

Eastman™ hydroquinone

Health, safety, and environmental information

Introduction

This publication provides information on health, safety, and environmental issues as well as handling considerations for hydroquinone. It is offered as information only and should be used solely as a guide in developing procedures and facilities for handling this product. Customers must determine for themselves the appropriate procedures and facilities for their operations.

The information in this publication, along with the data and information contained in Eastman's Material Safety Data Sheets (MSDS), needs to be reviewed and understood to help ensure the safe storage and handling of hydroquinone. It is the customer's responsibility to direct and control the unloading of any chemical or material into or from storage and handling facilities. Title to all chemicals and materials, unless otherwise specified, shall vest in a customer on delivery into the possession of the common carrier at Eastman's facilities or premises.

Federal, state, and local regulations regarding the handling and storage of chemicals may vary widely in the United States. The federal Occupational Safety and Health Administration (OSHA), Environmental Protection Agency (EPA), National Fire Protection Association (NFPA), and a user's insurance company also impose safety standards. Knowledge of these and other appropriate federal and state laws and regulations as well as consultation with the proper authority should provide guidance for developing adequate handling procedures and constructing appropriate storage facilities.

Applications

Hydroquinone (CAS: 123-31-9) has been used for more than 100 years as a developer for black and white film (including X-ray film). It is also used as a raw material in the production of antioxidants for rubber, food grade antioxidants, and liquid-crystal polymers; as a polymerization inhibitor for vinyl acetate and acrylic monomers; and as a topical skin-lightening agent.

Physical characteristics

Hydroquinone is a white, odorless, crystalline solid with an extremely low vapor pressure; it is moderately soluble in water and highly soluble in alcohol. In the presence of water, hydroquinone can slowly oxidize to quinone, which is more volatile.

Natural occurrence

Hydroquinone occurs naturally as a glucose ether (commonly known as arbutin) in the leaves of many plants and in fruit, coffee, and wheat products. Exposure to hydroquinone from these common foods probably explains the presence of low concentrations of hydroquinone in the urine and plasma of people who have no occupational or other known exposure to hydroquinone.

Human experience

Human experience from hydroquinone manufacturing operations and from the use of products containing hydroquinone provides information on the following potential adverse health effects: skin allergy, eye irritation, and impairment of vision.

Skin effects

Prolonged and repeated skin contact with photographic developers containing hydroquinone has been reported to cause an allergic skin rash. Such rashes, however, are rare in workers who manufacture or handle pure (dry) hydroquinone. When incorporated into skin-lightening creams that contain ingredients that promote dermal absorption, hydroquinone can cause a lightening of the skin's natural color by inhibiting the production of melanin pigment. Although there have been a few allegations that hydroquinone has caused permanent skin lightening following industrial use, there are no clearly confirmed cases.

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An infrequently reported observation related to the use of skin-lightening creams by women who have dark skin is localized ochronosis, a dark pigmentation of the skin. Although there are a few case reports from use of creams containing 2.0% or less hydroquinone, they appear to be limited to individuals who misuse the products or to products that contain other active ingredients.

Eye effects

Hydroquinone dust can cause eye irritation on direct contact. Additional eye effects were first reported in the 1940s in hydroquinone manufacturing employees following several years of prolonged and repeated eye exposure to high airborne concentrations of hydroquinone dust and quinone vapor. Initially, there was brown staining of the conjunctiva. This pigment deposition in the conjunctiva does not impair vision; however, its presence is evidence of exposure and its increase or decrease can be used as an indication of the severity of exposure to hydroquinone dust and quinone vapor.

With continued eye exposure to high concentrations of hydroquinone and quinone, pigment deposition can extend into the cornea and structural alterations of the cornea may occur that can impair vision. One of the first complaints of an individual with corneal involvement is difficulty driving at night as light beams from oncoming cars are scattered and reflected by the corneal alterations.¹ Continued over-exposure may lead to further corneal injury and serious impairment of vision.

The discovery of eye injury in hydroquinone manufacturing operations led to the establishment of occupational exposure limits. In the United States and Canada, these limits are 2 mg/m³ for hydroquinone dust² and 0.1 ppm for quinone vapor.³ It is believed that nearly all workers may be repeatedly exposed day after day to these occupational exposure limits without experiencing adverse health effects.

¹Other eye conditions such as cataracts may cause similar symptoms.

²TLV established in 1956 based on 1947 recommendation of Oglesby, et al.

³LV established in 1961 based on 1947 recommendation of Oglesby, et al.

Systemic effects

Adverse health effects produced by a chemical after it is absorbed into the body are referred to as systemic toxicity. No adverse systemic effects were detected by medical examination of workers exposed to a combination of hydroquinone dust and quinone vapor at concentrations high enough to cause eye injury. No increase in death rates due to cancer was observed in a study of photographic processors who used both hydroquinone and other photo processing chemicals. Similarly, no adverse systemic effects have been reported in employees involved in the manufacture of hydroquinone at Eastman Chemical Company; the general death rate and the death rate due to cancer among these workers were significantly lower than those for the general population and for another group of industrial workers.

Laboratory research on potential systemic effects

Since the opportunity to detect chemically induced effects in people under various conditions of exposure is limited, the potential systemic health effects of hydroquinone have been investigated through experimental studies conducted in animals. Hydroquinone is absorbed through the skin very slowly, and no systemic effect has been observed when it is applied to the skin as an aqueous solution. Studies in which animals are exposed to airborne dust are difficult to conduct and may cause undue stress on the animals. Therefore, the majority of information concerning systemic effects of hydroquinone comes from studies in which animals are given hydroquinone orally or by injection. These studies indicate that exposure to hydroquinone at or below applicable occupational exposure limits is not expected to cause significant systemic effects in humans, including cancer, adverse reproductive effects, or birth defects.

The systemic effects of hydroquinone in animals are dependent on species and strain, dose level, and route of exposure. These effects include tumor formation and effects on the kidneys, bone marrow, and nervous system. The following sections discuss these findings and their relevance to humans who may be exposed to hydroquinone.

Metabolism and systemic effects

Once they are absorbed, chemicals can be distributed to various organs where they undergo chemical changes; this chemical conversion is called metabolism. The products from hydroquinone metabolism and their disposition play a major role in hydroquinone toxicity. The composition and amounts of hydroquinone metabolites vary depending on the route of exposure and dose administered. This results in a corresponding variation in the type and severity of systemic effects. Following ingestion, hydroquinone is metabolized to water-soluble compounds in the liver, then filtered by the kidneys, and eliminated in the urine.

Genotoxicity and bone marrow effects

Genotoxicity is the ability of a chemical to interact with DNA in chromosomes and cause either mutations or alterations in physical structure (clastogenicity). Several test methods (including the use of animal cells and bacteria) have been developed to determine a chemical's ability to cause genotoxicity. The relevance of genotoxicity data in predicting human risk is unclear. However, since many chemicals that are genotoxic also may cause cancer and birth defects, such testing is used as a tool in screening chemicals for further study. Although studies for mutagenicity using bacteria (Ames' test) are generally negative, there is some evidence for clastogenicity and mutagenicity of hydroquinone from studies in animals, in isolated cells taken from animals and plants, and in other microorganisms. However, positive findings have typically been observed in tests done in vitro (outside the body, in an artificial environment) or by a route of exposure such as injection that bypasses or overwhelms detoxification processes. Therefore, the implications of genotoxicity data for human risk remain unclear.

Laboratory studies have shown that hydroquinone is toxic to bone marrow and immune-system cells, possibly through interaction with DNA. However, as with genotoxicity studies, the great majority of these findings are observed only in studies conducted in vitro or by a route of exposure that bypasses or overwhelms the ability of the liver to metabolize and detoxify hydroquinone.

Kidney effects and the question of cancer

Adverse kidney effects, referred to as chronic progressive nephropathy (CPN), have been observed in one strain of male rat (F-344) following chronic administration of oral doses of hydroquinone. While CPN occurs spontaneously as part of the aging process in nearly all male rats, hydroquinone appears to exacerbate this condition. Associated with the development of CPN is the subsequent formation of benign (nonmalignant) kidney tumors in a small number of male rats. It is important to note that tumor formation occurred only after CPN developed, only in regions of the kidney affected by CPN, and only in one strain of male rat. CPN did not occur in two other strains of rats, mice, or dogs. This high degree of specificity raises questions as to the relevance of this finding to the estimation of human risk as humans do not naturally develop CPN.

The exact mechanism by which hydroquinone produces kidney tumors in male F-344 rats is not known with certainty. A great deal of research has been directed at investigating the apparent relationship of nephropathy and tumor formation. Available data indicate that one of hydroquinone's metabolites may be reabsorbed in the kidney rather than eliminated, leading to localized cell damage. This damage induces an increase in the formation of new cells (cell proliferation) as part of the repair process. Many researchers believe that cell damage and subsequent cell proliferation contribute to the development of some tumors. Recent research suggests that at high levels of exposure hydroquinone-induced cell damage and proliferation may promote tumor formation when combined with the spontaneous chronic progressive nephropathy seen in this strain and sex of rats.

Additional effects have been reported in hydroquinone cancer studies. Increases in liver tumors (primarily benign) were noted in female mice, and an increase in leukemia was reported in the female F-344 rat; however, these findings were not reproduced in a subsequent study. Furthermore, recent reanalysis of the female rat data suggests that this finding was not a true increase but was within the normal background incidence for this sex and strain of rat. There was no evidence of cancer in male mice following chronic oral administration of hydroquinone. No

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tumors were reported in mice following long-term dermal application of hydroquinone. Therefore, the occurrence of tumors has not been consistent across species, sex, or route of exposure, nor in repeated studies.

The International Agency for Research on Cancer (IARC), a part of the World Health Organization, evaluates the carcinogenic risk of chemicals to humans and publishes its reviews in critically evaluated monographs. Reviews and evaluations are formulated by international working groups of independent scientists. Animal and human data are assessed separately and then combined into an overall evaluation. IARC recently reviewed the available human, animal, and genotoxicity data for hydroquinone and found that there is inadequate evidence for the carcinogenicity of hydroquinone in humans and limited evidence in experimental animals. Their overall evaluation is that hydroquinone is not classifiable as to its carcinogenicity to humans (Group 3).

When taken as a whole, the weight of evidence suggests that exposure to hydroquinone at or below current occupational exposure limits does not present a risk of cancer to humans.

Nervous system effects

High oral doses of hydroquinone stimulate the nervous system of animals, producing tremors of short duration. However, as doses are reduced, the tremors decrease. To further investigate this effect, a study specifically designed to detect functional impairment of the nervous system was conducted in rats. The animals were observed for changes in body position, degree of activity, coordination of movement, gait, behavior, sensory function, and strength. Nervous system tissues were examined for microscopic changes. Tremors and temporary minimal to mild depression of general activity were observed only at high doses. No abnormalities were seen in the microscopic examination of nervous system tissue from any dose.

Reproductive and developmental toxicity

The potential for hydroquinone exposure to cause adverse developmental or reproductive effects has been investigated in several animal studies. Reproductive toxicity addresses adverse effects on the male or female reproductive system from exposures of either parent prior to conception, during pregnancy, or after birth until puberty. Developmental

toxicity addresses adverse effects (such as birth defects) on the developing embryo and fetus prior to birth. Hydroquinone has not caused adverse reproductive effects in male or female animals or birth defects in their offspring when administered orally at dose levels not causing systemic toxicity in the mother. Based on these findings, hydroquinone is not expected to cause developmental or reproductive toxicity in humans under normal conditions of use.

Environmental effects

Due to its physicochemical properties, including low vapor pressure and sufficient solubility in water, hydroquinone will distribute mainly to surface and groundwaters when released into the environment. Since hydroquinone is degraded both photochemically and biologically, it is not expected to persist in the environment or bioaccumulate.

Since hydroquinone is highly toxic to fish and other aquatic organisms, it must not be discharged directly into streams, rivers, or lakes. At high concentrations, hydroquinone is somewhat toxic to sludge microorganisms; however, biodegradation takes place at lower concentrations. Since hydroquinone is readily degraded in acclimated activated sludge units, no significant concentration of hydroquinone should remain in the effluent from secondary wastewater treatment systems.

Safe handling recommendations

Eastman supplies hydroquinone as a dry, free-flowing, crystalline material. Hydroquinone is classified as a severe dust explosion hazard with an associated low minimum ignition energy (MIE = <10 mJ) and a high potential to generate static charge in the free-falling powder. Therefore, the following practices are recommended:

1. Operating personnel should be grounded by wearing static dissipative Type I footwear as described in ANSI Standard Z41-1991, Chapter 6. Wetting floors in the immediate operating areas with water before handling the hydroquinone may increase the dissipation of static charge accumulation.
2. Discharging hydroquinone from drums and supersacks can create significant static charge accumulation in the dry powder and should be done slowly. A good fugitive dust collection system is highly recommended to reduce the potential for personnel exposure during loading operations. Also see the personal protection information paragraph at the end of this section.
3. An inert gas atmosphere should be maintained at all times within any vessel into which hydroquinone is charged. The introduction of the dry powder can be the source for static discharge and ignition. When charging hydroquinone into an inerted vessel, it is recommended that the oxygen content of the vessel be monitored frequently since an oxygen-rich atmosphere can be created inside the vessel with the introduction of oxygen via the solid void space.
4. Minimize distances hydroquinone powder must free-fall in processing equipment.
5. Vessels and processing equipment should be electrically grounded.
6. Refer to National Fire Protection Association (NFPA) Pamphlet No. 654, *Prevention of Fire and Dust Explosions in the Chemical, Dye, Pharmaceutical, and Plastics Industries*.

Engineering controls should be used to contain hydroquinone dust and minimize exposure of workers and contamination of the workplace. It is very important to use good housekeeping and to minimize the generation of airborne dust. Spills should be cleaned up immediately; an industrial, explosion-proof canister vacuum is recommended for large spills. Floors and work surfaces can be cleaned using a water spray (see Environmental effects). Good general room ventilation must be provided and, where needed, local exhaust ventilation.

Skin and eye contact with HQ should be avoided through the use of personal protective equipment such as safety glasses (or goggles) with side shields and chemical resistant gloves. Based on reported breakthrough times, neoprene and nitrile rubber gloves are the most impermeable; for specific information, consult the glove manufacturer. Depending on the task or work environment, additional measures such as aprons or disposable coveralls may be needed to prevent possible skin contact. As in any chemical handling area, good personal hygiene practices should be encouraged, particularly avoiding hand-to-eye contact. Exposure of the eyes to hydroquinone dust (or quinone vapor) at concentrations greater than the exposure limits must be avoided (see Eye effects). If hydroquinone dust levels (or quinone vapor levels) exceed the exposure limits, an approved, full-face respirator for organic vapor and dust must be worn.⁴

Technical assistance

If you have questions concerning the handling of Eastman™ hydroquinone, contact your Eastman representative.

⁴Workplace concentrations may be measured using NIOSH Method 5004.

Appendix: Scientific literature¹

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¹Note: These references have been selected from the published scientific literature to highlight physical, chemical, and biological properties of hydroquinone, but are not intended to represent a comprehensive data source.



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