section 313(d)(2)(B) due to its potential to cause death in humans.

FOR FURTHER INFORMATION CONTACT: Daniel R. Bushman, Environmental Analysis Division, Office of Information Analysis and Access (2842T), Environmental Protection Agency, 1200 Pennsylvania Ave., NW, Washington, DC 20460; telephone number: 202-566-0743; fax number: 202-566-0677; e-mail: bushman.daniel@epa.gov, for specific information on this notice. For general information on EPCRA section 313, contact the Emergency Planning and Community Right-to-Know Hotline, toll free at (800) 424-9346 or (703) 412-9810 in Virginia and Alaska or toll free, TDD (800) 553-7672, http://www.epa.gov/epaoswer/hotline/.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Notice Apply to Me?

You may be potentially affected by this action if you manufacture, process, or otherwise use acetonitrile. Potentially affected categories and entities may include, but are not limited to:

Category	Examples of Potentially Affected Entities
Industry	Facilities included in the following NAICS manufacturing codes (corresponding to SIC codes 20 through 39): 311*, 312*, 313*, 314*, 315*, 316, 321, 322, 323*, 324, 325*, 326*, 327, 331, 332, 333, 334*, 335*, 336, 337*, 339*, 111998*, 211112*, 212324*, 212325*, 212393*, 212399*, 488390*, 511110, 511120, 511130, 511140*, 511191, 511199, 512220, 512230*, 519130*, 541712*, or 811490*. *Exceptions and/or limitations exist for these NAICS codes. Facilities included in the following NAICS codes (corresponding to SIC codes other than SIC codes 20 through 39): 212111, 212112, 212113 (correspond to SIC 12, Coal Mining (except 1241)); or 212221, 212222, 212231, 212234, 212299 (correspond to SIC 10, Metal Mining (except 1011, 1081, and 1094)); or 221111, 221112, 221113, 221119, 221121, 221122, 221330 (Limited to facilities that combust coal and/or oil for the purpose of generating power for distribution in commerce) (correspond to SIC 4911, 4931, and 4939, Electric Utilities); or 424690, 425110, 425120 (Limited to facilities previously classified in SIC 5169, Chemicals and Allied Products, Not Elsewhere Classified); or 424710 (corresponds to SIC 5171, Petroleum Bulk Terminals and Plants); or 562112 (Limited to facilities primarily engaged in solvent recovery services on a contract or fee basis (previously classified under SIC 7389, Business Services, NEC)); or 562211, 562212, 562213, 562219, 562920 (Limited to facilities regulated under the Resource Conservation and Recovery Act, subtitle C, 42 U.S.C. 6921 et seq.) (correspond to SIC 4953, Refuse Systems).
Federal Government	Federal facilities

This table is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Some of the entities listed in the table have exemptions and/or limitations regarding coverage, and other types of entities not listed in the table could also be affected. To determine whether your facility would be affected by this action, you should carefully examine the applicability criteria in part 372 subpart B of Title 40 of the Code of Federal Regulations. If you have questions regarding the applicability of this action to a particular entity, consult the person listed in the preceding **FOR FURTHER INFORMATION CONTACT** section.

B. How Can I Get Copies Of This Document and Other Related Information?

EPA has established a docket for this action under Docket ID No. **EPA-HQ-TRI-2006-0319.** All documents in the docket are listed in the www.regulations.gov index. Although listed in the index, some information is not publicly available, e.g., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, will be publicly available only in hard copy. Publicly available docket materials are available either electronically in www.regulations.gov or in hard copy at the OEI Docket, EPA/DC, EPA West, Room 3334, 1301 Constitution Ave., NW, Washington, DC. This Docket Facility is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566-1744, and the telephone number for the OEI Docket is (202) 566-1752.

II. Introduction

A. Statutory Authority

This action is taken under sections 313(d) and 313(e)(1) of EPCRA, 42 U.S.C. 11023. EPCRA is also referred to as Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA) (Pub. L. 99–499).

B. Background

Section 313 of EPCRA, 42 U.S.C. 11023, requires certain facilities that manufacture, process, or otherwise use listed toxic chemicals in amounts above reporting threshold levels to report their environmental releases and other waste management quantities of such chemicals annually. These facilities must also report pollution prevention and recycling data for such chemicals, pursuant to section 6607 of the PPA, 42 U.S.C. 13106. Congress established an initial list of toxic chemicals subject to reporting that comprised more than 300 chemicals and 20 chemical categories.

EPCRA section 313(d) authorizes EPA to add or delete chemicals from the list and sets criteria for these actions. EPCRA section 313(d)(2) states that EPA may add a chemical to the list if any of the listing criteria in Section 313(d)(2) are met. Therefore, to add a chemical, EPA must demonstrate that at least one criterion is met, but need not determine whether any other criterion is met. Conversely, to remove a chemical from the list, EPCRA section 313(d)(3) dictates that EPA must demonstrate that none of the listing criteria in Section 313(d)(2) are met. The EPCRA section 313(d)(2) criteria are:

> A) The chemical is known to cause or can reasonably be anticipated to cause significant adverse acute human health effects at concentration levels that are reasonably likely to exist beyond facility site boundaries as a result of continuous, or frequently recurring, releases.
>
> (B) The chemical is known to cause or can reasonably be anticipated to cause in humans–

(i) cancer or teratogenic effects, or

(ii) serious or irreversible–

(I) reproductive dysfunctions,

(II) neurological disorders,

(III) heritable genetic mutations, or

(IV) other chronic health effects.

(C) The chemical is known to cause or can be reasonably anticipated to cause, because of

(i) its toxicity,

(ii) its toxicity and persistence in the environment, or

(iii) its toxicity and tendency to bioaccumulate in the environment,

a significant adverse effect on the environment of sufficient seriousness, in the judgment of the Administrator, to warrant reporting under this section.

EPA often refers to the section 313(d)(2)(A) criterion as the "acute human health effects criterion;" the section 313(d)(2)(B) criterion as the "chronic human health effects criterion;" and the section 313(d)(2)(C) criterion as the "environmental effects criterion."

EPA issued a statement of petition policy and guidance in the **Federal Register** of February 4, 1987 (52 FR 3479) to provide guidance regarding the recommended content and format for submitting petitions. On May 23, 1991 (56 FR 23703), EPA issued guidance regarding the recommended content of petitions to delete individual members of the section 313 metal compounds categories. EPA has also published in the **Federal Register** of November 30, 1994 (59 FR 61432) a statement clarifying its interpretation of the section 313(d)(2) and (d)(3) criteria for modifying the section 313 list of toxic chemicals.

III. What is the Description of the Petition and the Regulatory Status of Acetonitrile?

Acetonitrile is on the list of toxic chemicals subject to the annual release reporting requirements of EPCRA section 313 and PPA section 6607. Acetonitrile was among the list of chemicals placed on the EPCRA section 313 list by Congress. Acetonitrile is listed under the Clean Air Act (CAA) as a volatile organic compound (VOC) and a hazardous air pollutant (HAP). Acetonitrile is also on the list of hazardous constituents (Appendix VIII to Part 261) and can qualify as listed hazardous waste (U003) under the Resource Conservation and Recovery Act (RCRA).

On February 4, 1998, EPA received a petition from BP Chemicals Inc. (BP) and GNI Chemicals Corporation (GNICC) to delete acetonitrile from the list of chemicals reportable under EPCRA section 313 and PPA section 6607, stating that acetonitrile meets all of the criteria for delisting under EPCRA section 313(d)(3). On March 5, 1999 (64 FR 10597), EPA denied the petition based on a determination that acetonitrile meets the listing criteria of EPCRA section 313(d)(2)(B) and (d)(2)(C) due to its potential to cause neurotoxicity and death in humans and its contribution to the formation of ozone in the environment.

In September 2000, based on additional reviews, EPA reversed its previous position that acetonitrile was a chronic neurotoxicant (Ref. 1).

On June 28, 2002, EPA received a second petition from BP to delete acetonitrile from the list of chemicals reportable under EPCRA section 313. Specifically, BP argues that acetonitrile meets all of the criteria for delisting under EPCRA section 313(d)(3) because: (1) under generally accepted scientific principles, chronic mortality is not an issue for concern; and (2) EPA's Office of Air Quality Planning and Standards (OAQPS) has concluded that acetonitrile does not have sufficient photochemical reactivity to contribute to ozone formation. Subsequent to BP's filing of the petition on June 28, 2002, BP formed Innovene USA LLC as its olefin,

derivatives and refining group, which was then acquired from BP by INEOS USA, LLC (INEOS), which has taken over the petition.

IV. What is EPA's Technical Review of Acetonitrile?

In response to the petition to delete acetonitrile from the list of chemicals reportable under EPCRA section 313 and PPA section 6607, EPA prepared a Technical Review of Acetonitrile (Methyl Cyanide) (Ref. 2). The sections below summarize the human health hazard information contained in the Technical Review. The review did not consider acetonitrile's status as a volatile organic compound (VOC) and thus its contribution to the formation of ozone in the environment since EPA no longer considers these factors as a basis for listing under EPCRA section 313(d)(2) (70 FR 37698).

A. Metabolism

Acetonitrile is metabolized to inorganic cyanide through the intermediate production of hydrogen cyanide. Data demonstrate that the metabolism to cyanide is oxygen- and NADPH-dependent (Ref. 3), and mediated by cytochrome P450 isozyme 2E1 (or P-450j) production of a reactive intermediate, methyl cyanohydrine (Refs. 4, 5, and 6). Formaldehyde and formic acid are also by-products of acetonitrile metabolism (Ref. 4). Cyanide is further oxidized and conjugated to thiocyanate, a less toxic compound that is excreted in urine, but one that has been shown to interfere with thyroid function (Ref. 7).

B. Toxicity Evaluation

1. *Effects of Acute Exposure*

Humans acutely exposed to sublethal doses of acetonitrile developed effects that are generally attributed to metabolism of acetonitrile to cyanide (Ref. 8). Several cases were reported in which children or adults ingested large amounts of acetonitrile (≈250 to 4,000

milligrams/kilogram (mg/kg)) (Ref. 9). Symptoms exhibited by poisoning victims include anxiety, confusion, hyperpnea, dyspnea, rapid pulse, unconsciousness, and convulsions (Ref. 9). Cyanide was detected in the blood of these individuals. Case reports of acute occupational exposure to acetonitrile indicate that workers exhibited nausea, shallow and/or irregular respiration, and impaired motor activity. An autopsy of a worker who died shortly after exposure revealed cerebral, thyroid, liver, splenic, and renal congestion (Ref. 9). Gastric erosion has been reported in individuals who ingested acetonitrile (Refs. 10 and 11).

In animals, oral LD_{50} values (i.e., the dose of a chemical that is lethal to 50 percent of the test organisms) have been reported for the mouse (269-453 mg/kg) and the rat (1,730-4,050 mg/kg) and inhalation LC_{50} values (i.e., the concentration of a chemical that is lethal to 50 percent of the test organisms) of 12,000, 16,000, and 7,551-12,435 parts per million (ppm) have been reported for the rat for 2, 4, and 8 hour exposures, respectively, and for the mouse following 1-2 hour exposures (2,300-5,700 ppm) (Ref. 9). A 1-hour LC_{50} estimate for acetonitrile in mice was reported to be 2,693 ppm (Ref. 6). A recent study (Ref. 12) reported a slightly higher oral LD_{50} of 617 mg/kg for Crl:CD-1(ICR)BR mice and an inhalation LC_{50} of 3,587 ppm for this strain. Observational signs of toxicity reported in animals after acute exposure to acetonitrile include dyspnea, tachypnea, tremors, and convulsions in various studies (Ref. 9).

2. *Effects of Subchronic and Chronic Exposure*

Subchronic inhalation exposure to acetonitrile resulted in an increase in mortality in rats at 1,600 ppm (calculates to approximately 505 mg/kg-day) and in mice at 800 ppm (calculates to approximately 402 mg/kg-day) (Ref. 13).

Following subchronic inhalation exposure in rats, the mortality incidence was 0/20 in each of the 0, 100, 200 and 400 ppm groups, 1/20 in the 800 ppm group (one death occurring on day 5), and 9/20 in the 1,600 ppm group (four deaths occurring on day 2, one each on days 7, 9, 10, 11, and 23) (Ref. 13). Clinical signs at the two high-concentration groups included hypoactivity and ruffled fur during the first week. Ataxia, abnormal posture, and clonic convulsions occurred in the 1,600 ppm males that died. In addition, a decrease in hematocrit, hemoglobin, and erythrocytes was observed in male rats at 1,600 ppm and in female rats at ≥800 ppm. Changes in organ weights were also observed, primarily at the highest dose in male rats and at ≥800 ppm in female rats, and include decreases in absolute and relative thymus weight, increases in absolute and/or relative liver and kidney weight, and decreases and increases in brain and heart weight, respectively. Histopathologic effects were limited to rats that died at 800 and 1,600 ppm; effects observed include congestion, edema, and hemorrhage in the lung alveoli.

Following subchronic inhalation exposure in mice, the mortality incidence was 0/20 in each of the 0, 100 and 200 ppm groups, 1/20 in the 400 ppm group (death occurring on day 13), 5/20 in the 800 ppm group (deaths occurring on days 20, 21, 45, 69, 89) and 20/20 in the 1,600 ppm group (all deaths occurring by day 21) (Ref. 13). Changes in organ weights were observed, including increased absolute and/or relative liver weight at ≥100 ppm in males and ≥400 ppm in females and increased relative lung weight at ≥200 ppm in males.

Effects were not observed in rats or mice following chronic inhalation exposure to 400 ppm (calculates to approximately 126 mg/kg-day) acetonitrile in rats and 200 ppm (calculates to approximately 100 mg/kg-day) acetonitrile in mice (Ref. 13). The concentrations at which effects were observed in the 13-week study were not tested in the chronic study, and, in addition, two of the three principal reviewers of the study suggested that the highest exposure

concentrations applied in the chronic study (200 ppm-mouse; 400 ppm-rat) were too low and one reviewer suggested concentrations should have been as high as 800 ppm (Ref. 13).

3. *Carcinogenicity*

There are no studies evaluating the carcinogenicity of acetonitrile in humans. Other data pertinent to the assessment of potential carcinogenicity include a National Toxicology Program (NTP) cancer bioassay in mice and rats. NTP concluded that the evidence for carcinogenicity via inhalation of acetonitrile in male F344/N rats was equivocal (Ref. 13). Although there was a statistically significant positive trend in the incidences of hepatocellular adenomas, carcinomas, and adenomas and carcinomas (combined) in male rats only, the incidences were not statistically significant by pairwise comparison or by life table analysis. There was no evidence of carcinogenicity in female rats or in either male or female B6C3F1 mice (Ref. 13).

4. *Developmental and Reproductive Toxicity.*

Following acute inhalation exposure to 3,800 ppm acetonitrile to hamsters on a single day during gestation day 8 (GD8), an increase in maternal toxicity and mortality was observed; at higher exposure concentrations (≥5,000 ppm), an increase in severe fetal abnormalities, including exencephaly, encephalocoele, and rib fusions was reported (Ref. 14). Following acute oral ingestion of acetonitrile in hamsters on a single day at GD8, a decrease in fetal body weight was observed at the lowest observed adverse effect level (LOAEL) of 100 mg/kg (the LOAEL for maternal toxicity was 300 mg/kg) (Ref. 14). In rats, a single oral dose of 2,000 mg/kg on GD10 resulted in dysmorphogenic features, including misdirected allantois and/or trunk and caudal extremity (Ref. 15). Mortality was not observed in dams exposed to 2,000 mg/kg acetonitrile on GD10; however, dams exhibited clinical signs of toxicity including piloerection, prostration, and/or tremors, and caused unspecified maternal weight loss between GDs 10 and 12

(Ref. 15). In a oral gavage study, New Zealand white rabbits were administered acetonitrile on GDs 6-18, which resulted in a decrease in the average number of live fetuses per litter at 30 mg/kg-day, as well as an increase in maternal mortality and anorexia, ataxia, decreased motor activity, bradypnea, dyspnea, and impaired righting reflex (Ref. 16).

Inhalation and oral exposure in rats and rabbits resulted in both maternal and developmental toxicity. Maternal mortality was observed in rats at inhalation concentrations of 1,827 ppm (Ref. 17) and oral doses of 275 mg/kg-day (Ref. 18), and at 30 mg/kg-day in rabbits (Ref. 16). In rats, inhalation exposure to 1,827 ppm resulted in an increase in the percentage of nonlive implants per litter and early resorptions (Ref. 17). In rats, there was an increase in post-implantation loss and in the number of fetuses with unossified sternebrae and a decrease in number of live fetuses per dam at the oral dose of 275 mg/kg-day (Ref. 18). A decrease in the average number of live fetuses per litter was observed in rabbits at 30 mg/kg-day (Ref. 16). While developmental toxicity was observed at doses that produced maternal toxicity or mortality, it is inadequate to assume that the developmental effects result only from maternal toxicity, and the results may indicate that both lifestages, the adult and developing offspring, are sensitive to the dose level (Ref. 19).

V. What is EPA's Summary of the Technical Review?

Based on the available data, and given the severity of the effect, mortality, EPA concludes that there is sufficient evidence to support a concern for moderately high toxicity from exposure to acetonitrile. In assessing mortality following acetonitrile exposure, the patterns in the timing of death across exposures demonstrates the chronic nature of the effect. Mortality was observed in the 13-week mouse inhalation study in the 800 and 1600 ppm treatment groups (Ref. 13). The first occurrence of mortality in the 800 ppm treatment group was not observed until day

20 and single deaths continued on days 21, 45, 69 and 89 of the 13-week study. This pattern of mortality is dissimilar to that observed in the 13-week mouse inhalation study at 1,600 ppm, where initial deaths were observed in the first week and all mice died by day 21 (Ref. 13).

Based on the observed pattern of death in the 800 ppm treatment group of the NTP 13-week mouse inhalation study, beginning at the end of the third week and extending through the termination of the study, it can be reasonably anticipated that additional acetonitrile-induced mortality would have continued beyond the termination of the study and the sacrifice of surviving animals. Because the mortalities extended from the third week of the study to study termination, the data indicates that the mortality observed in the 800 ppm treatment group is not due to a single acute exposure to sufficiently high acetonitrile concentrations, but rather is best explained as being the result of long-term repeated exposures. The observed exposure-response relationship for acetonitrile demonstrates that a threshold exists at which acetonitrile exposure levels are sufficient to cause mortality from chronic exposure, and, as such, mortality would not necessarily be expected following chronic exposure at the doses tested in the NTP 2-year study because the acetonitrile exposure levels in the study design were not sufficient to cause mortality.

In addition, in 1999, EPA's Integrated Risk Information System (IRIS) Toxicological Review of Acetonitrile (Ref. 8) set the reference concentration (RfC) for acetonitrile based on this same 13-week mouse inhalation study (Ref. 13). The IRIS Toxicological Review of Acetonitrile identified the 400 ppm concentration in the NTP (1996) mouse study as a frank effect level (FEL) and the critical effect in the derivation of the reference concentration (RfC), given the death of a mouse at week 2 at 400 ppm and the increased mortality at 800 ppm. The FEL is a level of exposure or dose that produces irreversible, adverse effects at a statistically or

biologically significant increase in frequency or severity between those exposed and those not exposed. The RfC is an estimate of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Such a "lifetime" exposure value, set by IRIS based on the 13-week mouse inhalation study, is based on chronic effects, and would be unnecessary if IRIS found only acute effects.

VI. What is EPA's Rationale for the Denial?

EPA is denying the petition to delete acetonitrile from the EPCRA section 313 list of toxic chemicals. This denial is based on EPA's conclusion that acetonitrile can reasonably be anticipated to cause serious or irreversible chronic health effects in humans. Based on the available data, and given the severity of the effect, mortality, EPA concludes that there is sufficient evidence to support a concern for moderately high toxicity from chronic exposure to acetonitrile.

Because EPA believes that acetonitrile has moderately high chronic toxicity, EPA does not believe that an exposure assessment is appropriate for determining whether acetonitrile meets the criteria of EPCRA section 313(d)(2)(B). This determination is consistent with EPA's published statement clarifying its interpretation of the section 313(d)(2) and (d)(3) criteria for modifying the section 313 list of toxic chemicals (59 FR 61432, November 30, 1994).

VII. References

EPA has established an official public docket for this action under Docket ID No. EPA-HQ-TRI-2006-0319. The public docket includes information considered by EPA in developing this action, including the documents listed below, which are electronically or physically located in the docket. In addition, interested parties should consult documents that are referenced in the

documents that EPA has placed in the docket, regardless of whether these referenced documents are electronically or physically located in the docket. For assistance in locating documents that are referenced in documents that EPA has placed in the docket, but that are not electronically or physically located in the docket, please consult the person listed in the above FOR FURTHER INFORMATION CONTACT section.

1. U.S. EPA. 2000. OPPT/RAD Decision on Neurotoxicity Endpoint for Acetonitrile. Office of Pollution Prevention and Toxics, Washington, DC.

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13. NTP (National Toxicology Program). 1996. Toxicology and carcinogenesis studies of acetonitrile (CAS NO. 75-05-8) in F344/N rats and B6C3F1 mice (inhalation studies). NTP Technical Report Series 447.

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17. Saillenfait, A.M., P. Bonnet, J.P. Guenier et al. 1993. Relative developmental toxicities of inhaled aliphatic mononitriles in rats. Fundam. Appl. Toxicol. 20:365-375.

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List of Subjects in 40 CFR Part 372

Environmental protection, Community right-to-know, Reporting and recordkeeping requirements, and Toxic chemicals.

Dated: February 25, 2013.

Arnold E. Layne,

Director, Office of Information Analysis and Access.

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