

## Free Executive Summary

### Epidemiologic Studies of Veterans Exposed to Depleted Uranium: Feasibility and Design Issues



Committee on Gulf War and Health: Updated Literature Review of Depleted Uranium, Institute of Medicine

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*Depleted uranium, a component of some weapons systems, has been in use by the U.S. military since the 1991 Gulf War. Military personnel have been exposed to depleted uranium as the result of friendly fire incidents, cleanup and salvage operations, and proximity to burning depleted uranium-containing tanks and ammunition. Under a Congressional mandate, the Department of Defense sought guidance from the Institute of Medicine in evaluating the feasibility and design of an epidemiologic study that would assess health outcomes of exposure to depleted uranium. The study committee examined several options to study health outcomes of depleted uranium exposure in military and veteran populations and concluded that it would be difficult to design a study to comprehensively assess depleted uranium-related health outcomes with currently available data. The committee further concluded that the option most likely to obtain useful information about depleted uranium-related health outcomes would be a prospective cohort study if future military operations involve exposure to depleted uranium. The book contains recommendations aimed at improving future epidemiologic studies and identifying current active-duty military personnel and veterans with potential DU exposure.*

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## SUMMARY

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The 1991 Persian Gulf War, although considered a successful military operation, had a profound impact on the lives of troops who served overseas. Returning veterans reported numerous health problems that they associated with wartime exposures, including fatigue, sleep disturbance, and cognitive difficulties. Troops in the 1991 Gulf War and in other conflicts, including the Iraq War (Operation Iraqi Freedom), were exposed to a variety of hazardous agents, including depleted uranium (DU). DU is used to strengthen armor and to increase the penetration effectiveness of munitions. Troops were potentially exposed to DU during friendly-fire incidents, cleanup operations, and accidents (including fires).

Section 716 of the 2007 John Warner National Defense Authorization Act required that the Department of Defense (DOD), the Department of Veterans Affairs, and the Department of Health and Human Services “conduct a comprehensive study of the health effects of exposure to depleted uranium munitions on uranium-exposed soldiers and on children of uranium-exposed soldiers who were born after the exposure of the uranium-exposed soldiers to depleted uranium.” In response to this charge to the agencies, DOD sought guidance from the Institute of Medicine (IOM) in evaluating the feasibility and design of an epidemiologic study that would assess health outcomes related to exposure to DU.

### CHARGE TO THE COMMITTEE

In response to DOD’s request, IOM entered into a contract to conduct the following study:

An IOM committee will examine and make recommendations regarding the critical elements needed for an epidemiologic study of veterans who were exposed to DU while on active duty. Those might include veterans who

- Were exposed to smoke from fires resulting from the burning of vehicles containing DU munitions or fires at depots at which DU munitions were stored.
- Worked in environments containing DU dust or residue from DU munitions.
- Were within a structure or vehicle when it was struck by DU munitions.
- Climbed on or entered equipment or structures struck by DU munitions.
- Were medical personnel who provided initial treatment to members of the armed forces who were exposed to DU.

The committee also will identify elements needed to study veterans' children who were born after parental exposure to DU.

### **COMMITTEE'S APPROACH TO ITS TASK**

To approach its task, the committee first considered the necessary elements of a comprehensive epidemiologic study to assess exposure to DU and related health outcomes (Chapter 2). The committee then evaluated DOD's available data and research efforts and identified limitations and data gaps in the databases (Chapter 3). Finally, it identified options for further study of potential health outcomes in DU-exposed military personnel and veterans (Chapter 4).

### **ELEMENTS OF AN EPIDEMIOLOGIC STUDY**

The elements of an epidemiologic study essential for assessing the relationship between exposure to DU and health outcomes include identification of a relevant study population of adequate size; a comprehensive assessment of uranium exposure in the population, including the use of biomarkers; an evaluation of long-term health outcomes; adequate followup time; use of reasonable methods for controlling confounding and minimizing bias; and appropriate statistical analyses.

### **AVAILABLE DATASETS**

The committee reviewed available datasets on health outcomes in DU-exposed military personnel and veterans and datasets on these populations that do not specifically assess DU exposure (they track health outcomes in general) but might be useful for future study. The datasets include the Depleted Uranium Medical Management Program, including the Depleted Uranium Follow-up Program at the Baltimore Veterans Affairs Medical Center (BVAMC); the Millennium Cohort study; and the DOD Birth and Infant Health Registry. In general, the studies are well designed; however, they lack either adequate sample size or accurate exposure information (for example, biomarkers of exposure and work-assignment locations) to assess fully whether DU exposure is associated with health outcomes.

### **CONCLUSIONS AND RECOMMENDATIONS**

The committee examined four approaches (case-control and cohort studies) to study health outcomes related to DU exposure in military and veteran populations. Two of the study designs use existing data, and two require collection of new data.

There are important limitations in each of the approaches, particularly the low statistical power and the lack of adequate and accurate exposure data. Given those limitations, it would be difficult to design a study to comprehensively assess the health outcomes of DU exposure in military and veteran populations with currently available data. Detecting a small increased risk for a given health outcome of DU exposure in those populations is not feasible in an epidemiologic study. Of the four approaches, the committee concludes that the one most likely to

obtain useful information about DU-related health outcomes would be a prospective cohort study if future military operations involve exposure to DU.

To gain a sense of the expected sample sizes required for a high-quality epidemiologic study, the committee calculated sample-size estimates for a cancer outcome (lung cancer) and a renal-function outcome (serum creatinine concentration); these outcomes, lymphoma, respiratory disease, neurologic outcomes, and adverse reproductive and developmental outcomes were identified as having high priority for further study in the committee's report *Gulf War and Health: Updated Literature Review of Depleted Uranium*.<sup>1</sup> The committee determined that more than 1 million DU-exposed people would be required to detect a statistically significant difference in risk of lung cancer, a relatively common cancer. Fewer DU-exposed people would be needed to evaluate renal disease than lung cancer because renal disease is more prevalent than lung cancer (a range of potential study sizes, with the associated assumptions, is provided in Chapter 2 of this report). Beyond the size of future DU-exposed military populations, the success of any cohort study would depend on DOD's ability to collect accurate and complete individual-level exposure information on military personnel who enter a war theater in which DU munitions and armor are used.

The committee made several additional recommendations:

- DOD should investigate available in vivo assay techniques other than measuring urinary uranium to determine whether they offer advantages (for example, increased sensitivity) over urinalysis.
- DOD should consider assessing uranium concentrations in lung, kidney, and brain tissues from military personnel who were potentially exposed to DU and died while on active duty. Analysis of uranium in autopsy tissue might provide information on concordance between renal uranium concentrations and model-based estimates. It also would provide information on pulmonary retention of DU, which has implications for estimating lung cancer risk, and insight into the toxicokinetics of DU.
- DOD should continue to link and integrate available databases so that information can be assessed.
- DOD should determine the feasibility of collecting biomarker data from people in the Millennium Cohort Study who reported being exposed to DU and from military personnel who were at Camp Doha during the time of the fire in 1991. Any study participants who have positive bioassay results for DU exposure should receive health monitoring through the Depleted Uranium Follow-up Program at the BVAMC throughout their lifespans.
- DOD should conduct further study of the potential reproductive and developmental toxicity of DU with animal models.

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<sup>1</sup>IOM (Institute of Medicine). 2008. *Gulf War and health: Updated literature review of depleted uranium*. Washington, DC: National Academies Press.

# Epidemiologic Studies of Veterans Exposed to Depleted Uranium

## Feasibility and Design Issues

**Committee on Gulf War and Health: Updated Literature Review  
of Depleted Uranium**

**Board on Population Health and Public Health Practice**

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—Goethe



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This report has been reviewed in draft form by persons chosen for their diverse perspectives and technical expertise in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards of objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following for their review of this report:

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by **David J. Tollerud**, Institute of Public Health Research, University of Louisville, and **Johanna T. Dwyer**, Tufts University School of Medicine and Friedman School of Nutrition Science, Tufts-New England Medical Center. Appointed by the Institute of Medicine and the National Research Council, respectively, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the author committee and the institution.



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