

herbicides and the outcome at any level of exposure.

The Secretary's determinations regarding individual diseases are based on all available evidence in Update 2002 and prior NAS reports. This notice generally states specific information only with respect to significant additional studies that were first reviewed by NAS in Update 2002. Information regarding additional relevant studies has previously been stated in VA's prior notices following earlier NAS reports, and will not be repeated here.

Hepatobiliary Cancers

Hepatobiliary cancers are cancers of the liver and intrahepatic bile ducts. There are a variety of known risk factors, including chronic infections with hepatitis B or C, exposure to aflatoxin, vinyl chloride and polychlorinated biphenyl (PCB), and smoking, that should be considered by a credible study.

NAS noted in VAO and subsequent reports that there were relatively few occupational, environmental, or veteran studies of hepatobiliary cancer. It also noted that most of the few existing studies addressing hepatobiliary cancer contain methodological difficulties such as small study size and inadequate control for life-style-related risk factors, or do not support an association with herbicide exposure.

An environmental study of the residents of Chapaevsk, Russia, an industrial community with documented contamination by dioxins and other chemicals of the food and water supply, revealed a higher incidence of liver cancer than in Russia as a whole or the Samara region of Russia, in which Chapaevsk is located, although no information was provided on exposed cases or estimated relative risk for morbidity. (Revich B, Aksel E, Ushakova T, Ivanova I, Zuchenko N, Lyuev N, Brodsky B, Sotsov Y. 2001. Dioxin exposure and public health in Chapaevsk, Russia. *Chemosphere* 43:951-966) In Update 2002, NAS determined that this study cannot be taken as strong evidence for an association between dioxins and liver cancer because the study failed to adjust for confounding by socioeconomic, lifestyle, comorbidity and other factors, and because of the likelihood of multiple exposures and concerns regarding the study design.

NAS found 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 hepatobiliary 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 hepatobiliary cancer outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

Nasopharyngeal Cancer

Nasal and nasopharyngeal cancers are relatively rare in the United States and thus difficult to study epidemiologically. Reported risk factors for nasal cancer include occupational exposure to nickel and chromium compounds, wood dust, and formaldehyde. Studies of nasopharyngeal cancer have reported associations with the consumption of salt-preserved foods, cigarette smoking, and Epstein-Barr virus. NAS noted in VAO and subsequent reports that there was inadequate or insufficient evidence to determine whether an association exists between herbicide exposure and nasal and nasopharyngeal cancer.

An environmental study of the residents of Chapaevsk, Russia, revealed a higher incidence of pharyngeal cancer in females than in Russia as a whole, although no information was provided on exposed cases or estimated relative risk for morbidity. (Revich et al., 2001.) Male residents of Chapaevsk did not show a higher incidence of pharyngeal cancer. NAS reported, in Update 2002, that the usefulness of these data is restricted because of factors such as lack of adjustment for confounding, the likelihood of multiple exposures, concern regarding the study design, and the absence of information on the completeness and accuracy of cancer incidence data.

NAS found 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 nasopharyngeal 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 nasopharyngeal cancer outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

Bone and Joint Cancer

NAS noted that bone cancer is more common in teenagers than adults, and,

therefore, the incidence among Vietnam veterans is quite low. Among the risk factors for adults contracting bone and joint cancer are exposure to ionizing radiation from treatment for other cancers and a history of certain noncancerous bone diseases. NAS found in VAO and subsequent reports that there is inadequate or insufficient information to determine whether an association exists between exposure to herbicides and bone cancer.

An environmental study of the residents of Chapaevsk, Russia, revealed seven deaths in male residents and seven deaths in female residents due to cancer of the bones or soft tissues. (Revich et al., 2001.) In Update 2002, NAS reported that these results cannot be taken as evidence for an association between bone cancer and dioxins, because cancers of the bone and soft tissue were combined in the analysis. Further, the increased risk for death due to bone cancer and soft-tissue cancer combined was not statistically significant.

NAS found 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 bone and joint 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 bone and joint cancer outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

Breast Cancer

NAS noted that breast cancer is the second most common cancer among women in the United States. Breast cancer incidence generally increases with age. Risk factors other than aging include a personal or family history of breast cancer and certain reproductive characteristics; specifically, early onset of menarche, late onset of menopause, and either no pregnancies or first full-term pregnancy after age 30. NAS noted in VAO and subsequent reports that there is inadequate or insufficient information to determine whether an association exists between exposure to herbicides and breast cancer.

In its prior reports, NAS reviewed several studies finding no increased risk of breast cancer associated with herbicide exposure or Vietnam service, and possibly even showing a limited protective effect for new incidence of breast cancer