

confidence interval (CI) of 0.8–3.2 for CLL. (Waterhouse D *et al.* 1996. Cancer incidence in the rural community of Tecumseh, Michigan: a pattern of increased lymphopoietic neoplasms. *Cancer* 77(4): 763–770). A population-based case-control study in an agricultural area of Italy noted an increased risk of CLL among farmers (Odds Ratio (OR) = 1.6, CI = 0.5–5.2) and animal breeders (OR = 3.1 CI = 1.1–8.3), although no information was provided on herbicide exposure in the study population. (Amadori D *et al.* 1995. Chronic lymphocytic leukaemias and non-Hodgkin's lymphomas by histological type in farming-animal breeding workers: a population case-control study based on job titles. *Occupational and Environmental Medicine* 52(6): 374–379). A study of cancer risk in Danish male gardeners reportedly exposed to pesticides and herbicides showed a significant increase in CLL (relative risk = 2.8, CI = 1.0–6.0), although no specific data on herbicide exposure were given. (Hansen ES *et al.* 1992. A cohort study on cancer incidence among Danish gardeners. *American Journal of Industrial Medicine* 21(5): 651–660). One study showed a significant increase in mortality due to CLL among farmers in Nebraska from 1957–1974 (OR = 1.7), although no data regarding herbicide exposure were given. (Blair A, White DW. 1985. Leukemia cell types and agricultural practices in Nebraska. *Archives of Environmental Health* 40(4): 211–214).

Two epidemiologic studies reported specifically on herbicide exposure and CLL. In a study of 1,675 white Iowa males who died of leukemia, CLL was significantly increased in farmers (OR = 1.9, CI=1.2–3.1). (Burmeister LF *et al.* 1982. Leukemia and farm practices in Iowa. *American Journal of Epidemiology* 115(5): 720–728). Further analysis showed a strong relationship of CLL deaths in counties with acres treated with herbicides. In a population-based case-control interview study of 578 white men with leukemia and 1,245 controls, CLL mortality was higher in farmers than nonfarmers. (Brown LM *et al.* Pesticide exposures and other agricultural risk factors for leukemia among men in Iowa and Minnesota. *Cancer Research* 50(20): 6585–6591). When risk was calculated for CLL subtype, odds ratios were significantly increased for use of any herbicide (OR = 1.4). The risk of CLL in farmers who ever handled 2,4-D was 1.3. The risk of CLL in men who first handled 2,4,5-T at least 20 years before interview was significantly increased (OR = 3.3, CI = 1.2–8.9).

NAS also noted that a recent follow-up study of residents of Seveso, Italy found no increased risk of lymphocytic leukemia. (Bertazzi PA *et al.* 2001. Health effects of dioxin exposure: a 20-year mortality study. *American Journal of Epidemiology* 153(11): 1031–1044).

NAS stated that the epidemiologic studies indicate that farming occupation is associated with significant risk of CLL, especially when there is exposure to the herbicides 2,4-D and 2,4,5-T. NAS further noted that CLL shares more traits with non-Hodgkin's lymphoma (NHL) than with other types of leukemia and could have a common etiology, and that many studies support the hypothesis that herbicide exposure can contribute to the risk of NHL. NAS also concluded, as in its prior reports, that a connection between exposure to TCDD, a contaminant of 2,4,5-T, and human health effects is considered biologically plausible.

IV. The Secretary's Determination on Chronic Lymphocytic Leukemia

After considering all of the evidence, the Secretary has determined that there is a positive association between the exposure of humans to an herbicide agent and the occurrence of CLL in humans. The studies cited by NAS consistently show an increased risk of CLL among agricultural workers and two of the studies show a significantly increased risk among farmers who were exposed to herbicides. Some of the findings noted by NAS are statistically significant, and the consistency of the findings overall supports the view that an association exists. Under these circumstances, the Secretary concludes that the credible evidence for an association between exposure to an herbicide agent and the occurrence of CLL in humans outweighs the credible evidence against such an association. Accordingly, the Secretary has determined that a presumption of service connection for CLL is warranted pursuant to 38 U.S.C. 1116(b).

This proposed rule does not reflect determinations concerning any disease other than CLL. The Secretary's determinations concerning other diseases discussed in the current NAS report will be addressed in future documents published in the **Federal Register**.

Unfunded Mandates

The Unfunded Mandates Reform Act requires, at 2 U.S.C. 1532, that agencies prepare an assessment of anticipated costs and benefits before developing any rule that may result in an expenditure by State, local, or tribal governments, in the aggregate, or by the private sector of

\$100 million or more in any given year. This rule would have no consequential effect on State, local or tribal governments.

Paperwork Reduction Act

This document contains no provisions constituting a collection of information under the Paperwork Reduction Act (44 U.S.C. 3501–3521).

Executive Order 12866

This document has been reviewed by the Office of Management and Budget under Executive Order 12866.

Regulatory Flexibility Act

The Secretary hereby certifies that this regulatory amendment will not have a significant economic impact on a substantial number of small entities as they are defined in the Regulatory Flexibility Act (RFA), 5 U.S.C. 601–612. The reason for this certification is that these amendments would not directly affect any small entities. Only VA beneficiaries could be directly affected. Therefore, pursuant to 5 U.S.C. 605(b), these amendments are exempt from the initial and final regulatory flexibility analysis requirements of sections 603 and 604.

The Catalog of Federal Domestic Assistance program numbers are 64.109 and 64.110.

List of Subjects in 38 CFR Part 3

Administrative practice and procedure, Claims, Disability benefits, Health care, Pensions, Veterans, Vietnam.

Approved: February 27, 2003.

Anthony J. Principi,

Secretary of Veterans Affairs.

For the reasons set forth in the preamble, 38 CFR part 3 is proposed to be amended as follows:

PART 3—ADJUDICATION

Subpart A—Pension, Compensation, and Dependency and Indemnity Compensation

1. The authority citation for part 3, subpart A continues to read as follows:

Authority: 38 U.S.C. 501(a), unless otherwise noted.

2. In § 3.309, paragraph (e) the listing of diseases is amended by adding “Chronic lymphocytic leukemia” between “Hodgkin's disease” and “Multiple myeloma” to read as follows:

§ 3.309 Diseases subject to presumptive service connection.

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