

DATE June 21, 1983

cc

SUBJECT PROTOCOLS FOR EPIDEMIOLOGIC STUDIES
OF THE HEALTH OF VIETNAM VETERANS

REFERENCE

TO M. C. Throdahl
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A great deal of effort has been expended in these protocols to ensure that an effect, if due to dioxin, will be detected. They will look for effects which have been identified by animal studies as well as by a variety of human studies and they acknowledge that there is still the real possibility they will have false positives, false negatives, and also equivocal findings despite this effort. I like the stated recognition that these protocols will be developmental and may change with time, but they do not state how they will be able to handle the biases if they later change protocols. If they change protocols, biases will be difficult to control.

In any of their three cohort studies, including "likely exposed" may identify a cohort with more combat duty, and with this selection there may be increased deaths, increased casualties, or even increased drug usage. This possibility is not considered in the protocol - maybe they can identify this possibility by comparison to the "likely not exposed", or even to cohort 3. World War I had its "gassed syndrome", World War II had its battle fatigue and tropical diseases, and Vietnam had its drugs and other known confounding factors.

I believe that the definition of cohorts in St. Louis should prevent biases, but the examinations of the veterans can be biased by the questioners, by the physical examiners, or even by those who decide they want to take the exams. From what I know of Ranch Hand, I believe that these possible biases have been well handled.

I now would like to list some of my specific comments for the various pages of this protocol:

Page 8, first paragraph. It states that it is possible that a significant exposure was from non-Ranch Hand applications. They do not give the basis for this statement and it would seem that this could not be a major source of exposure.

Page 9, second paragraph. It states that for the occupational exposure, the total number of exposed persons was usually not reported, but, in fact, this exposure list is recorded in a number of books and summaries. I believe this paragraph should also address the fact that 2,4,5-T was used widely and indiscriminately over a number of years in the United States and without reported effect over these many years.

Page 10, first paragraph. This paragraph talks about liver effects, but it does not acknowledge or recognize that these liver effects were temporary in practically all reported cases.

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Page 11, the last paragraph. The statement is made that literature suggests that Vietnam veterans differ from other veterans in a number of ways. This protocol does not state how they will deal with these many confounding factors.

Page 12, second paragraph. It states that the servicemen enjoyed better long-term health than their counterparts who did not serve in the military. I suspect that they are dealing with the so-called healthy worker effect. Nevertheless, a comparison between the military and non-military would be an interesting definition of long-term health status.

Page 12, last paragraph. The first sentence states that there are no studies comparing the health of combat veterans with those who did not participate in combat. I would think that the reason there are not reports is that those in combat did not suffer effects other than those who were not in combat. This would account for why there are not reports.

Page 17, ninth line from the bottom. It states that if differences existed and they applied to all veterans, then a valid study of Vietnam experience would not be possible. I don't see how they reach such a conclusion; if there is no difference seen, then there is not a Vietnam effect.

Page 18, second paragraph, fifth line. They are discussing the Swedish finding of soft tissue sarcomas but they fail to address the negative studies done similarly to the Swedish studies which found no effect. These studies include the Finnish and the New Zealand studies. See attached analysis.

Page 18, fourth from the last line on second paragraph. They state that other cancers could be added easily if an association was suggested. Based on a form of this lymphoma study, I don't see how the other cancers could be identified.

Page 35, first paragraph. This paragraph implies that the Swedish study has established an effect between the exposure and sarcomas. I have no problem with them attempting to prove Hardell's conclusions, but I do not believe that Hardell's conclusions are fact. I see no reason for not including cases which arose prior to 1984 as a part of the soft tissue sarcoma study. Again, see same attached analysis.

Page 44, first paragraph. This paragraph states that more emphasis will be given to dermatologic and immunologic studies for the Agent Orange cohort and for psychologic outcomes for the Vietnam cohort. Such an approach would encourage bias. The interviewer should not know which group an individual is in. A standard protocol should be used which would be constant, regardless of the response of the individual.

Page 44, second paragraph. It states that all the factors may be associated with service in Vietnam. They are indeed correct and these same confounders will be found not only in the non-service cohort but also in the Agent Orange cohort as well.

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Page 44, third paragraph, fourth line from bottom. Though the subject's perceptions about exposure to herbicides are indeed appropriate, the same question should be addressed to the "exposure unlikely cohort" as well as the third cohort. After receiving replies to these questions, the remainder of the questionnaire should be followed just as though there had been no discussion of exposure to herbicides. Only in this way will biases be prevented.

Page 46, paragraphs one and two. There is no question but that servicemen with complaints will be more likely to participate in the study than a man without complaints. This will create a bias. This section does deal with the importance of well-standardized, non-biased approaches and it certainly is well stated.

Page 71, first paragraph. Though it states that this high risk is generally suspected to be exposure to Agent Orange, one of the reasons CDC has been asked to do the study is that many experts do not think that exposure to Agent Orange produces risk. Nevertheless, it is the possibility of high risk that is the basis for this study by the CDC. As stated earlier in the protocol, there are many other factors which are, not may have been, factors which can confer an increased risk. The last sentence in this paragraph acknowledges that being in Vietnam poses health risks which should be identified.



George Roush, Jr., M.D.

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Attach.