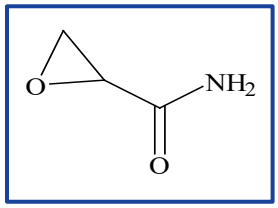
SUMMARY

Background: Glycidamide is a metabolite (substance generated during metabolism) of acrylamide, a chemical that is produced in the baking and frying of starchy foods, including French fries, potato chips, and bread, and is used in the production of dyes and plasticizers. Humans can be exposed to glycidamide through occupational settings, the diet, or the use of tobacco products. Although the toxicity of acrylamide in humans is well documented, the toxicity of glycidamide to humans is unknown. The effects of exposure to glycidamide in drinking water in male and female rats and mice were studied to identify potential toxicity or cancer-related outcomes and to determine whether it is the source of the carcinogenic activity of acrylamide.



Methods: Groups of 48 male and 48 female rats and mice were given drinking water containing 7.65, 15.3, 30.6, or 61.2 parts per million (ppm) glycidamide for 2 years. Control animals received 0 ppm (drinking water alone). Additional 2-week and 3-month studies were conducted to set appropriate doses and to identify target organs for subsequent studies. The animals were monitored for mortality or illness and body weight changes throughout the study. At the end of the study, tissues from more than 40 sites from every animal were examined for signs of disease.

Results: Male and female rats and mice exposed to glycidamide had lower survival rates than the control animals, and body weights were decreased in male and female rats exposed to glycidamide. The rates of several types of neoplasms (which can include benign or malignant growths) increased in each of the animal studies. Male and female rats exposed to glycidamide had increased rates of mononuclear cell leukemia (a cancer of cells with one nucleus such as white blood cells) and neoplasms of the thyroid gland and oral cavity; male rats had increased rates of neoplasms in the heart, epididymis (a tube behind the testes), and testes; and female rats had increased rates of neoplasms in the clitoral gland (a type of sebaceous gland in the genitals of female rodents), mammary gland, and forestomach (a tissue that stores undigested food). Male and female mice had increased rates of neoplasms in the Harderian gland (a gland in the eye), lung, skin, and forestomach, and female mice had increased rates of neoplasms in the mammary gland and ovary.

Conclusions: *The NTP four-point scale rates the level of evidence that a substance has the ability to cause cancer in laboratory animals. Under the conditions of these 2-year drinking water studies, there was clear evidence that glycidamide exposure has the ability to cause testicular, heart, and thyroid cancers, as well as neoplasms in the oral cavity of male rats; thyroid cancer, clitoral gland cancer, and neoplasms in the mammary gland and oral cavity of female rats; neoplasms in the Harderian gland, lung, skin, and forestomach of male mice; and mammary gland cancer, skin cancer, and neoplasms in the Harderian gland, lung, and forestomach of female mice. There was also some evidence that it has the ability to cause leukemia and neoplasms in the forestomach of female rats and equivocal (uncertain) evidence that it has the ability to cause leukemia in male rats and ovarian cancer in female mice. In addition, glycidamide exposure caused increased incidences of noncancerous tissue abnormalities in the brain in male and female rats; the epididymis in male rats; the liver in male rats and female mice; the bone marrow, spinal cord (lumbar section), and uterus in female rats; the eye, spleen, and forestomach in male and female mice; the preputial gland (gland in front of the genitals) in male mice; and the ovary and spinal cord (cervical section) in female mice. Because the same neoplasm sites were observed in rats and mice administered acrylamide, the carcinogenic activity of acrylamide is presumed to be due to its metabolic conversion to glycidamide.*