Sources of Exposure

General Populations

- Exposure risk of the general population to 3,3'-dichlorobenzidine is to be low as it is no longer used to manufacture soluble dyes in the United States. Additionally, its use in other manufacturing, processing, or other uses for commercial purposes has markedly decreased in the United States.
- Exposure of the general population to 3,3'-dichlorobenzidine may occur through contaminated water or soil near hazardous waste sites or near facilities where 3,3'-dichlorobenzidine is used and/or discharged.
- Exposure may occur through ingestion of paint chips containing 3,3'-dichlorobenzidine as a pigment. This is of particular concern for exposures of children.
- Exposure to trace amounts of 3,3'-dichlorobenzidine can occur in cosmetics sold abroad that use certain synthetic dyes as colorants, and in other foreign consumer skin care and personal hygiene products such as cosmetic facial masks.
- Exposure may also occur from dietary sources, including aquatic organisms and fruit, but the extent of the exposure is unknown.

Occupational Populations

- Workers in industries where 3,3'-dichlorobenzidine is used (dyes, plastics) may be exposed.
- Occupational exposure is most likely to occur through inhalation or dermal contact.

Toxicokinetics and Biomonitoring

Toxicokinetics

- 3,3'-Dichlorobenzidine is rapidly absorbed from the gastrointestinal tract in rats.
- In animals, 3,3'-dichlorobenzidine is thought to be widely distributed throughout the body.
- Evidence in humans and animals suggest that 3,3'-dichlorobenzidine undergoes metabolism through N-acetylation resulting in the metabolites N-acetyl-3,3'-dichlorobenzidine and N'N'-diacetyl-3,3'-dichlorobenzidine.
- Evidence in humans suggests 3,3'-dichlorobenzidine and its metabolites are excreted in urine. In animals, evidence suggests bile/feces as the major route of excretion followed by urine.

NHANES Biomonitoring

- There are no data regarding levels of 3,3'-dichlorobenzidine in the general population.

Biomarkers/Environmental Levels

Biomarkers

- Testing for 3,3'-dichlorobenzidine levels in urine and the detection of hemoglobin adducts are often used together to monitor exposure in humans.
- Detection of 3,3'-dichlorobenzidine adducts with hemoglobin in the blood is a marker of an early biological effect.
- There are no established baseline or "normal" human values for either urine or hemoglobin adduct levels for 3,3'-dichlorobenzidine.

Historical Environmental Levels

Air

- There are no recent monitoring data for air levels of 3,3'-dichlorobenzidine.

Water

- 3,3'-Dichlorobenzidine was found in surface water and groundwater in Oklahoma (2005–2006): range 0.65–0.90 µg/L

Sediment and Soil

- 3,3'-Dichlorobenzidine was found in wet sediment (range: not detectable to 69.66 mg/kg) near a U.S. lake (Michigan) (1993–2003), with the highest concentration measured 6 km from the source.

Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2022. Toxicological Profile for 3,3'-Dichlorobenzidine. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Services.

ToxGuide™ for 3,3'-Dichloro-benzidine

$C_{12}H_{10}Cl_2N_2$

CAS# 91-94-1

June 2022

U.S. Department of Health and Human Services
Public Health Service
Agency for Toxic Substances and Disease Registry
www.atsdr.cdc.gov

ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

Chemical and Physical Information

3,3'-Dichlorobenzidine is a White or Gray to Purple Crystalline Solid

- The 3,3'-dichlorobenzidine salts, 3,3'-dichlorobenzidine dihydrochloride, 3,3'-dichlorobenzide dihydrogen bis(sulphate), and 3,3'-dichlorobenzidine sulphate are a white to light-gray crystalline powder.
- 3,3'-Dichlorobenzidine and its salts have relatively low solubility in water but are soluble in alcohol and slightly soluble in hydrochloric acid.
- 3,3'-Dichlorobenzidine and its salts are not volatile.
- 3,3'-Dichlorobenzidine has low mobility in soil and binds strongly to solid phases in soil, sediment, and sludge.
- Previously, 3,3'-dichlorobenzidine and its salts were used in the manufacturing of dyes in the United States.
- Currently, 3,3'-dichlorobenzidine dihydrochloride is used in pigments in the United States. The manufacture of 3,3'-dichlorobenzidine has largely ceased in the United States; however, it is still imported.

Routes of Exposure

- Inhalation – Exposure to 3,3'-dichloro-benzidine in air is a minor route of exposure for workers and populations near industrial waste sites.
- Oral – The primary route of exposure to 3,3'-dichlorobenzidine for the general population may occur through ingestion of contaminated water.
- Dermal – Dermal contact via cosmetic products is a potential route of exposure to minute levels of 3,3'-dichlorobenzidine for the general population. Dermal contact is a minor route of exposure for workers.

3,3'-Dichlorobenzidine in the Environment

- In air, 3,3'-dichlorobenzidine is emitted as a vapor, but reacts with sunlight, with an estimated half-life of 10 hours.
- It is photolabile in water and susceptible to rapid photolysis in sunlit surface water and may yield benzidine. Its half-life in water when exposed to natural sunlight is approximately 90 seconds.
- 3,3'-Dichlorobenzidine binds to soil and sediment and can be transported relatively long distances.
- 3,3'-Dichlorobenzidine has the potential to concentrate in aquatic animals and has been detected in fruits.

Relevance to Public Health (Health Effects)

Health effects are determined by the dose (how much), the duration (how long), and the route of exposure.

Minimal Risk Levels (MRLs)

Inhalation

- No acute-, intermediate-, or chronic-duration inhalation MRLs were derived for 3,3'-dichlorobenzidine.

Oral

- No acute-, intermediate-, or chronic-duration oral MRLs were derived for 3,3'-dichlorobenzidine.

Health Effects

- Workers exposed to 3,3'-dichloro-benzidine may be at a higher risk of developing bladder cancer, and cancer appears to be the most sensitive effect of exposure.
- Limited evidence in workers has also observed dermatitis as an effect.
- 3,3'-Dichlorobenzidine is genotoxic in animals. There is strong evidence that 3,3'-dichlorobenidine exposure results in gene mutation in animal cells and deoxyribonucleic acid (DNA) damage in human cells when metabolized in the body.

Health Effects (Continued)

- One study in dogs noted the development of liver tumors.
- The U.S. Department of Health and Human Services (HHS) has classified 3,3'-dichlorobenzidine as reasonably anticipated to be a human carcinogen. The International Agency for Research on Cancer (IARC) classified 3,3'-dichlorobenzidine as possibly carcinogenic to humans, and the U.S. Environmental Protection Agency (EPA) classified it as a probable human carcinogen.

Children's Health

- It is not known if children exposed to 3,3'-dichlorobenzidine would be expected to experience effects similar to adults. There is insufficient evidence to determine if developmental effects occur in the fetus or the offspring of individuals exposed to 3,3'-dichlorobenzidine.
- There is indirect evidence that 3,3'-dichlorobenzidine or its metabolites can cross the placenta.
- It is unknown if infants can be exposed to 3,3'-dichlorobenzidine in breast milk.