Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, July 13, 2015 11:01 AM
To: (b) (6) (b) (6) (b) (6)
Subject: colon ca

Categories: Orange Category

Hi, guys, just want to point out that the 1999 Paulu study is an environmental not an occupational study for colon ca...

These templates are a useful start!! Thanks

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Tuesday, July 14, 2015 2:25 PM
To: (b) (6)
Subject: final revisions
Attachments: CLCW-BladderCA6.docx

(b) (6)

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Wednesday, July 15, 2015 1:18 PM
To: (b) (6) (b) (6)
Subject: FW: [EXTERNAL] SecVA briefing
Attachments: SecVA briefly.docx

(b) (6)

From: (b) (6)
Sent: Wednesday, July 15, 2015 1:17 PM
To: (b) (6) ; (b) (6)
Subject: FW: [EXTERNAL] SecVA briefing

Ignore that the doc. is called "briefly" instead of briefing.

Leukemia is too difficult to do quickly. Several different conditions.
I didn't have parkinsons done yet. Cant do it now but could tonight if you think it is needed.
Let me know if you want more references or anymore for these. I did NOT put in risk factor articles as I thought you wanted to compare other studies to ATSDR and not discuss risk factors. But I certainy can add that.

(b) (6)

(b) (6)

From: (b) (6)
Sent: Wednesday, July 15, 2015 1:11 PM
To: (b) (6)
Subject: [EXTERNAL] SecVA briefly

General reference for cancers from ATSDR:

Toxicological Profile for Trichloroethylene, (Draft), ATSDR October, 2014

http: //www.atsdr.cdc.gov/toxprofiles/tp19.pdf

A study of three Michigan communities in which people were exposed to chlorinated solvents including trichloroethylene in drinking water showed no significant increases in cancers among the exposed population, including leukemia (Freni and Bloomer 1988). However, the cohort size in this study was only 223.

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 (Agency for Toxic Substances and Disease Registry 1994, 1999; Burg and Gist 1999; Burg et al. 1995; Davis et al. 2005).

NOTE: Studies showing an increased risk were in those exposed to high levels for years. This risk needs to be compared to time at CL, levels measured at CL, and other risk factors.

Renal

Raaschou-Nielsen et al. (2003) reported an SIR of 1.6 (95% CI, 1.1-2.3) for occupational TCE exposure in men employed for 5 years or more.

Hansen: 2013 showed no increase in risk for developing renal cell cancer for those working directly with TCE. The median duration of employment in the company with TCE exposure was 6 years. It was determined that if TCE is a risk factor for kidney cancer, it was only at extremely high levels of exposure.

Vlaandern et al performed an analysis of occupational exposures in four Nordic countries for TCE and PCE found no association between these exposures and kidney cancer.

Charbotal suggests an association between exposures to high levels of TCE and
Increased risk of RCC. Respectively. A significantly increased risk of RCC
was identified for the highest cumulative dose: the
adjusted OR was 2.16 (1.02–4.60). Increased risk only for high cumulative dose which was much higher than the exposed does in CLCW

References:

Vlaanderen J et. Al. Occupational exposure to trichloroethylene and perchloroethylene and the risk of lymphoma, liver, and kidney cancer in four Nordic countries. Occup Environ Med. 2013 Jun; 70(6):393-401.

Raaschou-Nielsen O, Hansen J, McLaughlin JK, Kolstad H, Christensen JM, Tarone RE, Olsen JH. Cancer risk among workers at Danish companies using trichloroethylene: a cohort study. Am J Epidemiol. 2003 Dec 15;158(12):1182-92.

Hansen J1, Sallmén M, Seldén AI, Anttila A, Pukkala E, Andersson K, Bryngelsson IL, Raaschou-Nielsen O, Olsen JH, McLaughlin JK. Risk of cancer among workers exposed to trichloroethylene: analysis of three Nordic cohort studies. J Natl Cancer Inst. 2013 Jun 19;105(12):869-77.

BARBARA CHARBOTEL*, et al, Case–Control Study on Renal Cell Cancer and Occupational Exposure to Trichloroethylene. Part II: Epidemiological Aspects. Ann. Occup. Hyg., Vol. 50, No. 8, pp. 777–787, 2006.

Prostate

Paulu. A study regarding health effects of the contaminated drinking water in Massachusetts evaluated cancer effects and found no elevated risk of prostate cancer.

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). 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. 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.

The Radican study found no increased incidence of prostate cancer in workers exposed to TCE 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. None was statistically significant.

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.

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. 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).

Paulu C, Aschengrau A, Ozonoff D. Tetrachloroethylene-contaminated drinking water in Massachusetts and the risk of colon-rectum, lung, and other cancers. Environ Health Perspect. 1999 Apr;107(4):265-71

Morgan, J., & Cassady, R. (n.d.). Community Cancer Assessment in Response to Long-Time Exposure to Perchlorate and Trichloroethylene in Drinking Water. Journal of Occupational and Environmental Medicine 44.2 (2002) 616-21.

Radican L, Blair A, Stewart P, Wartenberg D. Mortality of aircraft maintenance workers exposed to trichloroethylene and other hydrocarbons and chemicals: extended follow-up. J Occup Environ Med. 2008 Nov;50(11):1306-19

Christensen KY, Vizcaya D, Richardson H, Lavoué J, Aronson K, Siemiatycki: Risk of selected cancers due to occupational exposure to chlorinated solvents in a case-control study in Montreal. J Occup Environ Med. 2013 Feb; 55(2):198-208.

Lipworth, L. Cancer mortality among aircraft manufacturing workers: an extended follow-up. J Occup Environ Med. 2011 Sep;53(9):992-1007

Colorectal

Environmental studies evaluating possible relationship between CRC and exposure to the chemical found in CLCW are somewhat limited.

Paulu et al. 1999 observed that the adjusted ORs for colon-rectum cancer were modestly elevated among ever-exposed subjects as more years of latency were assumed [OR and CI, 1.7 (0.8-3.8) and 2.0 (0.6-5.8) for 11 and 13 years of latency, respectively]. These elevated ORs stemmed mainly from associations with rectal cancer. Adjusted ORs for rectal cancer among ever-exposed subjects were more elevated [OR and CI, 2.6 (0. 8-6.7) and 3.1 (0.7-10.9) for 11 and 13 years of latency, respectively] than were corresponding estimates for colon cancer [OR and CI, 1.3 (0.5-3.5) and 1.5 (0.3-5.8) for 11 and 13 years of latency, respectively]." While the odds ratio are somewhat elevated the CI were below 1 which means the conclusion could be due to chance alone. Therefore this data does not rise to the level of certainty to support a link between exposures to CLCW.

Morgan et al. in a 2002 study, found no increased risk of colon and rectal cancers in California communities exposed to drinking water contaminated with TCE.

Lipworth et all, in 2011 publication evaluated TCE, PCE and mixed solvent exposures, concluded that there was "no consistent evidence of increased cancer" with long term exposure to the above chemicals in aircraft workers.

Hansen et al, in a pooled cohort study published in 2013 study documented no increased risk of colo-rectal cancer due to exposure to TCE and its metabolites.

References

Lipworth L, Sonderman JS, Mumma MT, Tarone RE, Marano DE, Boice JD Jr, McLaughlin JK. Cancer mortality among aircraft manufacturing workers: an extended follow-up. J Occup Environ Med. 2011 Sep;53(9):992-1007.

Paulu C, Aschengrau A, Tetrachloroethylene-contaminated drinking water in Massachusetts and the risk of colon-rectum, lung, and other cancers. Ozonoff D Environ Health Perspect. 1999 Apr;107(4):265-71

Hansen J1, Sallmén M, Seldén AI, Anttila A, Pukkala E, Andersson K, Bryngelsson IL, Raaschou-Nielsen O, Olsen JH, McLaughlin JK. Risk of cancer among workers exposed to trichloroethylene: analysis of three Nordic cohort studies. J Natl Cancer Inst. 2013 Jun 19;105(12):869-77.

Morgan JW1, Cassady RE. Community cancer assessment in response to long-time exposure to perchlorate and trichloroethylene in drinking water. J Occup Environ Med. 2002 Jul;44(7):616-21.

Parkinson's

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Tuesday, March 31, 2015 5:31 PM
To: (b) (6)
Subject: FW: esophageal cancer discussion of risk factors

Maybe we should do esophageal ca next.

From: (b) (6)
Sent: Tuesday, March 31, 2015 5:29 PM
To: (b) (6)
Subject: esophageal cancer discussion of risk factors

Hey (b) (6), this is my most reecent take on an esophageal ca case

Discussion of risk factors for esophageal cancer:

PCE: The USDHHS 13th report on carcinogens has ascertained PCE to be 'reasonably anticipated to be a human carcinogen" based on sufficient evidence from animal studies (17). In humans esophageal cancer has been suspected to be linked to PCE exposure, but studies have been unclear, confounding by smoking and other chemical exposure could not be ruled out, and the case numbers in the cohort studies were small (17). I am not aware of any studies definitively linking PCE exposure to esophageal cancer at the low levels of exposure measured at CL.

TCE: The USDHHS 13th report on carcinogens has ascertained TCE to be 'reasonably anticipated to be a human carcinogen" based on sufficient evidence from animal studies and also from evidence in human studies (17). However, I am not aware of any studies definitively linking TCE exposure to esophageal cancer at the low levels found in CL.

Vinyl chloride and benzene: Vinyl chloride and benzene exposure have not been linked to adenocarcinoma of the esophagus to my knowledge. Cigarette smoking is a significant source of benzene exposure. (17) I am not aware of any community studies definitively linking benzene or vinyl chloride exposure to esophageal cancer at the low levels found in CL.

Community/drinking water studies: There are no known community or drinking-water studies which have definitively implicated exposure to CLCW solvents and esophageal cancer to my knowledge. The Bove et al study evaluated CL civilians with an average employment on base of 2.5 years (18). They found no association with CL employment and death from esophageal cancer (Hazard ratio was 0.58 (the death rate was higher in unexposed Camp Pendleton employees than CL exposed employees). However, the Bove et al study of CL marines with an average exposure of 18 months found a nonstatistically significant increase in esophageal cancer (hazard ratio 1.43 with 95% CI of 0.85-2.38). The interpretation is somewhat unclear as the there is a chance these findings could be due to chance alone,

smoking, alcohol and obesity data were not available in these studies, and no dose-response relationship was identified (20).

Occupational data: While the occupational data has been somewhat conflicting, no studies
have found a definitive association between occupational solvent exposure of the type found at CL and esophageal cancer (2,3,4). Reference a large case-control study which found no evidence of an association between esophageal cancer risk and exposure to chlorinated solvents (3), which studied high occupational exposure (5 years or more working directly with solvents) in general much higher exposures and longer duration than this veteran was working there, and much higher doses than the levels measured in Camp LeJeune (5). Most occupational studies of perchlorethylene (PCE)such as in dry cleaners and esophageal cancer risk are hampered by inability to control for other risk factors such as smoking/drinking. Calvert et al (21) found elevated risks of esophageal cancer in dry cleaners. They found esophageal cancer risk was highest among those employed in a PCE-using shop for 5 years with 20 years' latency since first such employment (SMR was , 2.16 (0.85 to 4.54) for < 5 years exposure and < 20 years latency but was 4.78 (2.68 to 7.91) with > 5 years exposure and > 20 years latency). The authors cite a lack of information about smoking and drinking as a weakness of these evaluations as smoking was found to be more prevalent in PCE-exposed workers.

Non-CLCW risk factors: In contrast to the somewhat conflicting data from solvent studies, smoking has been determined to be a well defined risk factor for adenocarcinoma and squamous cell carcinoma of the esophagus (13-16, 19). A mechanism has been established; tobacco condensates, particularly nitrosamines, have been found to come in contact with the esophageal mucosa in smokers. Epidemiologic studies have found a direct correlation between the amount smoked and the risk of esophageal adenocarcinoma (19).

Summary:

##########

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Critical review of the epidemiological literature on occupational exposure to perchloroethylene and cancer.
Mundt KA, Birk T, Burch MT.
SourceApplied Epidemiology, Inc., Amherst, Massachusetts 01002-2424, USA.
kmundt@appliedepidemiology.com

3) Christiansen Y.K. et al, Risk of selected cancers due to occupational exposure to chlorinated solvents in a case-control study in Montreal. JOEM, 55, (2) 2013;

198-208;
Bernardini P, Scoppetta C
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Public Health Service Agency for Toxic Substances and Disease Registry
August 2007;

5) Contaminated Water Supplies at Camp Lejeune: Assessing Potential Health Effects. The National Research Council of the National Academy of Sciences.
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6) U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Agency for Toxic Substances and Disease Registry
Division of Toxicology and Human Health Sciences Atlanta, GA 30333;ADDENDUM TO THE
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7) TOXICOLOGICAL PROFILE FOR Tetrachloroethylene); U.S. DEPARTMENT OF HEALTH AND HUMAN
SERVICES
Public Health Service Agency for Toxic Substances and Disease Registry
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Agency for Toxic Substances and Disease Registry PUBLIC HEALTH STATEMENT Benzene

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Body mass index in relation to oesophageal and oesophagogastric junction adenocarcinomas: a pooled analysis from the International BEACON Consortium.
Hoyo C, Cook MB, Kamangar F, Freedman ND, Whiteman DC, Bernstein L, Brown LM, Risch HA, Ye W, Sharp L, Wu AH, Ward MH, Casson AG, Murray LJ, Corley DA, Nyrén O, Pandeya N, Vaughan TL, Chow WH, Gammon MD.

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Rubenstein JH, Taylor JB. Veterans Affairs Center of Excellence for Clinical Management Research, Ann Arbor, MI, USA. jhr@umich.eduSource Department of Obstetrics and Gynecology, Duke University School of Medicine, Durham, NC 27710, USA. cathrine.hoyo@duke.edu

12) Gut. 2008 Feb;57(2):173-80. Epub 2007 Oct 11.
Combined effects of obesity, acid reflux and smoking on the risk of adenocarcinomas of the oesophagus.Whiteman DC, Sadeghi S, Pandeya N, Smithers BM, Gotley DC, Bain CJ, Webb PM, Green AC; Australian Cancer Study.Division of Population Studies and Human Genetics, Queensland Institute of Medical Research, PO Royal Brisbane Hospital, Queensland 4029, Australia.

david.whiteman@qimr.edu.au

13) J Gastrointest Cancer. 2013 Jun;44(2):143-51. doi: 10.1007/s12029-013-9480-z.
Risk factors for rising incidence of esophageal and gastric cardia adenocarcinoma.
Carr JS, Zafar SF, Saba N, Khuri FR, El-Rayes BF.
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA.

14) Recent Results Cancer Res. 2010;182:1-17. doi: 10.1007/978-3-540-70579-6_1.
Epidemiology of adenocarcinoma of the esophagus, gastric cardia, and upper gastric third.
Vial M, Grande L, Pera M

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Epidemiology of adenocarcinoma of the esophagus, gastric cardia, and upper gastric third.
Vial M, Grande L, Pera M.

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Epidemiology and risk factors for gastroesophageal junction tumors: understanding the rising incidence of this disease.
Buas MF, Vaughan TL.Program in Epidemiology, Fred Hutchinson Cancer Research Center, Seattle, WA, USA

17. Report on Carcinogens, Thirteenth Edition; U.S. Department of Health and Human Services
Public Health Service, National Toxicology Program.2014

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20) Bove, FJ et al; Evaluation of mortality among marines and navy personnel exposed to contaminated drinking water at USMC base camp Lejeune; a retrospective cohort study. Environ health 2014, 13;10.

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Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Thursday, April 02, 2015 4:15 PM
To: (b) (6)
Subject: FW: for action - VHA/VBA - Sen Burr - lejuene clinical guidelines update and grant/denial rates
Attachments: talking points updated.docx

Does this sound ok to you?

From: (b) (6)
Sent: Thursday, April 02, 2015 4:14 PM
To: (b) (6); (b) (6); (b) (6); (b) (6)
Cc: (b) (6)
Subject: RE: for action - VHA/VBA - Sen Burr - lejuene clinical guidelines update and grant/denial rates

Is this what they want? Is this too much detailed information to give them? The process I discuss has just gotten underway.

From: (b) (6)
Sent: Thursday, April 02, 2015 3:57 PM
To: (b) (6); (b) (6); (b) (6); (b) (6)
Cc: (b) (6)
Subject: RE: for action - VHA/VBA - Sen Burr - lejuene clinical guidelines update and grant/denial rates
Importance: High

All,
10NC has come back needing the following to be **addressed in the last response** (#4) in order to clear our submission:

Issues to address:

1. Articulate initial education plan or core topics covered rather than "trainings"
2. Literature searches sound haphazard.
3. Use citations.

Please provide by 9am tomorrow morning.

Thank you,
(b) (6)

I CARE
DEPARTMENT OF VETERANS AFFAIRS

(b) (6)
Office of Disability and Medical Assessments (10NC8)

Department of Veterans Affairs
810 Vermont Ave., NW, Ofc 971
Washington, DC 20420
(b) (6)
Fax: (202) 495-5168
(b) (6)

From: (b) (6)
Sent: Thursday, April 02, 2015 12:25 PM
To: (b) (6); (b) (6); (b) (6)
Cc: (b) (6)
Subject: FW: for action - VHA/VBA - Sen Burr - lejuene clinical guidelines update and grant/denial rates

From: (b) (6)
Sent: Thursday, April 02, 2015 12:24 PM
To: (b) (6)
Cc: VHA 10NC8 Action; VHA CO 10NC Front Office HSSs
Subject: RE: for action - VHA/VBA - Sen Burr - lejuene clinical guidelines update and grant/denial rates

10NC8 submits the attached talking points.

(b) (6)
Office of Disability and Medical Assessments (10NC8)
Department of Veterans Affairs
810 Vermont Ave., NW, Ofc 971
Washington, DC 20420
(b) (6)
Fax: (202) 495-5168
(b) (6)

From: (b) (6)
Sent: Tuesday, March 31, 2015 11:40 AM
To: VHA 10NC8 Action
Cc: VHA CO 10NC Action; VHA CO 10N Front Office
Subject: FW: for action - VHA/VBA - Sen Burr - lejuene clinical guidelines update and grant/denial rates

Good Morning 10NC8,

Please submit the request below to **the VHA CO 10NC Front Office HSSs mail group** by **Noon Thursday April 2, 2015** to allow time for clearance and submission to 10B3 by their deadline. Thank you.

Best regards,

(b) (6)

827 A (Office) (b) (6)

From: (b) (6)
Sent: Tuesday, March 31, 2015 11:07 AM
To: VHA 10N Action; VHA 10NC8 Action
Subject: FW: for action - VHA/VBA - Sen Burr - lejuene clinical guidelines update and grant/denial rates

Good Morning,

Senators Burr (NC) and Nelson (FL) have requested a briefing to discuss the item noted below. Please provide SME(s), talking points and available dates/times (next week if possible) to 10B3 by 4pm Thursday, April 2. The staff prefer to accomplish this on Friday April 10th if possible..

a. Please update us on the analytical and deliberative process utilized by VHA Occupational Health Subject Matter Experts when they assess disability claims from veterans seeking a service connected rating for exposure to the known and possible human carcinogens in the base water supply while serving at Camp Lejeune between 1953-1987. We are particularly interested in the quantitative methodology within these SME assessments and how VA ensures SMEs are not approaching any claim with a predetermined or unsubstantiated bias and how VA is ensuring its SMEs are trained on the most up to date, valid science, to include CDC-ATSDR reports.

Thank you,
(b) (6)

From: (b) (6)
Sent: Thursday, March 26, 2015 9:56 AM
To: (b) (6)
Cc: (b) (6); (b) (6); (b) (6)
Subject: [EXTERNAL] RE: Follow Up Notes from Joint Briefing/Discussion with ATSDR and VA on Camp Lejeune Scientific Studies

(b) (6) Following up on some items of ongoing interest regarding Lejeune. Recently, IOM released a report on Lejeune and the 15 conditions in the law. IOM made specific recommendations for VA to review and implement as necessary. (b) (6) and I would like to get an update on the process that VA will follow to review the IOM's recommendations and if a working group has been formed at VA to conduct the review of this specific IOM report. (b) (6) and I are also interested in receiving, as part of that briefing, information on the analytical and deliberative process utilized by VHA Occupational Health Subject Matter Experts when they assess disability claims from veterans seeking a service connected rating for exposure to the known and possible human carcinogens in the base water supply while serving at Camp Lejeune between 1953-1987. We are particularly interested in the quantitative methodology within these SME assessments and how VA ensures SMEs are not approaching any claim with a predetermined or unsubstantiated bias and how VA is ensuring its SMEs are trained on the most up to date, valid science, to include CDC-ATSDR reports. Lastly, we request, as part of this briefing, an update on the most recent status of cumulative disability claim grants and

denials data out of the Louisville VARO for the Lejeune population, broken down by health condition (VA has provided this report previously in a spreadsheet format)

Given the upcoming recess, it would be ideal if we could receive the briefing on Friday, April 10 in the late morning or afternoon. Please let us know if you need anything more from us in preparation for the briefing.

(b) (6)
National Security and Veterans' Affairs
Office of Senator Richard Burr (R-NC)
217 Russell Senate Office Building
Washington, DC 20510
(b) (6)
202-228-2981 Fax
(b) (6)

From: (b) (6)
Sent: Monday, March 09, 2015 10:12 AM
To: (b) (6)
Cc: (b) (6); (b) (6); (b) (6); (b) (6); (b) (6); (b) (6); (b) (6); (b) (6)
Subject: RE: Follow Up Notes from Joint Briefing/Discussion with ATSDR and VA on Camp Lejeune Scientific Studies

Please see below for the Department's responses. All questions, except for 6, were responded to by VHA.

Question 1: VA and ATSDR will designate a point person for the interagency communications on the ATSDR studies and inputs for VA's utilization. In the opinion of Congressional Staff, this should be an SES-level person and of equivalent ranks on both sides. (b) (6) said he would be willing to fulfill that role for ATSDR. Please advise from VA's side who of an equivalent rank will be designated from VA.

Response: (b) (6) Office of Public Health is designated as the point person for interagency communications with ATSDR

Question 3: ATSDR stated that the three studies cited by VBA Occupational Health SME's (studies by Christensen, Hansen, and Zhao) were of limited utility. They recommended SMEs refer to the National Toxicology Program profile on TCE, as well as IARC and EPA literature for the most current scientific analysis of TCE and other known and probable carcinogens in the Camp Lejeune water system. EPA designated TCE a "known human carcinogen" in 2013. Could you please explain the range of info that the SME's use?

Response: VHA appreciates ATSDR's recommendations for background medical literature and looks forward to continuing this dialogue. The recommendation to refer SMEs to the summary

documents mentioned above is a good one. VHA will ensure these documents are disseminated to examiners.
In order to provide the most comprehensive evaluation of each case for Veterans, VHA often needs specific details from the medical literature. The above summary documents are enormously useful to this end but may not always provide the study detail needed for completing opinions. VHA often needs to evaluate the relevance of specific medical literature to the individual needs of Camp Lejeune Marines in order to draw conclusions about each case.
Most available studies in the medical literature by themselves as single entities are of limited use for the specific purpose of evaluating these cases. Applicability to the Camp Lejeune water contamination situation is often not perfect. For example, the majority of studies available in the medical literature for related solvents are performed in occupational rather than water-contamination settings. (The applicability of these studies depends on the specifics of each study.) Despite limitations in comparison, VHA considers these studies listed, and many others to which are referred, to be relevant to the task. It is because of individual study limitations and at times unclear study relevance that many articles are used in drawing conclusions.
Of note: The National Toxicology Program profile mentioned in the question considers the Zhao 2005 study to be of "high" utility and the Hansen 2013 study to be of "moderate" utility. The Christensen 2013 article was considered of "low/moderate utility."
With regard to the range of information that SMEs use, there is no identified limitation of information available in the medical literature. Most commonly information is obtained from: peer-reviewed journals, Meta-analyses, monographs, position statements, governmental organizations, educational institutions, and data bases such as Up-to-Date.

Question 4: Why are Occupational Health SMEs reading scientific abstracts to form the basis of their understanding for input on Lejeune disability claims? "This labor intensive approach appears to be an onerous and tedious means of staying current on the available science

Response: VHA understands this question to be asking why VHA refers to specific scientific studies in the medical literature rather than obtaining information and staying current on the science from Monographs or summaries.
As noted in the previous question, SMEs may need more data than is available in a monograph or a summary, or even a Meta-analysis. A summary document is an excellent place to start and at times may be sufficient. However, each Camp Lejeune case is different and requires a different amount of detail and research. Though it may be "onerous and tedious" at times, it is important to be aware of published scientific articles that relate to the exposures at CLCW in order to incorporate the most updated science in our opinions. Some of these may be more recently published than the summary documents. The goal is to provide the best and most scientifically-sound medical opinions.

Question 5: There was also some discussion regarding the preponderance of findings from "meta-analysis", which one VBA SME stated in a VBA denial letter in 2014 was not conclusive based on their review of "virtually every review" of cohort studies and meta-analysis over two decades established there is "no causal association between occupational exposure to TCE and cancer". Given that ATSDR emphatically stated TCE is known to cause kidney cancer, there appears to be some gap in understanding of the prevailing science on the part of at least one VBA SME, perhaps others.

Response: VHA agrees with ATSDR and recognizes that TCE is a potential human carcinogen. VHA cannot speak specifically to any case from which the above statement may have been extracted; however VHA will ensure that all SMEs are aware of this. Meta-analyses are helpful summaries that provide increased statistical power due to larger numbers of cases. There is utility in

reviewing these articles, but we recognize that reviewing such studies does not indicate that all available information has been reviewed.

Question 6: The acknowledged disparities and errors in data captured on Male and Female Breast Cancer grants and denials at the Louisville VARO was discussed. Last month, VBA told ATSDR CAP that errors had been uncovered and corrected the record. How did these errors occur and will VBA now be taking a close look at the data on all the grants and denials for other conditions to identify any other problems?

Response: (*VBA*)During the ATSDR Community Assistance Panel (CAP) quarterly meeting in January 2015, VBA gave a summary of the findings of a review of completed male and female breast cancer claims that had been requested by the CAP. These claims were identified by searching VBA's database using a unique four digit diagnostic code in VA's Schedule for Rating Disabilities. The search resulted in 117 claims filed by male Veterans and 89 by female Veterans. However, when reviewing the files, it was determined that only 47 of the male Veterans had breast cancer, and 73 of the female Veterans had breast cancer. The other claims were found to have various diagnoses such as gynecomastia, breast lumps, fibrocystic disease, etc. There were also claims denied because there was no evidence of service at Camp Lejeune, or the Veteran did not serve during the period of water contamination.

At no time was it stated that errors in the processing of these claims were discovered. No errors were discovered during this review. During the last two fiscal years, VBA's internal quality review process identified one error in FY 2013 and no errors in FY 2014 in Camp Lejeune claims that have been decided.

Question 7: Congressional Staff brought the VHA Public Health website on Camp Lejeune to (b) (6) (b) (6) attention. One segment of that site contains a narrative that seems to rely upon or emphasize the "outdated" (ATSDR's characterization) National Research Council (NRC) 2009 literature review (not a scientific study). The specific wording from the site is as follows (segments highlighted to specify outdated or inaccurate information as of 2015) –

a. Are we working on updating the website? Can we provide a timeline that it will be updated?

Response: Following the ATSDR/VA discussion, the Office of Public Health updated the referenced portion of our Public Health website http://www.publichealth.va.gov/exposures/camp-lejeune/research.asp. VHA is confident that this update addresses the concerns brought forward. In particular the commentary on the 2009 NRC study has been reduced. VHA also provided a direct link to the ATSDR website so readers can access these important ATSDR studies and also view ATSDR's commentary.

Question 8: (b) (6) stated after the meeting that changes had been made to this page based on input from the ASTDR Community Assistance Panel in January 2015. Below is a pasted copy of the same webpage before changes were made last month. It appears the earlier version contained more specific wording regarding the studies and that the version above reemphasizes the conclusion of the NRC review and quotes specifically from that review. Absent are any extracts from ATSDR's studies or any information to indicate the NRC review is "outdated" or "overcome" by the ATSDR studies since 2009.

a. Please advise

Response: Following the ATSDR/VA discussion, the Office of Public Health updated the referenced portion of our Public Health website http://www.publichealth.va.gov/exposures/camp-lejeune/research.asp. VHA is confident that this update addresses the concerns brought forward for our

attention. In particular the commentary on the 2009 NRC study has been reduced. VHA also provided a direct link to the ATSDR website so readers can access these important ATSDR studies and also view ATSDR's commentary.

From: (b) (6)
Sent: Monday, February 02, 2015 5:16 PM
To: (b) (6); (b) (6)
Cc: (b) (6); (b) (6); (b) (6); (b) (6); (b) (6); (b) (6); (b) (6); (b) (6)
Subject: [EXTERNAL] Follow Up Notes from Joint Briefing/Discussion with ATSDR and VA on Camp Lejeune Scientific Studies

(b) (6) and (b) (6)

Sending this before my memory gets sketchy on what was discussed and what constitutes the various "ways forward" for the oversight and interagency communication pieces. In order to further greater understanding and awareness of the value inherent in ATSDR's studies to date, the following issues were discussed. Please let us know how VA and ATSDR will proceed on these various inputs. For sake of follow up, a response from both agencies/departments by end of February, at the latest, is desired.

- VA and ATSDR will designate a point person for the interagency communications on the ATSDR studies and inputs for VA's utilization. In the opinion of Congressional Staff, this should be an SES-level person and of equivalent ranks on both sides. (b) (6) said he would be willing to fulfill that role for ATSDR. Please advise from VA's side who of an equivalent rank will be designated from VA.

- (b) (6) indicated he would develop a comprehensive letter, in form of agency to agency correspondence, detailing the current state of scientific play and understanding on Lejeune for VA senior leaders to ensure a uniform understanding going forward. (We would like to ask that our offices be provided a copy of that letter and also one be sent to the Senate Veterans Affairs Committee Chairman and Ranking Member.)

- ATSDR stated that the three studies cited by VBA Occupational Health SME's (studies by Christensen, Hansen, and Zhao) were of limited utility. They

recommended SMEs refer to the National Toxicology Program profile on TCE, as well as IARC and EPA literature for the most current scientific analysis of TCE and other known and probable carcinogens in the Camp Lejeune water system. EPA designated TCE a "known human carcinogen" in 2013.

- One follow on question for VBA is "Why are Occupational Health SMEs reading scientific abstracts to form the basis of their understanding for input on Lejeune disability claims?" This labor intensive approach appears to be an onerous and tedious means of staying current on the available science.

- There was also some discussion regarding the preponderance of findings from "meta-analysis", which one VBA SME stated in a VBA denial letter in 2014 was not conclusive based on their review of "virtually every review" of cohort studies and meta-analysis over two decades established there is "no causal association between occupational exposure to TCE and cancer". Given that ATSDR emphatically stated TCE is known to cause kidney cancer, there appears to be some gap in understanding of the prevailing science on the part of at least one VBA SME, perhaps others.

- The acknowledged disparities and errors in data captured on Male and Female Breast Cancer grants and denials at the Louisville VARO was discussed. Last month, VBA told ATSDR CAP that errors had been uncovered and corrected the record. How did these errors occur and will VBA now be taking a close look at the data on all the grants and denials for other conditions to identify any other problems?

- Congressional Staff brought the VHA Public Health website on Camp Lejeune to Dr. Erickson's attention. One segment of that site contains a narrative that seems to rely upon or emphasize the "outdated" (ATSDR's characterization) National Research Council (NRC) 2009 literature review (not a scientific study). The specific wording from the site is as follows (segments highlighted to specify outdated or inaccurate information as of 2015) –

"Camp Lejeune Research Studies

Drinking-water systems that supplied two areas of housing at Camp Lejeune were contaminated with industrial chemicals from at least 1953 to 1985. The contaminated wells were shut down in February 1985. The duration and intensity of the exposure at Camp Lejeune are unknown. The geographic extent of contamination by specific chemicals also is unknown. Health effects from toxic water exposure Studies currently being conducted by The Agency for Toxic Substances and Disease Registry (ATSDR) may, in the future, provide scientific information to help evaluate possible service-connection for health effects or to make policy changes. A study on birth defects and childhood cancers released by the ATSDR in Dec. 2013 shows some evidence of an increased risk of neural tube defects, oral clefts, and childhood hematopoietic cancers (such as leukemia) in children whose mothers were exposed to contaminated Camp Lejeune water. The small number of cases in the study did not allow any firm conclusions to be drawn as to whether this small increased risk was caused by exposure to chemicals or occurred by chance. Scientific studies show some evidence of an increased risk of kidney cancer in workers exposed to high levels of TCE over many years. High-level benzene exposure is associated with an increased risk of leukemia. According to the National Research Council 2009 report, Contaminated Water Supplies at Camp Lejeune: "It cannot be determined reliably whether diseases and disorders experienced by former residents and workers at Camp Lejeune are associated with their exposure to contaminants in the water supply because of data shortcomings and methodological limitations, and these limitations cannot be overcome with additional study." - See more at:
http://www.publichealth.va.gov/exposures/camp-lejeune/research.asp#sthash.4e33Rb86.dpuf "

- (b) (6) stated after the meeting that changes had been made to this page based on input from the ASTDR Community Assistance Panel in January 2015. Below is a pasted copy of the same webpage before changes were made last month. It appears the earlier version contained more specific wording regarding the studies and that the version above reemphasizes the conclusion of the NRC review and quotes specifically from that review. Absent are any extracts from ATSDR's studies or any information to indicate the NRC review is "outdated" or "overcome" by the ATSDR studies since 2009.

Camp Lejeune Research Studies D
housing at Camp Lejeune were co
to 1985. The contaminated wells w
primarily were: Perchloroethylene
Trichloroethylene (TCE) (76 KB,
a fuel component Vinyl chloride (
broken down The duration and int
The geographic extent of contamir

Health effects from toxic water ex
Agency for Toxic Substances and
scientific information to help eval
make policy changes.

A study on birth defects and child
shows some evidence of an increa

1) Please update us on the analytical and deliberative process utilized by VHA Occupational Health Subject Matter Experts when they assess disability claims from veterans seeking a service connected rating for exposure to the known and possible human carcinogens in the base water supply while serving at Camp Lejeune between 1953-1987.

The SME panel estimates solvent exposure in the most favorable manner for the Veterans requesting evaluation for claims secondary to Camp Lejeune Contaminated Water (CLCW) exposure. The exposure evaluation takes into account, ingested and inhaled exposure as well as dermal exposure as appropriate. The exposure history is evaluated in light of current medical literature including the Agency for Toxic Substances and Disease Registry (ATSDR) data.

There are no industrial hygiene data available on daily water supply to scientifically analyze the level and duration of exposure.

Therefore, the SMEs are instructed to review the Veteran's duration of stay as well as their military occupation while they were stationed at Camp Lejeune.

2) We are particularly interested in the quantitative methodology within these SME assessments.

The SMEs review the available exposure levels from Camp Lejeune. They review research that has exposure data; quantitative or qualitative. This is most often occupational exposure data. The SMEs compare, to the degree possible, exposures in the studies with estimated exposure levels at Camp Lejeune. They also compare length of stay at Camp Lejeune (CL) with years of exposure in the studies.

Similarly, we can estimate benzene exposure from cigarette smoking and compare that with estimated benzene exposure from CLCW.

The SMEs can also calculate estimated exposure at CL based on several Veteran-specific factors and compare that exposure to the EPA RfD (oral reference dose) or other standard toxicology measures. They can subsequently estimate whether the exposure at CL rises to the level of that thought to cause a specific endpoint or ill health effect in general.

The SMEs compare odds ratios between risk of a given health effect from CLCW contaminants and risk of the health effect from a Veteran's known risk factors. They look at this in conjunction with a Veteran's specific information including length of time of exposure.

3) How does the VA ensure SMEs are not approaching any claim with a predetermined or unsubstantiated bias?

All the selected SMEs are highly experienced professionals who have been directly or indirectly involved with care and/or assessment of our Veterans at VA Medical Centers. Cases are assigned to SMEs located

throughout the country. They are not sent based on jurisdiction. All SME's conduct a thorough case review and provide unbiased opinions.

The SMEs do not have predetermined opinions or decisions on these cases. All SMEs go through the laborious task of literature review and case research for each claim. There would be no reason for this extra work if there were a predetermined or other bias.

4) **How is VA is ensuring its SMEs are trained on the most up to date, valid science, to include CDC-ATSDR reports?**

Formatted: Font: Bold

The SMEs have initial in-person trainings as new SMEs where they discuss the body of quality literature to date. The topics covered at our most recent training were: History of Camp Lejeune, Forensic Medicine Overview, Toxicological Consequences of the Major Contaminants, Health Care Law, Decoding the Service Record.

~~Monthly SME conference calls are held where they discuss new scientific studies and reports. Conference call minutes are sent out for those who were unable to attend the call.~~Comprehensive literature reviews and interpretation of such are being developed for the most common disease end points. These reviews will have references cited for use in SME reviews. These will be available to all SMEs.~~Conference call minutes are sent out for those who were unable to attend the call.~~The plan is to ensure that a literature review/update is performed every 6 months for each condition. When new pertinent research is found in the interim,~~-~~ this will be discussed on our monthly SME conference calls. Conference call minutes are sent out for those who were unable to attend the call ~~Group emails are sent to examiners when new scientific information is discovered. A few of the more experienced SMEs look for literature updates on a regular basis in order to keep the group current.~~. The SME leaders and Physician Assistant Reviewer routinely review the literature for updates. All SMEs are encouraged to do so as well.

All SMEs are aware of the Centers for Disease Control and Prevention-ATSDR reports. The Bove study is being mentioned in the SME reports to ensure that it is reviewed by each SME. They have also read the Institute on Medicine report, and at this time there is no plan to change the current SME practice.

Parrillo, Jeffrey M. (VACO)

From: [redacted]
Sent: Wednesday, October 14, 2015 9:52 AM
To: [redacted]
Subject: FW: Suspense: COB Thursday 15 October Report to SecVA on Camp Lejeune ATSDR Report and possible presumptions
Attachments: Camp Lejeune VA Task Force Report 10-13-15 Draft.docx; ATSDR summary of the evidence for Presumption_draft for VA 9.21.15.docx

Importance: High

Categories: Orange Category

Not sure if you got this. What do you think?

From: [redacted]
Sent: Wednesday, October 14, 2015 9:08 AM
To: [redacted]
VBAVACO
Cc: [redacted]
Subject: Suspense: COB Thursday 15 October Report to SecVA on Camp Lejeune ATSDR Report and possible presumptions
Importance: High

[redacted] and Team:

Thank you for your patience. Please find attached the draft document for your critical review. I have also attached the ATSDR document for your reference. I will need your edits by COB on Thursday, 15 October as we have a very tight turn on this for SecVA.

Unless you think it is REALLY NECESSARY, please DO NOT REPLY ALL, but just send me your edits.

In writing this document I unilaterally added to the membership of the Technical Work Group the following individuals as I feel that we will benefit from their participation:

[redacted]

[redacted] We will need a Commo Plan to accompany this effort.

[redacted] Thanks for already developing the timeline for rules/regulations.

Normally this document would be staffed through the IOM Task Force (USH, USB, etc...) and would be signed by [redacted] (OPP) prior to being sent to SecVA. We'll need to discuss if we need that step given our short timeline.

We will also need guidance about whether or not using VAIQ is necessary for formal staffing.

Once this document is nearly finalized, I will work with you all to prepare the necessary ppt slides.

I'm hoping that OPP will help me with the decision memo that will go to SecVA.

All the best,
(b) (6)

(b) (6)
Office of Public Health
810 Vermont Ave NW (10P3)
Washington, DC 20420
(b) (6)
Fax (202) 495-5973
(b) (6)
"Le Grand Schtroumpf"
Integrity-Commitment-Advocacy-Respect-Excellence

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, April 06, 2015 8:36 AM
To: (b) (6)
Subject: FW: thyroid

From: (b) (6)
Sent: Saturday, April 04, 2015 2:14 PM
To: (b) (6)
Subject: FW: thyroid

Forwarded;

From: (b) (6)
Sent: Tuesday, March 24, 2015 8:27 AM
To: (b) (6)
Subject: RE: thyroid

Hi (b) (6)

I am experimenting with a new style for my discussion, hitting all the CLCW specific exposures first (including USDHHS data), then environmental studies (including Bove, even when it doesn't address the situation), then occ studies, then non-CLCW risk factors.

Let me know what you think.

%%%%%%%%%%%%%%%%%%%%%%%%%

Thyroid cancer discussion

PCE: The USDHHS 13th report on carcinogens has ascertained PCE to be "reasonably anticipated to be a human carcinogen" based on sufficient evidence from animal studies. Animal studies have found evidence of renal tubule tumors in exposed rats. However, in human epidemiological studies thyroid cancer has not been definitively linked to low dose PCE exposure in this or other documents to my knowledge. I am not aware of any human studies definitively linking PCE exposure to thyroid cancer at the low levels found in CL.

TCE: The USDHHS 13th report on carcinogens has ascertained TCE to be 'reasonably anticipated to be a human carcinogen" based on sufficient evidence from animal studies and also from evidence in human studies. The IARC has determined TCE to be a group 1 carcinogen stating there is sufficient evidence linking exposure with renal cancer. However, evidence with regard to thyroid cancer is

not addressed in most statements; However, I am not aware of any studies definitively linking low dose TCE exposure to thyroid cancer at the low levels measured at CL.

Vinyl chloride and benzene: these are both known carcinogens according to the USDHHS report , but not known to cause thyroid cancer. Low-dose or community Vinyl chloride and benzene exposure have not been linked to thyroid cancer to my knowledge. I am not aware of any studies definitively linking low dose benzene or vinyl chloride exposure to thyroid cancer at the low levels found in CL. Benzene exposure is also found in cigarette smoke. However, some occupational studies suggest that 10 years or more of occupational high level exposure to benzene may increase the risk for thyroid cancer. See occupational studies below.

Community/drinking water studies: There are no known community or drinking-water studies which have definitively implicated exposure to CLCW solvents and thyroid cancer to my knowledge. The Bove et al study evaluated CL civilians with an average employment on base of 2.5 years (23). Thyroid cancer was not specifically studied. They did study "all cancers" They found nonstatistically elevated rates of all cancer in exposed CL cohorts compared to a Camp Pendleton cohort (Hazard ratio was 1.10 and the 95% confidence interval was 092-1.36). A Bove et al study of CL marines with an average exposure of 18 months (18) did not study thyroid cancer but found a nonstatistically significant increase in "soft tissue cancer" (hazard ratio 1.23 with 95% CI of 0.60-2.64). Since thyroid cancer was not evaluated, no conclusions can be drawn whether this evidence supports an association between thyroid cancer and residence at CL..

Occupational data:
Thyroid cancer was found to be elevated in studies of female Swedish shoe and leather industry employees (7), electromagnetic field exposures (8), individuals with certain genetic mutations (6), radiation exposed workers and healthcare operations (9). The Aschebrook-Kilfoy metaanalysis of 30 occupational studies found inconsistent evidence regarding pesticide exposure but otherwise no associations for most professions (9). Wong et al (12) found elevated risk of thyroid cancer in Chinese workers with 10 or more years of exposure to benzene (HR 6.43 CI 1.08-38) and an elevated rate in workers exposed to "organic or inorganic gases (HR=8.35 CI 1.14-51) and formaldehyde (8.33 CI=1.16-60), but these findings are preliminary. The author cited few other studies to support this association and need for more studies to corroborate these findings was recommended.

Leux (4) has summarized the literature regarding risk factors for the role of environmental chemicals causing thyroid tumors as " Epidemiological results provide insufficient evidence of a causal link between exposure to environmental chemicals and thyroid tumors, but raise the hypothesis of an increased risk of thyroid neoplasm for workers in the leather, wood, and paper industries, and those exposed to certain solvents and pesticides."

Non-CLCW risk factor analysis:
In contrast to the lack of information linking low dose CLCW exposures to thyroid cancer, studies and a large meta-anlysis finds that obesity is associated with a significantly increased risk of thyroid cancer (adjusted RR=1.33; 95% CI, 1.24-1.42; I2=25% (10).

Risk Factors: the proportion of thyroid cancer accounted for by genetic factors was 53% which is higher than for any other form of malignancy [2]
-Age between 25 and 65 years old.
-female (3:1 female vs. male)
- exposure to radiation to the head and neck as a child or being exposed to radiation from an atomic bomb. The cancer may occur as soon as 5 years after exposure.

-Dental xrays (Memon 2010) exposure to dental x-rays was significantly associated with an increased risk of thyroid cancer (odds ratio = 2.1, 95% confidence interval: 1.4, 3.1) (p=0.001) with a dose-response pattern (p for trend <0.0001)
-history of goiter (enlarged thyroid).
-a family history of thyroid disease or thyroid cancer.
- certain genetic conditions such as familial medullary thyroid cancer (FMTC), multiple endocrine neoplasia type 2A syndrome, and multiple endocrine neoplasia type 2B syndrome.

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Summary; Review of CLCW specific chemical exposure data, occupational data, community study data and information from animal studies have not found a definitive association between low dose or community exposure to CLCW solvents at the number of days this veteran was exposed and thyroid cancer. In contrast, he has a well defined non-CLCW risk factor in his elevated body mass index.

&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&&

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Supporting Evidence of Carcinogenic Hazard
Ivan Rusyn1, Weihsueh A. Chiu2, Lawrence H. Lash3, Hans Kromhout4, Johnni Hansen5,
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25. TCE: Mechanistic, Epidemiologic and Other
Supporting Evidence of Carcinogenic Hazard
Ivan Rusyn1, Weihsueh A. Chiu2, Lawrence H. Lash3, Hans Kromhout4, Johnni Hansen5,
and Kathryn Z. Guyton. Pharmacol Ther. 2014 January ; 141(1): .
doi:10.1016/j.pharmthera.2013.08.004.

From: (b) (6)
Sent: Monday, March 23, 2015 12:16 PM
To: (b) (6)
Cc: (b) (6)
Subject: RE: thyroid

Don't forget to send. Thanks!

From: (b) (6)
Sent: Friday, March 20, 2015 11:25 AM
To: (b) (6)
Subject: RE: thyroid

This seems very brief and starts with papillary thyroid ca which is only 1 type.

I just did a thyroid cancer case and did some research on this. Can I send it to you?

(b) (6)

From: (b) (6)
Sent: Thursday, March 19, 2015 9:40 AM
To: (b) (6)
Subject: FW: thyroid

(b) (6) can you look at this too?

From: (b) (6)
Sent: Thursday, March 19, 2015 11:43 AM
To: (b) (6)
Cc: (b) (6)
Subject: thyroid

Here are my comments so far. You have the Bove article listed, but I don't see where they addressed thyroid cancer in that study.

(b) (6)

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, April 20, 2015 8:59 AM
To: (b) (6); (b) (6)
Subject: prostate
Attachments: CLCW-ProstateCa-2015v1.docx

Ready to post! References fixed. I changed language to remove additional references that are UNWANTED, not UNUSED.

We can send out an email that prostate and thyroid are done and on the server. Working on lung and multiple myeloma presently.

(b) (6)

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: 90 Minutes
****
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:

****
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 veterans 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
****

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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Literature review

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Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, May 18, 2015 10:04 AM
To: (b) (6)
Cc: (b) (6)
Subject: RE: CL

Will you send out a reminder w/the agenda? Is (b) (6) participating?

From: (b) (6)
Sent: Monday, May 18, 2015 10:01 AM
To: (b) (6)
Cc: (b) (6)
Subject: RE: CL

(b) (6) please speak to the topic, I don't know if I will even be on the call.

Agenda:

1. TCE and kidney cancer
2. CAP meeting
3. Writing in layman's terms
4. Clinical templates
5. NRC Report

From: (b) (6)
Sent: Monday, May 18, 2015 10:00 AM
To: (b) (6)
Cc: (b) (6)
Subject: RE: CL

Sounds good. (b) (6) can you talk on writing on Layman's terms?

Add to the agenda the sharepoint templates.

And the NRC report

From: (b) (6)
Sent: Monday, May 18, 2015 9:53 AM
To: (b) (6)
Cc: (b) (6)
Subject: RE: CL

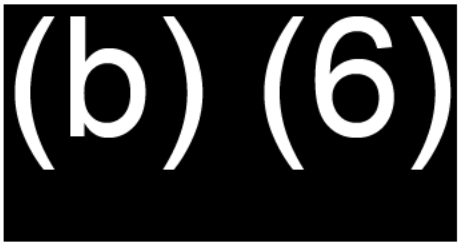
Tomorrow.
Possible agenda topics:

1. TCE and kidney cancer
2. CAP meeting
3. Writing in layman's terms

From: (b) (6)
Sent: Monday, May 18, 2015 9:43 AM

To: (b) (6)
Subject: CL

Hi, (b) (6) I hope you had a good weekend. When is out next CL conf call?



Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Tuesday, July 28, 2015 11:18 AM
To: (b) (6); (b) (6)
Subject: RE: CLCW: Bladder Cancer

It looks good.

From: (b) (6)
Sent: Tuesday, July 28, 2015 11:16 AM
To: (b) (6); (b) (6)
Subject: RE: CLCW: Bladder Cancer

You had asked me to send to (b) (6) for comments; I have made the changes suggested and noted in my last email to you to please review the final version....

From: (b) (6)
Sent: Tuesday, July 28, 2015 10:15 AM
To: (b) (6)
Cc: (b) (6)
Subject: RE: CLCW: Bladder Cancer

I haven't but if there are no changes I am good with it. I reviewed it carefully last go around.

From: (b) (6)
Sent: Tuesday, July 28, 2015 11:15 AM
To: (b) (6)
Cc: (b) (6)
Subject: CLCW: Bladder Cancer

(b) (6),

Have you had time to review the bladder cancer template? Can (b) (6) post? Please advise.

(b) (6)
Office of Disability & Medical Assessment
Department of Veterans Affairs
810 Vermont Ave. NW
Washington, DC 20420
(b) (6)

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Tuesday, March 17, 2015 3:37 PM
To: (b) (6) (b) (6) VHA CO CLCW SME
Cc: (b) (6) (b) (6) (b) (6) (b) (6) ; (b) (6) P SAMVAMC
Subject: RE: CLCW: CLCW IOM Report released today;

I agree. We need to keep the health law and disability separate from each other and using this document would blur the lines, in my opinion.

From: (b) (6)
Sent: Tuesday, March 17, 2015 2:27 PM
To: (b) (6) VHA CO CLCW SME
Cc: (b) (6) ; (b) (6) ; (b) (6) ; (b) (6) ; (b) (6)
Subject: RE: CLCW: CLCW IOM Report released today;

Please be aware this document was written in support of the Health Care Law.

It is still very valuable information but the burden of proof for disability is very different than the health care law. I would discourage anyone from using this document to support a nexus.

From: (b) (6)
Sent: Wednesday, March 11, 2015 10:50 AM
To: VHA CO CLCW SME
Cc: (b) (6) ; (b) (6) ; (b) (6) ; (b) (6) ; (b) (6)
Subject: CLCW: CLCW IOM Report released today;

Per (b) (6) : Please see the newly released report from IOM entitled Review of VA Clinical Guidance for Health Conditions Identified by the Camp Lejeune Legislation.

http://books.nap.edu/openbook.php?record_id=18991

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, June 29, 2015 10:49 AM
To: (b) (6) ; (b) (6)
Cc: (b) (6)
Subject: RE: CLCW: Request

We should just send our prior answer. We've answered this for the senators already.

From: (b) (6)
Sent: Monday, June 29, 2015 10:47 AM
To: (b) (6) ; (b) (6)
Cc: (b) (6)
Subject: CLCW: Request

Good Morning,

DMA has a meeting tomorrow to discuss the receipt of the letter from congress on CLCW. Please see the attached doc and provide me with a paragraph to address the ask by tomorrow at noon. I also attached the original letter from congress.

(b) (6)
Office of Disability & Medical Assessment
Department of Veterans Affairs
810 Vermont Ave. NW
Washington, DC 20420
(b) (6)

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, May 18, 2015 3:50 PM
To: (b) (6)
Subject: RE: Lung Ca template DRAFT
Attachments: CLCW-Lung Ca DRAFT7 (4).docx

From: (b) (6)
Sent: Monday, May 18, 2015 3:43 PM
To: (b) (6)
Subject: RE: Lung Ca template DRAFT

Back at ya....

From: (b) (6)
Sent: Monday, May 18, 2015 2:00 PM
To: (b) (6)
Cc: (b) (6)
Subject: RE: Lung Ca template DRAFT

A few more comments. See what you think.

From: (b) (6)
Sent: Monday, May 18, 2015 12:39 PM
To: (b) (6)
Cc: (b) (6)
Subject: Lung Ca template DRAFT
Importance: High

Good morning,

I never did receive any feedback from (b) (6) which he had indicated he would submit last Tuesday, even after several additional prompts. However, I did include in this draft the article he indicated as being relevant (citation 23). Please provide a final review, and if satisfied I can remove the watermark and submit to (b) (6) for posting on the SP site. I will try to work some on the renal and bladder Ca drafts this week if time allows.

(b) (6)

Name:
SSN:
Date:
Date of Birth:
Sex: male
Dates of military service: DD214
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
****
Contention, the veteran claims the following condition as secondary to exposure to CLCW:

Contention 1: Lung Cancer

Diagnosis:

Nexus: The diagnosis above Choose an item.

Case Specific Discussion:

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

VBMS/Claims file review:

VVA/VistaWeb/CARPI review:

Other possible veteran risk factors:
Employment history prior to military service:
Smoking:

Alcohol use:
Obesity: BMI—
Genetic:
Employment history after military service:
Hobbies/recreational leading to possible chemical exposure: UNK

Disease Specific Discussion, Lung Cancer:

Disease Description: The National Cancer Institute defines lung cancer as: cancer that forms in tissues of the lung, usually in the cells that are lining air passages. The two main types are small cell lung cancer and non-small cell lung cancer. These types are diagnosed based on how the cells look under a microscope.

Incidence: Lung cancer is the most common cancer worldwide. Lung cancer (both small cell and non-small cell) is the second most common cancer in both men and women (not counting skin cancer). Lung cancer accounts for about 13% of all new cancers. Overall, lung cancer is more common in men than women [1]. Lung cancer accounts for about 27% of all cancer deaths in the US, each year, and more people die of lung cancer than of colon, breast, and prostate cancers combined. Approximately 10-15% of all lung cancers arise in individuals that have never smoked, thus resulting in one of the leading causes of cancer-related mortality [2].

Comment [HD1]: Is this in the US? I don't know...this is your article. LOL.

Estimated new cases and deaths from lung cancer (non-small cell and small cell combined) in the United States in 2015:

- New cases: 221,200
- Deaths: 158,040

Risk Factors: Lung cancer has several known risk factors with the most important being smoking, second hand smoke, radon exposure, asbestos exposure (home and work), personal history of radiation treatment (chest or breast), and genetic factors (positive family history) [3]. Additional risk factors with consistent evidence of increased lung cancer risk include: older age, acquired lung diseases (COPD -2.8 times increased risk 95% CI, 1.8-4.4), TB, pneumoconiosis, idiopathic pulmonary fibrosis (7 times increased risk) and systemic sclerosis [1]. HIV infection increases lung cancer risk independent of smoking by at least 2.5 fold.

IARC has classified numerous occupational exposures as carcinogens for the lung: aluminum production, arsenic, asbestos, beryllium, bis(chloromethyl)ether, chloromethylmethyl ether, cadmium, chromium(VI), coal, coal-tar pitch, coke production, diesel engine exhaust, hematite mining, iron and steel founding, nickel , painting, plutonium, radon-222 and its decay products, rubber production industry, crystalline silica dust, soot, sulfur mustard, secondhand tobacco smoke, X-radiation, and gamma-radiation. There is limited evidence for strong inorganic acid mists, manufacture of glass, exposure to oxidized and hard bitumens, carbon electrode manufacture, alpha-chlorinated toluenes and benzoyl chloride, cobalt metal with tungsten carbide, creosotes, occupational exposures in spraying and application of insecticides, printing processes, 2,3,7,8-tetrachlorodibenzopara-dioxin, welding fumes, or living where there is air pollution [4].

The CDC reports that tobacco smoke contains a mix of more than 7,000 chemicals. Hundreds are toxic and approximately 70 are carcinogenic. The most important, based on their carcinogenic potency and

established levels in cigarette smoke, were polycyclic aromatic hydrocarbons, N-nitrosamines, aromatic amines, 1,3-butadiene, benzene, and various aldehydes [5]. The ATSDR Tox Guide for Benzene states: "About 50% of the entire nationwide exposure to benzene results from smoking tobacco or from exposure to tobacco smoke." The ATSDR Public Health Statement reports: "The average smoker (32 cigarettes per day) takes in about 1.8 milligrams (mg) of benzene per day. This amount is about 10 times the average daily intake of benzene by nonsmokers."

The American Cancer Society states that at least 80% of lung cancer deaths are thought to result from smoking, and this number is probably even higher for small cell lung cancer. The risk of lung cancer in smokers relative to non-smokers is in the order of over 20 fold [6]. The greater the length and quantity of smoking, the greater the cancer risk. Former smokers continue to have an elevated risk for lung cancer years after quitting. There is not a decrease in risk until 5 years of smoking cessation. During the first 5 years following stopping smoking, the risk of former cigarette smokers was high (RR = 16.1), but as cessation continued, it declined steeply. In a cohort of Veterans followed from 1954-1980, the relative risk (RR) for lung cancer for former cigarette smokers was 3.6. However, after 40 years of smoking cessation, the risk of lung cancer among former smokers has decreased, but remains elevated compared with never smokers [1]. The cumulative lung cancer risk among heavy smokers may be as high as 30 percent, compared with a lifetime risk of lung cancer of 1 percent or less in never smokers.

Second hand smoke can increase the risk for developing lung cancer [7]. A 2014 pooled analysis of 18 case-control studies found that among never smokers, the odds ratios (OR) comparing those ever exposed to secondhand smoke with those never exposed was 1.31 (95% CI: 1.17-1.45) for all cell types combined, 1.26 (95% CI: 1.10-1.44) for adenocarcinoma, 1.41(95% CI: 0.99-1.99) for squamous cell carcinoma, 1.48 (95% CI: 0.89-2.45) for large cell lung cancer, and 3.09 (95% CI: 1.62-5.89) for small cell lung cancer [8]. The estimated excess risk of lung cancer for never smokers married to smokers has been reported as 23-27% [2]. A more recent study reported that passive smoking during childhood increased lung cancer risk in adulthood by 3.6 fold [9].

Smoking cigars or a pipe is also associated with an increased risk of lung cancer. In a cohort study that followed pipe-only and cigar-only smokers, findings confirmed a carcinogenic effect to the lungs for both. The hazard ratio for incident cases was 3.9 for cigar smokers and 13.3 for pipe smokers [10]. The risk of lung cancer correlated with the intensity and duration of smoking. Other studies have shown similar results.

Marijuana smoke contains tar and many of same cancer-causing substances that are in tobacco smoke. Marijuana cigarettes are typically smoked all the way to the end, where tar content is the highest, are non-filtered, and inhaled very deeply [11]. The smoke is traditionally held in the lungs for a longer time than with cigarettes, which gives any cancer causing substances more opportunity to deposit in the lung. Nitrous oxides, hydrogen cyanide, and aromatic amines were present in marijuana smoke at levels 3-5 times higher than in mainstream tobacco smoke, while ammonia was present at levels 20 times higher than tobacco [12].

Radon is an inert gas that is produced naturally from radium in the decay series of uranium. Two of the decay products of radon emit particles that by virtue of their high energy and mass can cause damage to the DNA of cells of the respiratory epithelium. Radon enters buildings in the form of a gas derived from the soil. There is significant evidence that exposure to radon in indoor air is associated with an increased risk for lung cancer [1].

Genetic factors can affect both the risk for and prognosis of lung cancer. Individuals with a first-degree relative with lung cancer had a 2-3-fold increase in the risk of developing lung cancer, after adjustment for smoking and other potential confounders [13]. There is a similar magnitude of effect of family history on lung cancer risk in nonsmokers, suggesting familial risk for lung cancer is independent of those risks associated with cigarette smoking" [14].

Scientific Review:
NCR 2009 report: This reported concluded that there was limited/suggestive evidence of an association between exposures to CLCW and lung cancer. Limited and suggestive evidence of an association is defined as "evidence from available studies suggests an association between exposure to a specific agent and specific health outcome in human studies, but the body of evidence is limited by the inability to rule out chance and bias, including confounding, with confidence." Therefore, this level of proof does not rise to the level of at least as likely as not.

Comment [HD2]: I'm not sure there is value in using this report in this case. We are not citing studies from it and the conclusion is irrelevant now since there is new info since then. BUT IT IS A REFERANCE POINT FOR IOM REVIEWED STUDIES PRIOR TO 2008...WE ONLY WANT TPD LOOK AT LITERATURE MORE RECENT, SO IT'S A BENCHMARK. But do we need to use the limited/suggestive language? That's what they are opposed to since then the research has found different things for, for example, kidney cancer and TCE. If you want to leave it in like this it's fine. Just wondering.

In the body of this report there is no reported association between vinyl chloride and benzene and lung cancer. A recent cohort mortality study showed that there was no increased risk of lung cancer in workers exposed to vinyl chloride [15]. There is a paucity of literature on benzene and lung cancer. Benzene is a component of smoking and air pollution and thus it is difficult to isolate benzene exposure.

Environmental Exposure Literature Review: Extensive research of the scientific literature, found only limited data regarding environmental exposures to PERC and TCE. The study regarding health effects of the contaminated drinking water in Massachusetts evaluated cancer effects and found no elevated risk of lung cancer [16]. 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) [17]. Significantly fewer cases were observed than expected for cancer of the lung and bronchus (SIR, 0.71; 99% CI, 0.61 to 0.81). 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.

A Bove et al. study evaluated CL civilians with an average employment on base of 2.5 years [18]. They found non-statistically significant elevated rates of lung cancer in the exposed CL cohort compared to a Camp Pendleton cohort (Hazard ratio was 1.25 and the 95% confidence interval was 0.89-1.75). Another Bove et al. study of CL marines with an average exposure of 18 months found a slight and non-statistically significant increase in lung cancer (hazard ratio 1.16 with 95% CI of 0.96-1.40) [19]. The interpretations were not definitive as there were a low number of lung cancer deaths, the confidence intervals were wide and thus there remained a significant possibility that these findings could be due to chance alone. In addition, lung cancer risk factors such as asbestos exposure, family history, smoking and passive smoking were not available in these studies and no definitive dose-response relationships were identified for lung cancer. Therefore no definitive diagnostic conclusions can be drawn from this data.

Occupational Exposure Review: Two case-control studies of occupation and lung cancer were conducted in Montreal, and included 2016 cases and 2001 population controls [20]. When the two studies were pooled, there were indications of an increased risk of lung cancer associated with occupational exposure to perchloroethylene (OR (any exposure) 2.5, 95% CI 1.2 to 5.6; OR (substantial exposure) 2.4, 95% CI 0.8 to 7.7) and to carbon tetrachloride (OR (any exposure) 1.2, 95% CI 0.8 to 2.1; OR (substantial exposure) 2.5, 95% CI 1.1 to 5.7). No other chlorinated solvents showed both

statistically significant associations and dose-response relationships. ORs appeared to be higher among non-smokers. TCE results were ambiguous. There was a non-significant indication of excess risk among those exposed at any level, especially for adenocarcinomas, but there was no evidence of excess risk among those with relatively high or long exposure. There were suggestive, albeit inconsistent, indications that occupational exposure to perchloroethylene and carbon tetrachloride may increase the risk of lung cancer. The evidence remains inconclusive on the role of these agents on lung cancer risk.

A cohort of over 6800 workers was studied over a 50 year period at the Paducah Gaseous Diffusion Plant (PGDP) in Kentucky. Trichloroethylene (TCE) used in cleaning process equipment was a concern. Analysis of the data found a low SMR (0.75, 95% CI: 0.72-0.79) for trachea, bronchus, and lung cancer. Lung cancer results reflected regional mortality patterns [21].

A Swedish study sought to determine carcinogenic risks associated with occupational exposure to perchloroethylene (PERC). A national cohort of dry-cleaning and laundry workers comprised of over 10,000 members identified in 1984 were monitored for new cancer diagnoses for 21 years. Over 90% follow-up was completed for the cohort. The authors concluded that "no clear associated between PERC exposure and subsequent cancer morbidity in workers was evident from this historical prospective cohort" [22].

A recent 2014 analysis conducted using data from one of the largest population-based, case–control studies investigating occupational risk factors in respiratory cancer, the ICARE study, did not suggest any association between TCE and lung cancer [23]. Results suggest that exposure to PCE may constitute a risk factor for lung cancer, especially among females, who seemed to have a higher prevalence of exposure than males. The authors preferred to focus on the consistency of the results rather than their statistical significance. These results suggest that the exposure to PCE may be a risk factor for lung cancer; however the results are not statistically significant and further investigations are necessary to replicate these results in a larger exposed population.

Summary:
Exposure to cigarette smoke is by far the greatest risk factor for the development of lung cancer. Several environmental studies have documented no increase lung cancer risk from environmental exposure to the solvents found in CLCW. Literature also suggests that there is no conclusive evidence for an association between lung cancer and occupational exposure to solvents. Occupational exposure is typically more extensive than environmental exposure, suggesting no increased risk for lung cancer from exposure to the solvents found in CLCW.

Literature review:

1. Alberg AJ1, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013 May;143(5 Suppl)
2. Samet, J., Avila-Tang, E., Boffetta, P., Hannan, L., Olivo-Marston, S., Thun, M., & Rudin, C. (n.d.). Lung Cancer In Never Smokers: Clinical Epidemiology And Environmental Risk Factors. Clinical Cancer Research. 2009 Sept 15; 15(18):5626-5645.
3. What Are the Risk Factors for Lung Cancer? (2014, May 6). Retrieved April 24, 2015, from http://www.cdc.gov/cancer/lung/basic_info/risk_factors.htm
4. (n.d.). Retrieved April 24, 2015, from http://www.atsdr.cdc.gov/toxprofiles/tp19.pdf
5. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. 2004. Tobacco Smoke and Involuntary Smoking. IARC Monogr. 83. Lyon, Fr.: IARC
6. Boffetta, P., & Boccia, S. (n.d.). A Quick Guide to Cancer Epidemiology, Spring 2014.

Comment [HD3]: What is n.d. and what is this reference? If we delete it will mess up our citations THIS IS THE WAY THE CITATION NOTATION LINK SPIT IT OUT FOR APA FORMAT FOR A WEBSITE; THE ASTRIX BELOW FOR IARC WAS THE CITATION FINDER COUL D NOT LOCATE THIS OR ANY OTHER REFEREANCES ASTRIXED

Comment [HD4]: What is this? A book? No year or edition. TEXTBOOK-SPRINGER 2014

7. Richard Taylor, Farid Najafi, and Annette Dobson. Meta-analysis of studies of passive smoking and lung cancer: effects of study type and continent Int. J. Epidemiol. (2007) 36 (5): 1048-1059
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11. WU, T., Tashkin, D. P., Djahed, B., & Rose, J. E. Pulmonary Hazards of Smoking Marijuana as Compared with Tobacco. New England Journal of Medicine. 1988 Feb 11;318(6):347-51
12. Moir, D., Rickert, W. S., Levasseur, G., Larose, Y., Maertens, R., White, P., & Desjardins, S. (2008). A Comparison of Mainstream and Sidestream Marijuana and Tobacco Cigarette Smoke Produced under Two Machine Smoking Conditions. Chemical Research in Toxicology. 2008 Feb; 21(2):494-502.
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14. Cote, Michele. Increased risk of lung cancer in individuals with a family history of the disease: A pooled analysis from the International Lung Cancer Consortium. European Journal of Cancer. 2012: 48(13), 1957-1968
15. Carreón T1, Hein MJ, Hanley KW, Viet SM, Ruder AM. (2104). Coronary artery disease and cancer mortality in a cohort of workers exposed to vinyl chloride, carbon disulfide, rotating shift work, and o-toluidine at a chemical manufacturing plant. Am J Ind Med. 2014 Apr;57(4):398-411
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22. Seldén, A. I., & Jr, G. A. Cancer morbidity in Swedish dry-cleaners and laundry workers: historically prospective cohort study. International Archives of Occupational and Environmental Health. 2011 Apr;84(4):435-43
23. Francesca Mattei et al. Exposure to chlorinated solvents and lung cancer: results of the ICARE study. Occup Environ Med 2014 71: 681-689, July 11, 2014

ADDITIONAL REFERENCES (FOR USE ON CASE SPECIFIC BASIS-REMOVE UNWANTED PRIOR TO SUBMISSION):

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- Brownson R, Reif J, Keefe T, Ferguson S, Pritzl J. Risk Factors for Adenocarcinoma of the Lung. Am J Epi 125(1): 25-34.
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- Occupational Cancers, Anttila, S., Boffetta, P. Springer 2014
- IARC. List of Classifications by cancer sites with sufficient or limited evidence in humans, Volumes 1 to 108*; 2013http://monographs.iarc.fr/ENG/Classification/Table 4.pdf
- David Schottenfeld, Jennifer L. Beebe-Dimmer, Patricia A. Buffler,7 and Gilbert S. Current Perspective on the Global and United States Cancer Burden Attributable to Lifestyle and Environmental Risk Factors, Annu. Rev. Public Health 2013. 34:97–117
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- Blair A, Stewart PA, Tolbert PE, Grauman D, Moran FX, Vaught J, et al. Cancer and other causes of death among a cohort of dry cleaners. Br J Ind Med. 1990;47:162–168.
- Weiss, ST. Chronic obstructive pulmonary disease: Risk factors and risk reduction. In: UptoDate, Stoller, J (Ed), UptoDate, Waltham, MA, 2013.

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, June 08, 2015 12:22 PM
To: (b) (6)
Subject: RE: Meeting next week, vacation
Attachments: CLCW-Renal CA DRAFT8.docx

Just one comment and I fixed that reference.

From: (b) (6)
Sent: Monday, June 08, 2015 12:16 PM
To: (b) (6)
Subject: RE: Meeting next week, vacation
Importance: High

For your review.

(b) (6)

From: (b) (6)
Sent: Monday, June 08, 2015 10:49 AM
To: (b) (6)
Subject: RE: Meeting next week, vacation

K well let's finalize.

From: (b) (6)
Sent: Monday, June 08, 2015 9:03 AM
To: (b) (6)
Subject: FW: Meeting next week, vacation

I have not had any additional feedback from (b) (6) re: the RCC template, nor from (b) (6). And have heard nothing from (b) (6), as usual.

(b) (6)

From: (b) (6)
Sent: Friday, June 05, 2015 1:43 PM
To: (b) (6); (b) (6); (b) (6)
Cc: (b) (6)
Subject: Meeting next week, vacation

Hi guys,

I want to give you a heads up so my queue doesn't get too backed up;

I have a C&P meeting next week Tues 6/9 and will be unable to do CLCW exams then.

Also, I have vacation Tues 6/23 and 6/30 and will be unable to do CLCW exams then.

My next available Tues for CLCW will be on 6/16 and the next after that will be 7/7/15.

Thanks

(b) (6)

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, June 22, 2015 8:58 AM
To: (b) (6) (b) (6)
Cc: (b) (6)
Subject: RE: NRC Report

The 15 conditions listed in the NRC report as having limited suggestive evidence were determined as such based on literature through 2008, and does not address the body of literature from the last 7 years. Limited suggestive does not indicate sufficient data and there is no scientific basis for using this list as definitive.

From: (b) (6)
Sent: Friday, June 19, 2015 1:54 PM
To: (b) (6) ; (b) (6)
Cc: (b) (6)
Subject: NRC Report

In prep for the briefing with Sec VA on Camp Lejeune. I need a one liner concerning the 15 conditions of NRC report and the limited suggestive evidence. Please advise.

(b) (6)
Office of Disability & Medical Assessment
Department of Veterans Affairs
810 Vermont Ave NW
Washington, DC 20420
(b) (6)

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, June 08, 2015 4:00 PM
To: (b) (6)
Cc: (b) (6)
Subject: RE: RCC template

Then post

From: (b) (6)
Sent: Monday, June 08, 2015 3:59 PM
To: (b) (6)
Cc: (b) (6)
Subject: RE: RCC template

Only those you requested☺

(b) (6)

From: (b) (6)
Sent: Monday, June 08, 2015 2:58 PM
To: (b) (6)
Cc: (b) (6)
Subject: RE: RCC template

I'm assuming it's fine. If there has been no change, (b) (6)

From: (b) (6)
Sent: Monday, June 08, 2015 3:42 PM
To: (b) (6)
Cc: (b) (6)
Subject: RCC template
Importance: High

Please find attached the Renal Ca template for your final review. If no additional changes/edits/corrections are needed, (b) (6) when you are satisfied you can post it to the SP site unless (b) (6) has any concerns.

Bladder next....

(b) (6)

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Thursday, March 26, 2015 12:52 PM
To: (b) (6)
Subject: RE: TC draft
Attachments: CLCW-Thyroid Ca-DRAFT5.docx

How is this? Please proof it. I am tired of looking at it|!!!

From: (b) (6)
Sent: Wednesday, March 25, 2015 11:18 AM
To: (b) (6)
Subject: RE: TC draft

ATSDR has stated that the Bove et al study reported an increased risk of death in the Camp Lejeune cohort from several causes including cancers of the cervix, esophagus, kidney, and liver, Hodgkin's lymphoma, and multiple myeloma. "However, due to its limitations it does not provide definitive evidence for causality nor can it answer the question whether an individual has been affected by these exposures at Camp Lejeune."

From: (b) (6)
Sent: Wednesday, March 25, 2015 10:15 AM
To: (b) (6)
Subject: RE: TC draft

I put Asian at the top. DOesn't matter where it is. I know it's lay people but I just like to omit needless words.

You didn't attach anything...

W Bove I think we need to always put something about not thinking it is a good study, even if we cite it. Otherwise it looks like sometimes we are using it and sometimes not. Those couple sentences from the critical reviews about it.

(b) (6)

From: (b) (6)
Sent: Wednesday, March 25, 2015 11:09 AM
To: (b) (6)
Subject: RE: TC draft

You had taken the Asian RF out.....I am fine either way, just wanted you to know I am not crazy☺

I think our demographic are lay people....

I cleaned up DRAFT5 that I sent you this am, look it over one more time with the edit I made...I was just confused about the reference to citation number 6#, but that could be just me.

I think we are almost there,
(b) (6)

From: (b) (6)
Sent: Wednesday, March 25, 2015 10:04 AM
To: (b) (6)
Subject: RE: TC draft

I meant to write that under bove. Did I write it under the wrong article?

You can move those back to risk factors. I just like the "being" part taken out. That is written for lay people. I like to just list them.

(b) (6)

From: (b) (6)
Sent: Wednesday, March 25, 2015 10:41 AM
To: (b) (6)
Subject: TC draft
Importance: High

Looks good to me. The only part I am not clear on is reference number #6 when you note: Despite concerns about the validity of this study, which would lead to over estimation of risk.... I have attached the abstract for this article below for our reference. I only have the abstract so maybe this is more evident when reading the entire article?

The NCI list of risk factors: http://www.cancer.gov/cancertopics/pdq/treatment/thyroid/Patient#Keypoint2
-Being between 25 and 65 years old.
-Being female.
-Being exposed to radiation to the head and neck as a child or being exposed to radiation from an atomic bomb. The cancer may occur as soon as 5 years after exposure.
-Having a history of goiter (enlarged thyroid).
-Having a family history of thyroid disease or thyroid cancer.
-Having certain genetic conditions such as familial medullary thyroid cancer (FMTC), multiple endocrine neoplasia type 2A syndrome, and multiple endocrine neoplasia type 2B syndrome.
-Being Asian

J Occup Environ Med. 2002 Jul;44(7):616-21.
Community cancer assessment in response to long-time exposure to perchlorate and trichloroethylene in drinking water.
Morgan JW1, Cassady RE.

Author information

Abstract

In response to concerns about cancer stemming from drinking water contaminated with ammonium perchlorate and trichloroethylene, we assessed observed and expected numbers of new cancer cases for all sites combined and 16 cancer types in a California community (1988 to 1998). The numbers of observed cancer cases divided by expected numbers defined standardized incidence ratios (SIRs) and 99% confidence intervals (CI). No significant differences between observed and expected numbers were found for all cancers (SIR, 0.97; 99% CI, 0.93 to 1.02), thyroid cancer (SIR, 1.00; 99% CI, 0.63 to 1.47), or 11 other cancer types. Significantly fewer cases were observed than expected for cancer of the lung and bronchus (SIR, 0.71; 99% CI, 0.61 to 0.81) and the colon and rectum (SIR, 0.86; 0.74 to 0.99), whereas more cases were observed for uterine cancer (SIR, 1.35; 99% CI, 1.06 to 1.70) and skin melanoma (SIR, 1.42; 99% CI, 1.13 to 1.77). These findings did not identify a generalized cancer excess or thyroid cancer excess in this community

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Thursday, June 25, 2015 11:34 AM
To: (b) (6)
Subject: RE: White paper
Attachments: Definition of Renal Toxicity-White Paper.docx

comments

From: (b) (6)
Sent: Thursday, June 25, 2015 9:23 AM
To: (b) (6); (b) (6)
Subject: FW: White paper

From: (b) (6)
Sent: Thursday, June 25, 2015 8:21 AM
To: (b) (6)
Subject: White paper

Characterization of Renal Toxicity

The Institutes of Medicine (IOM) was tasked with characterizing "renal toxicity" as mandated for coverage in the Honoring America's Veterans and Caring for Camp Lejeune Families Act. This same issue has plagued both VBA and VHA as to what conditions should be considered for Subject Matter Expert (SME) review as potentially arising out of exposure to Camp Lejeune contaminated water (CLCW). Currently, a wide array of medical conditions are submitted for SME evaluations under the umbrella of renal toxicity, which at some point appears to have become interpreted as "kidney conditions" in general. The Honoring America's Veterans and Caring for Camp Lejeune Families Act, provides health benefits to both veterans and family members under a "no-fault" system for 14 health conditions, including renal toxicity as a result of solvent exposure. ~~Having~~ We have current guidance provided by the IOM for conditions which they have deemed, based on the latest scientific literature review, do not meet the threshold for inclusion for healthcare. This data should also benefit both VBA and VHA in determining which conditions would be unlikely to arise out of exposure secondary to CLCW; and therefore should not be submitted to VHA for Compensation and Pension purposes other than on a direct basis.

Among the contaminants ~~residents~~ at Camp Lejeune ~~were exposed to~~, TCE and PCE (PERC) were the most likely to be responsible for acute kidney injury and potentially subsequent chronic renal disease. In general, human and animal studies demonstrate that high-dose exposures are required for acute renal effects to be observed and that such effects are variable among species. The IOM report noted that, "There is no evidence for an increased incidence of chronic kidney disease in those who resided at Camp Lejeune during the time of the contaminated drinking water." This was primarily attributed to the fact that the documented levels of PCE and TCE in the drinking water at Camp Lejeune were much lower than those in human and animal studies reviewed, and the duration of exposure would likely have been much shorter for Camp Lejeune residents. The clinical guidance and algorithm for renal toxicity requires that the clinician assesses whether it is likely that the chronic kidney disease (CKD) is attributable to a known cause other than solvent toxicity. If there is no apparent evidence for alternate causation, CKD could be due to toxic exposure. If the evaluation shows that the patient's kidney disease is compatible with another etiology, such as diabetic nephropathy or hypertensive nephrosclerosis, it is unlikely that solvent exposure at Camp Lejeune was the causative agent. ~~Other m~~Medical conditions associated with CKD that should be excluded.include:

Diabetic nephropathy

Hypertensive nephrosclerosis

- Acute tubular necrosis resulting from hypotension, rhabdomyolysis, or nephrotoxic agents (e.g., chemotherapeutics, IV radiocontrast media, immunosuppressives)
- Atheroembolic renal disease
- Glomerulonephritis associated with IgA nephropathy, postinfection, membranous, membranoproliferative, other systemic diseases
- HIV-associated nephropathy
- Immune-mediated renal disease
- Interstitial renal disease caused by an allergic reaction or analgesic agents
- Light-chain disease
- Polycystic kidney disease
- Prerenal disease, volume depletion, congestive heart failure, liver failure
- Renovascular disease

If medical evidence for such conditions exists and the veteran's course is consistent with those conditions (the "renal disease is ~~as~~ more likely as not associated" with those conditions), CKD should be attributed to those entities and not CLCW exposure. 50/50 we have to evaluate

While not specifically discussed by the IOM report, kidney stones/nephrolithiasis should also be exempted from consideration under the umbrella of renal toxicities. Nephrolithiasis are not part of the spectrum of CKD.A review of the literature through PubMed noted only a potential association with cadmium and Trimethyltin (TMT) exposure reported; neither of which are noted to be associated with Camp Lejeune.

A new understanding that renal toxicity has been defined as Chronic Kidney Disease by the IOM and not generalized kidney conditions will assist VBA and VHA in evaluating only those claims potential associated with solvent exposure, reduce the number of claims pending and negative MO, while increase SME availability.

Parrillo, Jeffrey M. (VACO)

From: (b) (6)
Sent: Monday, April 20, 2015 11:23 AM
To: (b) (6)
Subject: so far
Attachments: CLCW-Lung Ca DRAFT3.docx; Lung ca in never smokers.pdf; vinyl chloride and ca.pdf

Categories: Red Category

And 2 new studies.

(b) (6)