



# Breast Cancer and Environmental Risk Factors

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FACT SHEET #17

Q & A's from the Cornell University Program on Breast Cancer  
and Environmental Risk Factors in New York State

## Pesticides and Breast Cancer Risk, An Evaluation of Cyanazine

### What is cyanazine?

Cyanazine, 2-[[4-chloro-6(ethylamino)-1,3,5-triazin-2-yl]amino]-2-methylpropionitrile, is a synthetic chemical that is widely used as an herbicide to control broad-leaf weeds and grasses in agricultural crops. This chemical is in the *s*-triazine family of herbicides. Some common trade names for cyanazine include Bladex and Fortrol. Cyanazine is also available commercially premixed with another *s*-triazine, atrazine.

### What is the history of cyanazine's use?

Cyanazine was first registered for use as an herbicide by Shell Chemical Company in 1971. In the U.S., over 90% of its use in agriculture is to control weeds in corn fields. Its highest use is in corn-growing states of the Midwest. It is used primarily as a *pre-emergent* herbicide on corn. It is usually applied once during the growing season to control weeds before the corn-seedlings emerge from the soil. It is also used to control weeds in sorghum, cotton, barley, wheat, oil rape seed, sugar cane, potatoes, and in forestry.

### What is the usage of cyanazine?

Cyanazine ranked as the 5th most used herbicide in U.S. agriculture in 1990-93, with an estimated 32 million pounds of active ingredient (AI) used per year. Cyanazine was third in herbicide usage in New York State (NYS), with 650

thousand pounds of AI used annually during the same time period.

### What is the current regulatory status of cyanazine?

Cyanazine is classified as a *Restricted Use Pesticide*. Applicators must be certified in order to use this pesticide. Cyanazine, along with the *s*-triazine herbicides atrazine and simazine, was placed under Special Review by the U.S. Environmental Protection Agency (EPA) in 1994. Cyanazine was placed under Special Review because of concerns raised about its cancer-causing potential in experimental animals and possible risks to humans exposed to this herbicide. On August 2, 1995, Du Pont Chemical Co., then the primary manufacturer and registrant, voluntarily proposed to phase out its production of cyanazine and to stop production for use in the U.S. by December 31, 1999. Sale and use of existing stocks of cyanazine will be prohibited after September 30, 2002.

### How do our federal agencies regulate cyanazine to protect the consumer?

The EPA sets the maximum levels of cyanazine allowed in public drinking water supplies. The *maximum contaminant level* (MCL) for cyanazine has been set at no more than 1 microgram per liter of drinking water (one microgram is one-millionth of a gram, one liter is approximately one quart). The EPA also sets the limits on the maximum levels of cyanazine residues allowed in food for human consumption, and in animal



feed. These maximum levels are called *tolerances*. The Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA) are the federal agencies responsible for monitoring the residues of cyanazine in domestic and imported foods. Foods that exceed the tolerances can be seized or destroyed by local or federal government officials.

### **Who might be exposed to cyanazine?**

People possibly exposed to cyanazine include:

- Agricultural workers who have mixed, handled or applied cyanazine, or herbicide mixtures containing cyanazine
- Family members that had lived on farms that have used cyanazine
- People who have been involved in cyanazine's manufacture, or in preparing commercial mixtures of herbicides that contain cyanazine
- People who have handled or laundered clothing contaminated with cyanazine
- People who have consumed cyanazine-contaminated water
- People who have consumed foods with residues of cyanazine and its breakdown products

### **Is cyanazine found in water, rainfall, soil, or food?**

**Water:** In the 1970s and 1980s there were many reports published that found cyanazine in surface and ground water, especially in the Midwest where cyanazine's herbicide use is the highest in the U.S. However, the frequency of detections for cyanazine were lower than that of other *s*-triazines, such as atrazine and simazine. This may be because cyanazine is broken down faster than atrazine and simazine in soil.

There are relatively few reports available on cyanazine residues in NYS waterways. A recent survey by the U.S. Geological Survey of pesticide residues in the surface waters of the Hudson River basin of NYS detected cyanazine residues in 17% of the water samples taken. However, most of the levels reported were very low. The median levels of cyanazine were 33 times lower than the MCL for drinking water set by the EPA. Most detections were observed in the spring and summer, which probably reflects the higher use of cyanazine during the growing season.

**Rainfall:** Studies have reported cyanazine in rainfall samples in the Midwest. A study conducted in Iowa detected cyanazine in 25% of the samples analyzed. Most of the detections occurred in the spring and early summer months of the growing season. There is some concern that cyanazine and other triazine herbicides can be deposited by rainfall to distant sites, including sensitive ecosystems or on organic farms.

**Soil:** Most of the degradation of cyanazine in soil is through breakdown by bacteria. Cyanazine is broken down more quickly than other *s*-triazine herbicides. About half of cyanazine applied to soil is detected 12 to 108 days after it is applied. This is in contrast to simazine and atrazine where half the amount applied has been detected up to 2 years later. Cyanazine can also be partially degraded in surface soils from exposure to sunlight. There is little information available on the persistency of cyanazine breakdown products in soil.

**Food:** The EPA has evaluated whether the residues of cyanazine and its breakdown products in treated foods (corn, wheat, sorghum) and in red meat, poultry, and eggs, pose a cancer risk. Studies evaluated by the EPA have estimated that the maximum risk of cancer from eating foods with residues of cyanazine is low, at 2.9 in 100,000.

### **Does cyanazine cause cancer in experimental animals?**

Rats and mice fed cyanazine for long periods of time did not develop tumors at non-breast sites.

### **Does cyanazine cause cancer in humans?**

Studies conducted in the Midwest have not found a significant increased risk of leukemia, a skin cancer called myeloma, or a cancer of the lymph system called non-Hodgkin's lymphoma in male agricultural workers with past, self-reported exposures to cyanazine.

### **Does cyanazine cause breast cancer?**

No studies have been published that have evaluated breast cancer risk in women exposed to cyanazine. There is some evidence that cyanazine is a breast carcinogen in experimental animals. While cyanazine does not induce breast tumors in mice, in one study, female rats fed moderate or high levels of cyanazine for long periods of time developed significantly more malignant breast tumors than rats that received a diet



without cyanazine. The way cyanazine causes the breast tumors in rats is not known.

Studies on other *s*-triazine herbicides (simazine and atrazine) also have shown that treatment with these herbicides over long periods of time induces breast tumors in female laboratory rats. Some researchers have suggested that atrazine affects the levels of hormones in the bodies of rats, and that these hormonal changes may play a role in the development of breast tumors. It is not known whether cyanazine-treated rats have altered levels of hormones.

### **Is there other evidence that cyanazine may affect breast cancer risk?**

Some studies have found that cyanazine is a mutagen, while others studies have not been able to demonstrate that cyanazine is a mutagen. Mutagens are substances that can cause changes in the genetic material of a cell that can sometimes lead to the development of cancer.

Other studies have not shown that cyanazine has the potential to affect breast cancer risk.

- Laboratory tests have shown that cyanazine does not act like estrogen. Estrogen is a hormone that has been implicated in breast cancer risk.
- There is no information available on whether cyanazine affects the rate of cell division in normal breast cells or breast cancer cells.

### **Conclusions**

We could not evaluate whether cyanazine increases breast cancer risk in humans, because no studies have evaluated the incidence of breast cancer in women with past exposures to cyanazine. There is some evidence from one study in rats that cyanazine is a breast carcinogen in experimental animals. There is evidence that cyanazine has some mutagenic potential. Cyanazine does not act like estrogen. Because the evidence of cyanazine's potential to affect breast cancer risk is limited to one animal study and some mutagenic potential, we conclude that the evidence is not adequate at the present time to show that cyanazine is a human breast carcinogen.

### **Further research needs**

Because the sale and use of cyanazine is scheduled to be discontinued by the year 2002, it is anticipated that the

potential for exposure to this chemical in the future will be limited. However, given the high use of cyanazine in the past, its detection in rainfall, and waterways, and evidence of its potential to cause breast tumors in animals, additional studies that evaluate cancer risks in individuals with past exposures to cyanazine should be considered.

- Studies are needed to determine if there is a higher incidence of breast cancer in women with past exposures to cyanazine. This should include women who have been exposed to cyanazine as agricultural workers, pesticide applicators or those who have lived on farms, especially in Midwestern states where cyanazine was used extensively as a corn herbicide. A study sponsored by the National Cancer Institute, the Agricultural Health Study, is currently evaluating the health effects of exposure to cyanazine and other agricultural chemicals in 58,000 male farm workers and pesticide applicators, and 35,000 women who are spouses of farm workers or are farmers or pesticide applicators themselves. Risk of cancer, including breast cancer, as well as other health effects will be evaluated in this 10-year long study being conducted in Iowa and North Carolina.
- If cyanazine is still produced for export after 2002, those involved in the manufacture of cyanazine-containing products will still have the potential for exposure. This population should be monitored to determine if there are any adverse health effects in men or women with long-term cyanazine exposure in the workplace.
- More studies are needed to determine how cyanazine causes breast tumors in experimental animals, and the relevance of these findings to humans.
- Studies are needed to determine the persistency of cyanazine breakdown products in soil, and if these breakdown products may pose any health risks.

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An extensive bibliography on *Cyanazine and Breast Cancer Risk* is available on the BCERF web site (<http://www.cfe.cornell.edu/bcerf/>)

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