

that NAS determine, to the extent possible: (1) Whether there is a statistical association between the suspect diseases and herbicide exposure, taking into account the strength of the scientific evidence and the appropriateness of the methods used to detect the association; (2) the increased risk of disease among individuals exposed to herbicides during service in the Republic of Vietnam during the Vietnam era; and (3) whether there is a plausible biological mechanism or other evidence of a causal relationship between herbicide exposure and the suspect disease. Section 3 of Pub. L. 102-4 also required that NAS submit reports on its activities every 2 years (as measured from the date of the first report) for a 10-year period.

Section 1116(b) of title 38, United States Code, as enacted by the Agent Orange Act of 1991, Pub. L. 102-4, provides that whenever the Secretary determines, based on sound medical and scientific evidence, that a positive association (*i.e.*, the credible evidence for the association is equal to or outweighs the credible evidence against the association) exists between exposure of humans to an herbicide agent (*i.e.*, a chemical in an herbicide used in support of the United States and allied military operations in the Republic of Vietnam during the Vietnam era) and a disease, the Secretary will publish regulations establishing presumptive service connection for that disease. If the Secretary determines that a presumption of service connection is not warranted, he is to publish a notice of that determination, including an explanation of the scientific basis for that determination. The Secretary's determination must be based on consideration of the NAS reports and all other sound medical and scientific information and analysis available to the Secretary.

Although 38 U.S.C. 1116(b) does not define "credible," it does instruct the Secretary to "take into consideration whether the results [of any study] are statistically significant, are capable of replication, and withstand peer review." Simply comparing the number of studies which report a positive relative risk to the number of studies which report a negative relative risk for a particular condition is not a valid method for determining whether the weight of evidence overall supports a finding that there is or is not a positive association between herbicide exposure and the subsequent development of the particular condition. Because of differences in statistical significance, confidence levels, control for confounding factors, bias, and other

pertinent characteristics, some studies are clearly more credible than others, and the Secretary has given the more credible studies more weight in evaluating the overall weight of the evidence concerning specific diseases.

Section 2 of the Agent Orange Act of 1991, Public Law 102-4, provided that the Secretary's authority to establish presumptions of service connection under 38 U.S.C. 1116(b) would expire 10 years after the first day of the fiscal year in which the NAS transmitted its first report to VA. The first NAS report was transmitted to VA in July 1993, during the fiscal year that began on October 1, 1992. Accordingly, under the Agent Orange Act of 1991, Public Law 102-4, VA's authority to issue regulatory presumptions as specified in section 1116(b) expired on September 30, 2002. In December 2001, however, Congress enacted the Veterans Education and Benefits Expansion Act of 2001 (Benefits Expansion Act), Public Law 107-103. Section 201(d) of that Act extended VA's authority under section 1116(b) through September 30, 2015. Pursuant to the Benefits Expansion Act, Public Law 107-103, VA may issue new regulations between October 1, 2002, and September 30, 2015, establishing additional presumptions of service connection for diseases that are found to be associated with exposure to an herbicide agent.

### **I. History of Agent Orange Presumptions**

Pursuant to 38 U.S.C. 1116 and prior NAS reports received between July 1993 and April 2001, VA regulations contain presumptions of service connection for ten categories of disease based on exposure to an herbicide agent. Those diseases are listed in 38 CFR 3.309(e) as follows: Chloracne or other acneform disease consistent with chloracne, Type 2 diabetes (also known as Type II diabetes mellitus or adult-onset diabetes), Hodgkin's disease, Multiple myeloma, Non-Hodgkin's lymphoma, Acute and subacute peripheral neuropathy, Porphyria cutanea tarda, Prostate cancer, Respiratory cancers (cancer of the lung, bronchus, larynx, or trachea), and Soft-tissue sarcoma (other than osteosarcoma, chondrosarcoma, Kaposi's sarcoma, or mesothelioma).

If a veteran who was exposed to an herbicide agent in service subsequently develops one of the presumptive diseases, VA will presume the disease was caused by the exposure to an herbicide agent in service for purposes of establishing entitlement to service-connected benefits. To qualify for this presumption, chloracne and porphyria cutanea tarda must become manifest to

a degree of disability of 10 percent or more within one year after the date of last exposure. The other conditions are presumed service connected if they are manifest to a degree of disability of ten percent or more at any time after exposure. 38 U.S.C. 1116(a)(2). VA presumes that any veteran who served in the Republic of Vietnam during the period beginning on January 9, 1962, and ending on May 7, 1975, was exposed to an herbicide agent during such service. 38 U.S.C. 1116(f).

### **II. Prior Actions Concerning Leukemia**

In each of its four previous biennial reports under the Agent Orange Act of 1991, the NAS concluded that there was "inadequate/insufficient" evidence to determine whether an association exists between exposure to an herbicide agent and the subsequent occurrence of leukemia in exposed persons. After reviewing each of those reports, the Secretary determined that the credible evidence against an association exists between exposure to an herbicide agent and the occurrence of leukemia in exposed persons outweighed the credible evidence for such an association, and that a positive association therefore did not exist. 67 FR 42600, 42604 (June 24, 2002); 64 FR 59232, 59238 (Nov. 2, 1999); 61 FR 41442, 41445 (Aug. 8, 1996); 59 FR 341, 344 (Jan. 4, 1994).

### **III. Latest NAS Review of Chronic Lymphocytic Leukemia**

After receiving and reviewing the last prior NAS report in 2001, the Secretary asked that NAS' next report separately review the scientific evidence concerning the association between herbicide exposure and one particular form of leukemia, known as chronic lymphocytic leukemia (CLL). NAS issued its report, "Veterans and Agent Orange: Update 2002," on January 23, 2003. In that report, NAS concluded that "there is sufficient evidence of an association between exposure to at least one of the chemicals of interest (2,4-D, 2,4,5-T or its contaminant TCDD, picloram, or cacodylic acid) and CLL." The term "sufficient evidence of an association," as explained in the NAS report, means that a positive association has been observed between herbicides and the outcome in studies in which chance, bias, and confounding could be ruled out with reasonable confidence.

NAS discussed several studies that reported findings regarding the incidence of CLL as distinguished from other types of leukemia. One study of site-specific cancer incidence among 7,016 males and females in a rural farming community found a standard incidence ratio of 1.8, with a 95%