THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

convenes the

EXPERT PANEL MEETING

for the

CAMP LEJEUNE HEALTH SURVEY

MARCH 8, 2011

Meeting minutes of the Camp Lejeune Health Survey Expert Panel held at the ATSDR, Chamblee Building 106, Conference Room B, Atlanta, Georgia, March 8, 2011, 9:00 a.m.

STEVEN RAY GREEN AND ASSOCIATES
NATIONALLY CERTIFIED COURT REPORTING
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P A R T I C I P A N T S

(alphabetically)

EXPERT PANEL:
DELZELL, ELIZABETH, ScD
MANGIONE, THOMAS, PhD
MYERS, DOUGLAS, ScD
SMYTH, JOLENE, PhD

ATSDR:
BOVE, FRANK
HARRIS, CAROLYN
MASLIA, MORRIS
RUCKART, PERRI
SINKS, TOM

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P R O C E E D I N G S

(9:00 a.m.)

The meeting of the Expert Panel on the Camp Lejeune Health Survey was called to order. Participants and attendees were introduced. Panel members included Dr. Elizabeth Delzell, Dr. Thomas Mangione, Dr. Douglas Myers and Dr. Jolene Smyth.

Ground rules were outlined. Rather than a consensus, the most definitive guidance that can be given is sought. Summary notes will be produced. In order to encourage a free and open exchange, remarks will not be attributed to specific speakers. A draft will be shared with the panel for review and comment before the final summary is posted on the Web site. Panel members, therefore, were asked not to communicate with the press, but rather invite questioners to review the summary minutes when published.

BACKGROUND INFORMATION

A slide presentation began with background on

the site, describing the ten base family housing areas and the three water treatment plants providing drinking water to most of the base housing–Tarawa Terrace, Holcomb Boulevard and Hadnot Point. Tarawa Terrace closed in 1987; Holcomb Boulevard and Hadnot Point are still in operation. An aerial map showed the relationship of housing areas to each other and to other parts of the base.

The contamination of the wells at each of the treatment plants was outlined and contaminants listed. The wells at Tarawa Terrace were contaminated with perchloroethylene (PCE) by an off-base dry cleaner which opened in 1953, a year after the Tarawa Terrace drinking water system began operating. Hadnot Point had multiple sources of contamination, including leaking underground storage tanks (UST) and waste disposal sites. The USTs were installed in the 1940s and 1950s. Contaminants detected at Hadnot Point included trichlorotheylene (TCE), PCE, and benzene, toluene, ethylene, and xylene (BTEX compounds). It was emphasized that the information in the presentation is

provided as background since all the water modeling had not been completed. Continuing the background, previous ATSDR studies at Camp Lejeune were described and discussed briefly.

Recommendations by the 2005 ATSDR Scientific Advisory Panel on Camp Lejeune were enumerated, along with actions taken as a result of the recommendations. The 2005 panel recommended that mortality and cancer incidence studies should receive the highest priority and seemed to be the outcomes most feasible to study. The only computerized data for active duty Marines and civilian employees were the Defense Manpower Data Center (DMDC) data, and there were no electronic databases to identify children who lived on base. For active duty, the DMDC data has full last name from 1977 forward and social security number (SSN) for everyone, but the unit code that identifies the base where the person was stationed is only available from June 1975 forward. For civilian employees, the DMDC data began in December 1972 and includes duty location and SSN. However,

full name is only available from December 1981 forward. The employee action code, which provides information about hiring and promotions, is only available from June 1974 forward. Therefore, the following groups that we identified using Defense Manpower Data Center (DMDC) records will be included in the health survey/morbidity study: former active duty marines who were stationed at Camp Lejeune any time during June 1975 and December 1985 and civilian employees who worked at the base any time during December 1972 and December 1985. The survey also includes participants in a previous 1999-2002 ATSDR survey of childhood cancers and birth defects. Samples of active duty marines and civilian employees from Camp Pendleton will comprise the comparison population because the base is similar to Camp Lejeune but without VOC-contaminated drinking water. The comparison groups from Camp Pendleton include only those who were never stationed or employed at Camp Lejeune during the period when the drinking water was contaminated. The Camp Pendleton samples will consist of 50,000 Marine/Navy personnel

stationed at Camp Pendleton any time from 6/75 to 12/85, and approximately 10,000 civilians employed there at any time from 12/72 to 12/85. The Camp Pendleton sample will include all of the female marines and employees from Camp Pendleton in order to have the maximum number of females in the study. The National Defense Authorization Act for Fiscal Year 2008 mandated that everyone who registered with the USMC receive a health survey. To comply with this law, ATSDR will mail health surveys to all registrants. However, registrants will not be included in the morbidity study unless they are also a member of the morbidity study population. The surveys completed by registrants who are not members of the study population will be analyzed separately, primarily in a descriptive manner.

Items covered in the health survey were discussed briefly. The survey packets will be sent out in a series of approximately six waves, to about 300,000 people. The survey will include a consent form and ask about residential history and work activities on

base, occupational history (including chemical exposures), and risk factors such as alcohol and smoking. Information will be gathered on cancers and other diseases, along with an open-ended question to report other health concerns. The option to complete the survey on-line will be offered.

The design for mailed surveys was outlined, beginning with the pre-notice letter, signed by the deputy commandant of the USMC, notifying the recipients that the survey will be coming and encouraging their participation. The initial health survey mailing will include letters signed by the Commandant of USMC and ATSDR. Repeated contacts will include a thank you/reminder postcard, a second survey mailed to non-responders, and finally an automated telephone reminder to non-responders.

Depending on the recommendations of the panel and the results of the survey, the Agency will decide whether to move forward with confirmation of self-reported diseases in the health survey.

If the decision is made to proceed, the participants will be sent medical records release forms to obtain copies of their records, as well as to access information in cancer registries. The confirmation process will be extensive and thorough.

GENERAL DISCUSSION AND CLARIFICATIONS

The Web-based version of the survey will include a button to click, signifying agreement to participate. The mail-in version of the survey will require a signature of informed consent to participation. If it is not signed, attempts will be made to get a signature. If those attempts are unsuccessful, the participant's information cannot be included.

If a decision is made to proceed with confirmation of self-reported diseases, the medical records release form will be sent only to those participants reporting diseases of interest.

Because many providers will not accept the standard records release form, the contractors

are prepared to interact with providers and use their forms, if necessary.

In the future a cancer incidence study may be done using data linkage, but at this time the focus is on the health survey which would just confirm the self-reported diseases.
The value of a data linkage cancer incidence study has been discussed and will be decided based on the results of the health survey and mortality study.

A question was asked about ATSDR’s decision to not use financial incentives due to concern about response rates. According to the speaker, predominant findings in the literature are that financial incentives increase response rates. ATSDR responded that financial incentives would add a great expense to the study. Moreover, the community assistance panel (CAP) members have stated that the Commandant’s signature on the study invitation letter will motivate participation in the health survey and will be important than financial incentives.

A panel member expressed concern about past experience showing that military personnel are reluctant to reveal personal health information, even when strongly urged to do so by someone of higher authority, for fear it will in some way be used against them later. A panel member suggested that $50,000 could be contributed to the fund for disabled Marine veterans if the survey got a response rate of greater than 50 percent as an incentive for participation.

CHARGE TO PANEL

The panel was charged to provide expert scientific opinion to ATSDR regarding the progress, analysis, and reporting of results from the Camp Lejeune Health Survey (phase 1) and Morbidity Study (phase 2). Because of concerns raised by a previous expert panel of epidemiologists that the validity of the health survey may be affected by selection/non-response bias as well as low statistical power due to a low participation rate, the current panel is being asked to develop criteria that address these concerns at the initial meeting

prior to the start of survey data collection. These criteria can then be used by ATSDR as a basis for deciding whether to proceed with confirming the diseases reported in the surveys and completing the morbidity study phase. Basing a decision to proceed with the morbidity study phase on criteria developed prior to data collection would avoid the perception that the agency's decision is being driven solely by the survey data.

To focus the panel's discussions, the following four questions were put before the panel during the initial meeting.

Question 1: In your professional judgment, what participation rate(s) should the Director of ATSDR consider as sufficient, based on considerations of statistical power for the diseases of interest, before obligating resources to collect confirmation on reported diseases?

Discussion on Question 1:

Recent military population studies using mailed surveys reported a response rate of 30 to 35%.

ATSDR expects that the study invitation letter signed by the Commandant, which was recommended by the CAP, will serve as a strong incentive to increase participation even for Marines who are distrustful of the USMC. The letter from the Commandant, along with the repeated contacts for non-responders, is an effort to ensure as high a participation rate as possible for a mailed survey.

The panel agreed that there is no magic number for a “sufficient” participation rate. The question asks for a rate below which it would not be worthwhile to collect medical record information to confirm the participant-reported diseases. The panel noted that there will be criticism unless the participation rate is 100%, and that is unlikely. Opinions ranged from the belief that an adequate rationale was lacking for not specifying a sufficient participation rate to the suggestion that 20% was the lowest rate at which phase 2 (confirmation of self-reported diseases) should proceed. Panel members concurred that the results of the health survey could be

interpreted with much more confidence if the self-reported diseases were confirmed. The panel recommended that the agency move forward with the morbidity study phase of the health survey. A low response rate will result in the need for sensitivity analysis to quantify the amount of bias under a range of plausible assumptions about the associations of participation with exposure status and health status.

The panel members suggested it might be worthwhile to do a pilot study before mailing out over 300,000 surveys.

The participation rate number is political. People react viscerally and use it for their own purposes, whatever it is. While 25% might be acceptable in one study, it might be a problem in this one.

If the participation rate is low, the validity of the study will likely be attacked, especially by those who do not believe that exposures at the base were sufficient to cause

disease. A likely scenario is that the health survey will be completed; phase 2 will retrieve medical records and confirm the reported diseases, and results will show some higher rate of a particular cancer or another medical condition at Camp Lejeune than at Camp Pendleton. Complaints of bias will follow, and a record linkage type study, that would not be affected by selection/non-response bias, may be required, if feasible, to clarify the findings of the health survey.

ATSDR will conduct interim analyses of the participation rate.

Question 2: In your professional judgment, what measures should be used for evaluating non-response/selection bias?

Discussion on Question 2:

Non-response/selection bias should be the biggest concern. Participation rates aren't as important as the non-response/selection bias.

The issues of participation rate and response

bias or selection bias get intermingled. Part of the issue is the reason for the bias. Have people made a choice not to respond (and is that choice related to their exposure and health status)? Or was the information sent to the wrong address; was the non-responder out of the country, or was there another reason for non-response?

The panel hopes that people who choose not to participate will at least return the postcard and give their reasons for not participating, so something can be learned from that. That could also help in looking at biases for non-responders. It might be worthwhile trying to meet with a group of non-responders to learn why they didn't participate.

As responses begin to come in, a preliminary assessment of participation rates and the possibility and magnitude of non-response bias could be done. If the assessment indicates that the bias is not substantial, then the survey would move forward. If there appears to be substantial non-response bias, then the issue could be addressed by focusing on

internal (i.e., within-Lejeune) comparisons among exposure groupings. The panel felt that while the response rate will get the attention of the media, it is less important that the issue of bias.

To assess the extent of bias (e.g., disease underreporting) in the survey, it may be useful to see if known risk factor-disease associations (e.g., smoking and lung cancer, or a specific occupation and a disease known to be associated with that occupation) are present in the survey data. If these risk factor-disease associations are not observed in the survey, this may be an indicator of the presence of bias. However, ATSDR noted that the primary purpose of obtaining information on occupations and other risk factors such as smoking and alcohol consumption was to control for potential confounding by these factors of the associations between VOC drinking water exposures and diseases.

The panel noted that there may not be a lot of cancers reported in the first or second wave of

survey mailings. However, the contractor can be asked to look at the link between participation and exposure after the first or second wave is completed, in order to assess the possibility and extent of non-response/selection bias. Evaluating whether there is under- or over-reporting of diseases would come at the end of the survey (and at the end of the morbidity study phase if it is conducted).

Evaluation measures have to be reasonable and interpretable so that moving forward with confirming self-reported diseases is justified. Formal uncertainty analyses could be undertaken, and ATSDR is committed to conducting quantitative bias analyses for the health survey and morbidity study.

The decision about which analytic procedures will be used can't be made until the biases and the level of biases are determined.
The best exposure measures will be the exposure measures that are least subject to distortion in the results due to response bias. It was

noted that some people may have been stationed at the base, but deployed elsewhere (so not exposed to Camp Lejeune drinking water), and that information is not available.

ATSDR distributed a handout on "Proposed Analyses of the Camp Lejeune Health Study," which provided analysis simulations based on the water modeling for Tarawa Terrace in an effort to give the panel a sense of variability over time of the concentrations in the drinking water, not just of PCE, but other substances because of degradation. Each scenario was discussed in detail. ATSDR asked the panel what kinds of analyses would make sense to perform in order to help characterize the bias. The proposed analysis sheet mentions average exposure, but not duration or cumulative exposure, and these are key exposure measures that should also be evaluated.
Logistic regression modeling to look at the factors associated with response, as well as early and late response, was proposed as an option. Also mentioned were several approaches to sensitivity analyses, including quantitative

bias analyses.

Defining response rate by dividing the number of responses by the total eligible has been deemed most justified, although it combines known refusals with people who simply never received the packet. The only way to truly know who refused is if they return the postcard or call the help line.

Age as it relates to non-response rates was discussed, noting the rates are higher among younger people. It was observed that if the older people fail to participate, it will affect the power of the survey.

Question 3: In your professional judgment, are there any additional criteria to consider before obligating resources to confirm reported medical conditions?

Discussion on Question 3:

Pilot testing and focus groups would give better insight. A focus group could be held in advance by bringing in 50, or even less, people

from both Camp Lejeune and Camp Pendleton and, after having them review the materials, asking them if they would participate.

Another suggestion was to do a pilot study, then gather focus groups of 20 or 30 who didn't respond and ask them why, and discuss their reasons. ATSDR responded that the agency did consider a pilot study, but a plan to conduct a pilot study received negative feedback from Congress, the Department of the Navy and the CAP, mainly because the survey was mandated by Congress and had to be done anyway. Additionally, forming focus groups would require separate OMB and IRB approvals.

Question 4: When should ATSDR begin to process IRB approvals with the 50 state cancer registries, the VA cancer registry, and the DoD cancer registry?

Discussion on Question 4:

A general discussion ensued outlining the timing, budgetary considerations and burden of work involved in obtaining state cancer

registry IRB approvals. The benefit of proceeding with obtaining IRB approvals before making a decision to begin phase 2 may shorten the process by six months. The adverse effect is that it may waste the Navy's money if there is a decision not to proceed.

CDC’s Cancer Surveillance Branch works closely with all 50 state registries, and ATSDR has made contact with the registries via CDC to establish rapport and learn which states may have unique requirements. There may be no problems in obtaining the IRB approvals, but it will take considerable time to get everything in place. If there are likely problems, they need to be identified and flagged.
There will be some funds for the registries attached to this effort, through the contractor, to make working with ATSDR more appealing.

The plan is that ATSDR will provide the registries with the names of people who have self-identified their cancers. The registries will be asked for confirmation. There was

general agreement that processing IRB approvals with the 50 state cancer registries, as well as the VA and DoD cancer registries, should move forward.

GENERAL OBSERVATIONS:

ATSDR has always recognized the difficulty of using the health survey for a scientific study, acknowledging issues of participation rate and power. The issue is finding a way to make the survey a useful study.

Some of the issues raised concerned the impacts on statistical power of: (1) missing data due to incomplete (but returned) questionnaires; (2) low participation among the Camp Pendleton cohorts; and (3) possible non-cooperation by some cancer registries and some health providers in the effort to confirm the self-reported diseases. Another issue concerned the potential for significant differential bias due to differences in response between Camp Lejeune and Camp Pendleton. It was noted that Camp Pendleton cohorts will have less incentive to participate than Camp Lejeune cohorts.

While many suggestions for changes in approach, design, incentive, etc. are quite valid, they would also require IRB or OMB approval, which is not feasible at this point. What can and will be considered now are recommendations to incentivize participation that can be rolled into the current plan.

While low response rates may give people an opportunity to minimize the worth of a study, these critics need to make a case that significant bias exists – they cannot simply assume that significant selection/non-response bias is present because there is a low participation rate. They must show that participation was affected by both exposure and disease status. So, although people with cancers or other diseases may be more likely to participate, significant selection bias is not likely to occur unless participation was also related to exposure status.

With medical records verification as a part of this effort, there should be minimal bias due

to false positives (i.e., bias due to over-reporting of diseases should be minimal). However, bias due to under-reporting could still be a problem. In addition, there may be difficulty confirming some of the reported conditions because of lack of cooperation from health care providers and/or lack of available medical records.

An effort should be made to clarify that ATSDR will be reporting the survey results. A presentation at Camp Lejeune is anticipated and will also be available on the web site.

It is unfortunate that people were never informed of the water contamination issue until recently. It is anticipated that the VA will be deluged with inquiries from exposed veterans.

Around October 1, ATSDR will have to decide whether to go back to the Navy and ask for the money to proceed to Phase 2, to validate the information on health outcomes received from the survey.

A final matter suggested for discussion was how to promote the study. Examples cited were an ATSDR press release, asking the Navy and Marine Corps to make an announcement, and asking the CAP to spread the word. It was suggested the purpose of the survey could be touted as an effort to try to better understand health outcomes from living on military bases so that we can make improvements.

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Timing and details of the next panel meeting were to be resolved by e-mail at a later date.

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(Meeting adjourned at 3:45 p.m.)

CERTIFICATE OF COURT REPORTER

STATE OF GEORGIA

COUNTY OF FULTON

I, Steven Ray Green, Certified Merit Court Reporter, do hereby certify that I reported the above and foregoing on the day of March 8, 2011; and it is a true and accurate summary of the proceedings captioned herein.

I further certify that I am neither relation nor counsel to any of the parties herein, nor have any interest in the cause named herein.

WITNESS my hand and official seal this the 28th day of March, 2011.

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STEVEN RAY GREEN, CCR, CVR-CM, PNSC

CERTIFIED MERIT COURT REPORTER

CERTIFICATE NUMBER: A-2102