

estimation were not performed, and no confounding factors were considered besides age. NAS noted that the lack of complete information prevented conclusions based on the study.

NAS stated that the new studies add little information on the association between exposure to herbicides and the incidence of skin cancer.

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

Cognitive and Neuropsychiatric Effects

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 cognitive and neuropsychiatric effects.

Results of a Vietnam veteran study of cognitive functioning from an Air Force Health Study (AFHS) examination in 1982 were reviewed by NAS in Update 2002. (Barrett DH, Morris RD, Akhtar FZ, Michalek JE. 2001. Serum dioxin and cognitive functioning among veterans of operation ranch hand. *Neurotoxicology* 22:491–502.) NAS noted that cognitive functioning in the Ranch Hand veterans evaluated with about 33 measures assessed through a variety of tests found eight significant group differences that did not support a dose-effect relationship with TCDD; that is, worse performance was seen in the background or low-TCDD groups. Ranch Hand veterans with the highest TCDD exposure had significantly lower scores on Logical Memory (Wechsler Memory Scale Form 1 (WMS)). NAS stated that finding could be attributed to chance alone and was not in agreement with other administered tests of verbal memory. NAS further stated that overall, the significant weaknesses in the study design, analyses, and interpretation of the results in the examination of serum TCDD and cognitive functioning in the Ranch Hand veterans prevent an association between exposure and neuropsychologic effects from being established.

In Update 2002, NAS reviewed a 30-year follow-up occupational study of 13

men in Czechoslovakia with TCDD exposure during the production of 2,4,5-T. (Pelclova D, Fenclova Z, Blaskova Z, Urban P, Lukas E, Prochazka B, Rappe C. 2001. Biochemical, neuropsychological, and neurological abnormalities following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. *Archives of Environmental Health* 56:493–500.) TCDD was correlated significantly with the memory quotient from WMS, the verbal IQ from the Wechsler Adult Intelligence Scale-Revised (WAIS-R), and the Benton test of visual memory. Age-corrected norms were used to determine abnormal performance. Education did not affect the results, but no demographic data on education were presented. Ten of 13 subjects drank alcohol daily, but this was not taken into account in the analyses. NAS reported that the low-voltage electroencephalogram with increased beta activity seen in 7 subjects could be related to the daily alcohol consumption. NAS further noted that it is not possible to determine the relationship between TCDD and cognitive functioning without attention to confounding.

An environmental study (Gauthier E, Fortier I, Courchesne F, Pepin P, Mortimer J, Gauvreau D. 2001. Environmental pesticide exposure as a risk factor for Alzheimer's disease: A case-control study. *Environmental Research Section A* 86:37–45) found that long-term exposure to herbicides and insecticides was not significantly related to the development of Alzheimer's disease. Occupational exposure to neurotoxic substances, including pesticides, was also not significantly related to Alzheimer's disease.

NAS concluded that there is still inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and cognitive and neuropsychiatric effects.

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

Gastrointestinal Tract Tumors

The incidence of stomach, colon, rectal, and pancreatic cancers increases with age for individuals between 45 and 59 years old. Other risk factors vary for these cancers but always include family history of the same form of cancer,

certain diseases of the affected organ, and dietary factors.

NAS noted in VAO and subsequent reports that there was limited or suggestive evidence of no association between exposure to herbicides and gastrointestinal (GI) tract tumors.

An occupational study (Burns *et al.*, 2001) of mortality of male employees of the Dow Chemical Company found fewer deaths than expected from all malignant neoplasms and specifically cancers of the digestive organs and peritoneum.

An environmental study of residents of Chapaevsk, Russia (Revich *et al.*, 2001) showed a higher incidence of colon cancer in males than Russia as a whole or the Samara region of Russia. Female residents of Chapaevsk did not have a higher incidence. However, female residents of Chapaevsk did have a higher incidence of stomach cancer than Russia or Samara. Male residents of Chapaevsk had a lower incidence of stomach cancer than Russia, but higher than Samara. Both male and female residents of Chapaevsk had a lower incidence of rectal cancer than Russia or Samara. NAS stated that, because of the lack of adjustment for confounding, the likelihood of multiple exposures, the absence of information on the completeness and accuracy of cancer diagnoses, and the ecologic study design, this study provides little evidence for associations with gastrointestinal cancers.

NAS concluded that there was no new evidence to change the previous determination that there is limited or suggestive evidence of no association between exposure to herbicides and gastrointestinal tract 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 gastrointestinal tract cancer outweighs the credible evidence for such an association, and he has determined that a positive association does not exist.

Brain Tumors

Exposure to ionizing radiation is an established risk factor for brain cancer. Several other potential factors have been examined, but most brain cancers are not associated with any known risk factors. Brain cancer occurs relatively infrequently.

NAS noted in VAO and subsequent reports that there was limited or suggestive evidence of no association between exposure to herbicides and brain tumors.

Two occupational studies published since Update 2000 were reviewed by