Name:

SSN:

Date:

Date of Birth:

Sex: male

Dates of military service

Dates of service at Camp Lejeune:

The following report was based on record review.

Reviewer:

**Member, Subject Matter Expert Panel**

Camp Lejeune Contaminated Water Project

Time Dedicated to this review: XX Minutes

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Contention, the veteran claims the following condition as secondary to exposure to CLCW:

Contention 1: Prostate cancer

Diagnosis:

Nexus: The diagnosis above Choose an item.

**Case Specific Discussion**:

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Claims file and other available evidence of record was review, applicable evidence is summarized below:

**VBMS/Claims file review**:

**VVA/VistaWeb/CAPRI review**:

**Other possible risk factors**:

Employment history prior to military service:

Smoking:

Alcohol use:

Obesity:

Genetic:

Employment history after military service:

Hobbies/ recreational leading to possible chemical exposure: UNK

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**Disease Specific Discussion, Prostate Cancer:**

Disease Description: The National Cancer Institute (NCI) defines prostate cancer as cancer that forms in tissues of the prostate. The prostate gland is located between the bladder and rectum. Cancers arising from the bladder or rectum which extend into the prostate are NOT prostate cancer.

Incidence: After skin cancer, prostate cancer is the most common cancer in American men. The American Cancer Society notes that, “About 1 man in 7 will be diagnosed with prostate cancer during his lifetime.” Clinically diagnosed prostate cancer rarely occurs before the age of 40, but the incidence rises rapidly thereafter.

The widespread prevalence of occult prostate cancer in older men and the dramatic increase with age are illustrated by a review of autopsy studies conducted in multiple countries [1]:

●20 to 30 years, 2 to 8 percent of men with occult cancer

●31 to 40 years, 9 to 31 percent

●41 to 50 years, 3 to 43 percent

●51 to 60 years, 5 to 46 percent

●61 to 70 years, 14 to 70 percent

●71 to 80 years, 31 to 83 percent

●81 to 90 years, 40 to 73 percent

The NCI (2007-2011 SEER data) reports the incidence of new cases was greatest for black men (223.9/100,000) in comparison to white (139.9/100,000) and Hispanic (121.8/100,000) men [2].

**Risk Factors:** Prostate cancer (CaP) has several known risk factors, the most important being increasing age, ethnicity, genetic factors (positive family history, Lynch syndrome, BRCA1 and BRCA 2), obesity, smoking, and possibly dietary factors (diet high in processed meat or dairy foods). Prostate cancer has one of the strongest relationships between age and any human malignancy and is more common in African American than white or Hispanic men. U.S. rates are 1.6 times higher among African–American men than among Caucasian men [3]. In addition to higher incidence rates, the age of onset in African-American men is earlier than for comparative groups.

Recent genetic studies suggest that hereditary factors may be responsible for 5%–10% of prostate cancers [4]. Men with a first degree relative with prostate cancer have a two to three fold increase in risk relative to the general population. Men with two first-degree relatives have a five-fold increased risk, whereas, men with a family history of three first degree relatives with prostate cancer have an increased risk of 11-fold. In addition, relatives of early onset cases would have a higher risk of having prostate cancer than later onset cases. Men with brothers diagnosed under the age of 65 had a six-fold increased risk of developing prostate cancer under the age of 65 themselves [5].

Clinical reviews and meta-analyses such as the Allot paper have found that higher waist circumference and hypertension are associated with increased risks of prostate cancer [6, 7]. The Huncharek meta-analysis reported that smoking is associated with prostate cancer incidence and mortality. The heaviest smokers had a 24% to 30% greater risk of death from prostate cancer than did nonsmokers [8]. Carter et al. reported that mortality from prostate cancer was 43% higher (relative risk, 1.4; 95% CI, 1.2 to 1.7) among current smokers than among those who had never smoked [9]. Skeldon et al. have reported that cannabis use has been linked with several urological malignancies including prostate cancer [10].

**Scientific Review:**

NAS 2009 report: The water supply at Camp Lejeune was contaminated with benzene, vinyl chloride, tetrachloroethylene (PERC) and trichloroethylene (TCE). The NAS report found “inadequate/insufficient evidence to determine whether an association exists” between exposures to Camp Lejeune contaminated water supply and prostate cancer [11].

Literature review of pertinent publication subsequent to the NAS 2009 report including current ATSDR statements support the fact the benzene and vinyl chloride have not been shown to contribute to prostate cancer development. Only PERC and TCE have a plausible connection to future development of prostate cancer, therefore the following excludes a further discussion on vinyl chloride and benzene.

Environmental Exposure Literature Review: Extensive research of the scientific literature, found limited relevant data regarding environmental exposures to PERC and TCE. A study regarding health effects of the contaminated drinking water in Massachusetts evaluated cancer effects and found no elevated risk of prostate cancer [12]. In response to concerns about cancer stemming from drinking water contaminated with PCE and TCE, Morgan et al. in 2002 reviewed new cases for 16 cancer types in a California community with a population of 3.3 million people (1988 to 1998) [13]. This study did not observe an overall cancer excess. The standardized incidence ratio for prostate cancer was 1.11 (99% CI .98 – 1.25). This was not statistically significant. This study was conducted on a water supply that was contaminated with PERC from 5-98 parts per billion (PPB) and TCE levels from .09 to 97 ppb when monitoring began. Estimated time frame of contamination was “likely as much as a decade earlier” than the date of detection. These were measurements taken at well heads. The water was then distributed to the population in a co-mingled distribution system, including some water sources that were not contaminated, similar to what occurred at Camp Lejeune.

In the ATSDR Trichloroethylene Subregistry health survey of people exposed to trichloroethylene and other contaminants through drinking water in up to 15 locations across five states (Illinois, Indiana, and Michigan, Pennsylvania, and Arizona), no convincing evidence of a significant association between trichloroethylene and cancer was found at baseline assessment or at several follow-up time points [14]. One Bove et al study evaluated a cohort of CL civilians with an average employment on base of 2.5 years [15].  They found slightly elevated rates (which did not reach statistical significance) of prostate cancer in the exposed CL cohort compared to the control Camp Pendleton (CP) cohort (Hazard ratio (HR) was 1.17 and the 95% confidence interval (CI) was 0.49-2.8).  In addition, a Bove et al study of CL marines with an average exposure of 18 months found  a similar slight  increase in prostate cancer rates (which also did not meet statistical significance) compared to a CP control cohort  (HR was 1.23 with 95% CI of 0.60-2.49) [16].  The interpretations were not definitive as there were a low number of prostate cancer deaths, and the confidence intervals were wide and thus there remained a significant possibility that these findings could be due to chance alone.  In addition, prostate cancer risk factors such as obesity, family history, and smoking were not available in these studies and no definitive dose-response relationships were identified for prostate cancer. While these studies do not rule out a causal effect of CLCW exposure on prostate cancer, no definitive diagnostic conclusions can be drawn.

Occupational Exposure Literature Review: Most of the published studies are based on occupational exposures to mixed solvents including PERC and TCE. Occupational exposures to these solvents in the studies were much higher among workers as compared to the estimated residential exposures at Camp Lejeune. Even within the occupationally exposed workers, those researchers that have looked at the question have concluded that only the highest levels of exposure are associated with a potentially increased risk for the development of prostate cancer. Despite the limitations of industrial studies, the estimates of exposure in those studies are significantly higher than the estimates of CLCW exposure. It is likely that even the lower levels of workplace exposures exceed the low levels of exposure measured at Camp Lejeune.

Several cohort mortality studies explore the relationship between trichloroethylene exposure and development of prostate cancer. The NAS review summarizes 3 studies and finds a small excess risk in individuals with high exposures in those with more than five years of occupational exposure. Individuals with occupational exposure to trichloroethylene had between a 1.0 and 1.3 (OR) fold risk of developing prostate cancer. A case control study, summarized in the same review, documented a two-fold risk after high exposure.

The Radican study found no increased incidence of prostate cancer in workers exposed to TCE [17]. The exposure calculations were defined as: “Intermittent or continuous exposure was assigned to subjects who used TCE infrequently or regularly, respectively, throughout the day. Low or peak exposure was assigned to subjects who used TCE for bench top work (to clean small parts) or who worked with vapor degreasers, respectively. Four categories of TCE were then developed for each worker: low intermittent, low continuous, peak infrequent, and peak frequent. In addition, estimates of the frequency (times/day), duration (min/day) and intensity of TCE exposure (the latter as a score based on the limited measurement data) were developed.” They reported hazard ratios (95% confidence intervals) for prostate cancer of 1.22 (0.82–1.82) for low/ intermittent exposure, 1.30 (0.85–1.99) for low/continuous exposure, 1.02 (0.57–1.86) for peak/ infrequent exposure, 1.24 (0.81–1.92) for peak/ frequent exposure.

A 2007 study of aerospace and radiation workers in the US found an elevated odds ratio for prostate cancer in workers with high trichloroethylene exposure (OR = 2.1; 95% CI = 1.2 to 3.9). High exposure was not specifically described [18]. The authors also noted a positive trend between increasing levels of TCE exposure and prostate cancer (P-value for trend = 0.02).

Lipworth et al, in 2011 reported an extended follow up of aircraft manufacturing workers who were exposed to TCE, PCE, chromates and mixed solvents and found no increased risk of prostate cancer [19]. The evaluated the length of exposure and found no statistically significant increase risk of prostate cancer.

Hansen et al. published a follow up report on a large cohort of workers in Nordic countries who were exposed to Trichlorethylene [20]. The researchers took urine measurements to document exposure to TCE. The TCE levels indicated comparable to greater exposure in this population compared with that would have reasonably occurred at Camp Lejeune. For prostate cancer, the SIR (standardized incidence ratio) was .96 (95% CI 0.08 to 1.14). This is not statistically significant.

In a Canadian study published in February 2013 the authors found that the majority of the associations examined between chlorinated solvent exposures and the development of 11 sites of cancer were null [21]. The authors define substantial exposure as: exposed at a confidence level of probable or definite; a concentration or frequency of medium or high; and duration of greater than 5 years. Out of two associations that were found to have significantly elevated odds ratios (ORs), one was for substantial exposure to perchloroethylene and prostate cancer (OR = 4.3; 95% CI: 1.4 to 13). The association between any PERC exposure and prostate cancer was lower and the confidence interval included 1, indicated this could have occurred from chance alone (OR=2.2; 95%CI: 0.8 to 5.7).

Summary

In summary, some occupational studies noted above suggest that after substantial occupational exposures for at least 5 years, there may be an increased risk of developing prostate cancer. There are many other studies in the literature that have found no increase in risk after workplace exposure. Therefore, with the possible exception of significant work place exposure (which is greater than the estimated CLCW exposure) to PERC or TCE for greater than 5 years, there is limited scientific documentation linking exposure to either of these solvents and the development of prostate cancer.

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