

in relation to herbicides or their contaminants had been conducted since Update 2000. They concluded that there was no information contained in the research reviewed for Update 2002 to change the conclusion that there is inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and cancers of the female reproductive system.

Taking account of the available evidence and NAS' analysis, the Secretary has found that the credible evidence against an association between herbicide exposure and cancers of the female reproductive system outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

### Urinary Bladder Cancer

Urinary bladder cancer is the most common of the genitourinary tract cancers. Bladder cancer incidence increases greatly with age over 40 years. The most important known risk factor for bladder cancer is smoking. Occupational exposures to aromatic amines (also called arylamines), polycyclic aromatic hydrocarbons (PAHs), and certain other organic chemicals used in the rubber, leather, textile, paint products, and printing industries are also associated with higher incidence of bladder cancer. High-fat diets have been implicated as risk factors, along with exposure to the parasite *Schistosoma haematobium*. Exposure to inorganic arsenic is also a risk factor for bladder cancer, and cacodylic acid is a metabolite of inorganic arsenic. The data remain insufficient to conclude that studies of inorganic arsenic exposure are directly relevant to exposure to cacodylic acid. Therefore, NAS did not consider the literature on inorganic arsenic.

NAS noted in VAO and Update 1996 that there was limited or suggestive evidence of no association between exposure to herbicides used in Vietnam or the contaminant dioxin and urinary bladder cancer. NAS, beginning with Update 1998, changed that conclusion to inadequate or insufficient information regarding an association.

In Update 2002, NAS reviewed an updated occupational study of mortality in Dow chemical workers potentially exposed to herbicides (Burns CJ, Beard KK, Cartmill JB. 2001. Mortality in chemical workers potentially exposed to 2,4-dichlorophenoxyacetic acid (2,4-D) 1945–1994: an update. *Occupational and Environmental Medicine* 58(1):24–30), which found no increased risk of mortality due to bladder cancer.

NAS also reviewed Revich *et al.* (2001), in which an increase in age-adjusted bladder cancer incidence was shown in Chapaevsk compared to the Samara Region of the Russian Republic. NAS noted, however, that the study did not control for occupation and smoking history, and there was no information on the number of cases included in the analysis or the completeness of surveillance for cancer in Chapaevsk and the Samara region.

In Update 2002, NAS concluded that there is no evidence to support changing the “inadequate or insufficient” categorization for bladder cancer.

Taking account of the available evidence and NAS' analysis, the Secretary has found that the credible evidence against an association between herbicide exposure and urinary bladder cancer outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

### Renal Cancer

Renal cancer is twice as common in men as in women. With the exception of Wilm's tumor, which is more likely to occur in children, renal cancer is more common in individuals over age 50. Smoking is a well-established risk factor for renal cancer. Other potential risk factors include diet, weight, and occupational exposure to asbestos and cadmium. Firefighters, who are routinely exposed to the decomposition of organic substances caused by a rise in temperature, are a known higher-risk group.

NAS noted in VAO and subsequent reports that there was inadequate or insufficient information to determine whether an association exists between exposure to herbicides and renal cancer.

In Update 2002, NAS reviewed an updated occupational study of mortality in Dow chemical workers potentially exposed to herbicides (Burns *et al.*, 2001), which concluded that there was no evidence of an association between exposure to 2,4-D and mortality due to renal cancer. NAS noted that this study has low precision due to the small number of deaths from renal cancer.

NAS also reviewed the results of Revich *et al.* (2001), which found age-adjusted incidence of renal cancer to be similar between Chapaevsk and the Samara region. Incidence rates of renal cancer in all of Russia was slightly lower. However, NAS noted that no information was given on the number of cases in the calculation of those incidence rates or the stability of those rates in previous years, and does not consider confounders other than age.

NAS stated that there is no information contained in the research reviewed for Update 2002 to change the conclusion that there is inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and renal cancer.

Taking account of the available evidence and NAS analysis, the Secretary has found that the credible evidence against an association between herbicide exposure and renal cancer outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

### Testicular Cancer

Testicular cancer is far more likely in men younger than 40 than in those who are older. Undescended testicles is a major risk factor for testicular cancer. Family history of the disease also appears to be a risk factor for testicular cancer.

NAS noted in VAO and subsequent reports that there was inadequate or insufficient information to determine whether an association exists between exposure to herbicides and testicular cancer.

In Update 2002, NAS reviewed an update of an occupational study of mortality in chemical workers at Dow Chemical Company (Burns *et al.*, 2001). One death from testicular cancer was identified among 1,517 male Dow employees. The study concluded that there is no significant risk of testicular cancer in this cohort. NAS concluded that the updated study analysis provided no evidence to suggest that chronic herbicide exposure increases the risk of testicular cancer.

Taking account of the available evidence and NAS' analysis, the Secretary has found that the credible evidence against an association between herbicide exposure and testicular cancer outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

### Leukemia (Other than chronic lymphocytic leukemia (CLL))

There are four primary types of leukemia: The acute and chronic forms of lymphocytic leukemia and the acute and chronic forms of myeloid (or granulocytic) leukemia.

Acute lymphocytic leukemia (ALL) is a disease of the young and of individuals older than 70, and plays a small role in the age groups that characterize most Vietnam veterans. Exposure to high doses of ionizing radiation is a known risk factor. Acute myeloid leukemia (AML) is the most