



PUBLIC HEALTH STATEMENT

BENZIDINE

CAS#: 92-87-5

Division of Toxicology

September 2001

This Public Health Statement is the summary chapter from the Toxicological Profile for Benzidine. It is one in a series of Public Health Statements about hazardous substances and their health effects. A shorter version, the ToxFAQs™ is also available. This information is important because this substance may harm you. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present. For more information, call the ATSDR Information Center at 1-888-422-8737.

This public health statement tells you about benzidine and the effects of exposure. The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal cleanup activities. Benzidine has been found in at least 28 of the 1,585 current or former NPL sites. However, the total number of NPL sites evaluated for benzidine is not known. As more sites are evaluated, the sites at which benzidine is found may increase. This information is important because exposure to benzidine may harm you and because these sites may be sources of exposure.

When a substance is released from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. This release does not always lead to exposure. You are exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance, or by skin contact. If you are exposed to benzidine, many factors determine whether you'll be harmed. These factors include the dose (how much), the duration (how

long), and how you come in contact with it. You must also consider the other chemicals you're exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT IS BENZIDINE?

Benzidine is a manufactured chemical that does not occur naturally. It is a crystalline (sandy or sugar-like) solid that may be grayish-yellow, white, or reddish-gray. It will evaporate slowly from water and soil. Its flammability, smell, and taste have not been described. Benzidine also has other names, such as 4,4'-diphenylenediamine or Fast Corinth Base B (a registered trade name). In the environment, benzidine is found in either its "free" state (as an organic base), or as a salt (for example, benzidine dihydrochloride or benzidine sulfate). In air, benzidine is found attached to suspended particles or as a vapor.

In the past, industry used large amounts of benzidine to produce dyes for cloth, paper, and leather. However, it has not been made for sale in the United States since the mid-1970s. Major U.S. dye companies no longer make benzidine-based dyes. Benzidine is no longer used in medical laboratories or in the rubber and plastics industries. However, small amounts of benzidine may still be manufactured or imported for scientific research in laboratories or for other specialized uses. Some benzidine-based dyes (or products dyed with them) may also still be brought into the United States.

1.2 WHAT HAPPENS TO BENZIDINE WHEN IT ENTERS THE ENVIRONMENT?

In the past, benzidine entered the environment largely when it was being made or used to produce

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dyes. Industry released it to waterways in the form of liquids and sludges, and transported benzidine-containing solids to storage or waste sites. Benzidine was sometimes accidentally spilled, and it was released to the air as dust or fumes. For the most part, companies no longer make or use benzidine, and the government strictly regulates these activities. Today, most benzidine still entering the environment probably comes from waste sites where it had been disposed. Some may also come from the chemical or biological breakdown of benzidine-based dyes, or from other dyes where it may exist as an impurity. Only very small amounts of free benzidine will dissolve in water at moderate environmental temperatures. When released into waterways, it will sink and become part of the bottom sludge. Benzidine salts can dissolve more easily in water than free benzidine. Only a very small portion of dissolved benzidine will pass into the air. Benzidine exists in the air as very small particles or as a vapor, which may be brought back to the earth's surface by rain or gravity. In soil, most benzidine is likely to be strongly attached to soil particles, so it does not easily pass into underground water.

Benzidine can slowly be destroyed by certain other chemicals, light, and some microorganisms (for example, bacteria). Certain fish, snails, algae, and other forms of water life may take up and store very small amounts of benzidine, but accumulation in the food chain is unlikely.

1.3 HOW MIGHT I BE EXPOSED TO BENZIDINE?

The general population is not likely to be exposed to benzidine through contaminated air, water, soil, or food. Benzidine is a manufactured chemical that

does not occur naturally in the environment. Today, U.S. industry makes and uses very little (if any) benzidine, and no releases to air, water, or soil are reported on the Toxic Release Inventory (TRI). Only rarely has benzidine been detected in areas other than waste sites, and it has not been found in food. Some dyes used to color foods or drinks may contain impurities that can be broken down to benzidine once inside the body.

If you live near a hazardous waste site, you could be exposed to benzidine by drinking contaminated water or by breathing or swallowing contaminated dust and soil. Benzidine can also enter the body by passing through the skin. Some quantities of dyes made from benzidine may still be brought into the United States. These may contain small amounts of benzidine as a contaminant, or chemicals that may be broken down in the body to benzidine. If you use such dyes to dye paper, cloth, leather, or other materials, you may be exposed by breathing or swallowing dust, or through skin contact with dust. You may be exposed in a similar way if you work at or near hazardous waste sites.

1.4 HOW CAN BENZIDINE ENTER AND LEAVE MY BODY?

Benzidine can enter your body if you breathe air that has small particles of benzidine or dust to which benzidine is attached. It can also enter your body if you drink water or eat food that has become contaminated with benzidine. If your skin comes in contact with benzidine, it could also enter your body. Generally, it will take only a few hours for most of the benzidine to get into your body through the lungs and intestines. It may take several days for most of the benzidine to pass through your skin. Breathing, eating, or drinking benzidine-based dyes

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may also expose you to benzidine. Your intestines contain bacteria that can break down these dyes into benzidine.

Once in your body, only a small portion of benzidine will leave as waste in your urine and feces. Your body will change most of the benzidine into many different chemical forms (called metabolites), which dissolve readily in your bodily fluids and are easy for your body to remove. Some of these changed forms of benzidine appear to cause many of the chemical's harmful effects. Studies show that after benzidine has entered your body, most of it (and its changed forms) will be removed within a week.

1.5 HOW CAN BENZIDINE AFFECT MY HEALTH?

Very little information is available on the noncancer health effects that may be caused by exposure to benzidine. Benzidine contact with your skin could possibly cause a skin allergy. Except for the cancer discussed next, benzidine has not been definitely shown to cause major adverse health effects in humans.

To protect the public from the harmful effects of toxic chemicals and to find ways to treat people who have been harmed, scientists use many tests. One way to see if a chemical will hurt people is to learn how the chemical is absorbed, used, and released by the body; for some chemicals, animal testing may be necessary. Animal testing may also be used to identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method to get information needed to make wise decisions to protect public health. Scientists have the responsibility to treat

research animals with care and compassion. Laws today protect the welfare of research animals, and scientists must comply with strict animal care guidelines.

Benzidine can cause cancer. This has been shown in studies of workers who were exposed for many years to levels much higher than the general population would experience. It is important to note that most of the workers did not develop cancer, even after such high exposures. When cancer does occur, most often it is cancer of the urinary bladder. Some evidence suggests that other organs, such as the stomach, kidney, brain, mouth, esophagus, liver, gallbladder, bile duct, and pancreas, may also be affected. Experiments with animals have also shown benzidine to be a carcinogen (a cancer causing substance). The Department of Health and Human Services (DHHS), the International Agency for Research on Cancer (IARC), and the EPA have determined that benzidine is a human carcinogen. In addition, dyes made from benzidine, such as Direct Blue 6, Direct Black 38, and Direct Brown 95, have been shown to cause cancer in animals, and there is some evidence that they may cause bladder cancer in humans. DHHS has determined that Direct Black 38 and Direct Blue 6 cause cancer in animals, and IARC has also determined that Direct Black 38, Direct Blue 6, and Direct Brown 95 cause cancer in animals.

1.6 HOW CAN BENZIDINE AFFECT CHILDREN?

This section discusses potential health effects from exposures during the period from conception to maturity at 18 years of age in humans. Potential effects on children resulting from exposures of the parents are also considered. Children might be

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exposed to benzidine if they eat small amounts of soil contaminated with benzidine. However, studies suggest that it is difficult to release benzidine once it becomes attached to most types of soils. Exposure by contaminated soil may occur if the children live in an area near a source of the chemical (such as a hazardous waste site that contains benzidine). There are no studies on health effects in children exposed to benzidine. There is no information on whether benzidine causes birth defects in children. It is unknown whether birth defects would occur in the newborn babies of animals that breathed or ate benzidine, or had it on their skin while they were pregnant. There is no information to determine whether children differ from adults in their sensitivity to the health effects of benzidine. There is indirect evidence that benzidine or its breakdown products can cross the placenta, but it is not known whether it can be transferred to the young through the mother's milk.

1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO BENZIDINE?

If your doctor finds that you have been exposed to significant amounts of benzidine, ask whether your children might also be exposed. Your doctor might need to ask your state health department to investigate. Benzidine has no agricultural or food chemical uses, so exposure to it by eating contaminated food is not likely. Impurities in certain food dyes can be transformed inside the body to benzidine. Children may be exposed to benzidine if they eat small amounts of soil contaminated with benzidine. Children should be prevented from eating soil; make sure they wash their hands frequently, and before eating. Discourage your children from putting their hands

in their mouths or from doing other hand-to-mouth activities.

1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO BENZIDINE?

Several tests have been developed to help determine whether you have been exposed to benzidine. Although these tests must be performed by experts in special laboratories, your doctor can collect the blood or urine samples and send them to an appropriate testing facility. Benzidine and its breakdown products can be detected in your urine, but only within about 2 weeks after your last exposure. Benzidine and some of its changed forms will bind to proteins within your red blood cells, and this can be detected for up to 4 months after your last exposure. Benzidine in some of its forms can bind to the DNA found in most of your cells. There are extremely sensitive tests that can detect such binding; scientists continue to investigate whether these tests can detect benzidine only or other similar chemicals too. None of these tests, however, can predict whether harmful effects will occur later.

1.9 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the FDA. Recommendations provide valuable guidelines to

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protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH). Regulations and recommendations can be expressed in not-to-exceed levels in air, water, soil, or food that are usually based on levels that affect animals; then they are adjusted to help protect people. Sometimes these not-to-exceed levels differ among federal organizations because of different exposure times (an 8-hour workday or a 24-hour day), the use of different animal studies, or other factors. Recommendations and regulations are also periodically updated as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for benzidine include the following: Because benzidine can cause cancer, the EPA has issued regulations that list it as a "priority" chemical, subject to rigid inspection and control. EPA allows 0.10 parts of benzidine per million parts of waste (0.10 ppm) that is brought to waste disposal sites. EPA also requires that any release of one pound or more of benzidine or its salts to the environment must be reported to the federal government's National Response Center. EPA's Office of Water also has water quality guidelines to protect human health. These guidelines suggest that benzidine concentration limits should be maintained at less than 1 part benzidine in a trillion parts of water (ppt). Although zero benzidine is preferred, lifetime exposure to these concentrations is estimated to result in no more than one additional case of cancer in a million persons exposed. OSHA considers benzidine to be a carcinogen, and has issued regulations to reduce the risk of exposure in any

workplace in which it might still be found. These regulations include entry controls, housekeeping and disposal rules, other rules on operating and handling procedures, and requirements that employers make showers and dressing rooms available. NIOSH recommends that worker exposure to benzidine-based dyes be kept to the lowest feasible concentration, and it considers benzidine to be an occupational carcinogen. EPA's Office of Water has set a discharge limit for benzidine-based dye applicators of 10 micrograms per liter (10 µg/L) (one µg is one millionth of a gram) over any calendar month or not more than 25 µg/L in any working day. FDA allows a maximum of 1 part of benzidine per billion parts (ppb) of some color additives for foods.

1.10 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns, please contact your community or state health or environmental quality department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop F-32
Atlanta, GA 30333

Information line and technical assistance:

Phone: 888-422-8737
FAX: (770)-488-4178

ATSDR can also tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses resulting from exposure to hazardous substances.

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To order toxicological profiles, contact:

National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161
Phone: 800-553-6847 or 703-605-6000

Reference

Agency for Toxic Substances and Disease Registry (ATSDR). 2001. Toxicological profile for Benzidine. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

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www.atsdr.cdc.gov/

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