V. FOLLOW-UP

Although DoD extensively researched various DU munitions' environmental and medical effects before the Gulf War (See Tab L), during the war DoD identified several data gaps requiring further investigation. This Section discusses environmental assessments of DU battlefield contamination, recent environmental studies of various DU munitions, the results of current medical studies, and ongoing and planned research.

A. Environmental Assessments

Some have suggested that since US forces used more than 300 tons of DU munitions in the Gulf War, it is reasonable to expect the entire battlefield was contaminated with dangerous levels of uranium aerosols, which could have exposed hundreds of thousands of Gulf War participants to harmful DU amounts. As noted earlier, when DU hits a target, small fragments can break off, burn, and produce uranium aerosols, of which possibly up to 35% are respirable. However, the tank round's entire mass does not aerosolize. In addition, the claims fail to consider the differences between tank rounds and 30mm rounds fired from A-10s. The Army fired 9,552 DU tank rounds [121] (approximately 50.55 tons) while A-10s fired 783,514 30mm DU rounds [122] (approximately 259 tons). The tank rounds were much more likely to hit their intended target than the 30mm rounds, though the exact number of 30mm rounds that struck targets in the Gulf War is unknown. Actual combat simulations conducted before the Gulf War indicate only a small percentage of the A-10 aircraft rounds (less than 10%) actually hit the target, e.g., during 9 passes with the A-10s firing 2-second bursts, only 93 of 957 rounds actually hit the targets. [123] The smaller caliber DU munitions fired from aircraft can miss the target entirely, hit the target and ricochet, or embed in the target without penetrating. Each of these circumstances leaves the penetrator almost entirely intact and produces little or no aerosol or fine particles. In this regard, we should point out that the average concentration of natural uranium in soil is about 4 tons per square mile in the top 12 inches of soil.

Figure 9. Dr. Rostker (Special Assistant for Gulf War Illnesses) in Kuwait's Iraqi Tank Yard

Since the Gulf War, DoD has conducted routine environmental surveillance in the Gulf region. Both the US Army and Air Force monitored DU contamination at existing or proposed areas of personnel concentration throughout the region. The US Army Center for Health Promotion and Preventive Medicine (USACHPPM) conducted the most extensive environmental sampling, with separate surveys in 1991, 1993, 1994, 1996, and 1998. This sampling did not include major tank battlefield areas where DU was fired or targets struck. Except for the Iraqi Tank Yard in Kuwait where captured Iraqi equipment is stored, scientists concentrated their sampling in areas where US personnel lived. These surveys are described below.

USACHPPM initially sampled soil in 1991 in response to the Kuwait oil well fires. From May 5 to December 3, 1991, USACHPPM collected samples at 9 sites in Kuwait and Saudi Arabia where personnel were concentrated. At each location, USACHPPM collected 3 to 5 composite samples from
grids measuring 100 by 100 yards. To better represent the site's contamination, each composite sample consisted of 50 to 100 sub-samples, depending on the consistency of the soil or sand and the sampling depth.

Except for King Khalid Military City (KKMC), USACHPPM returned to the same sampling locations in 1993 to collect additional samples. USACHPPM modified the soil sampling procedures slightly. Instead of composite samples, it collected 15 to 25 individual samples from the same grids sampled in 1991.

USACHPPM conducted its 1994 sampling to support Operation Vigilant Warrior; consequently it sampled only three sites. US forces occupied two of the sites during the operation and stored Iraq's captured and damaged equipment at the third location, the Iraqi Tank Yard. The sampling methodology was similar to the 1991 effort, except the sampling grids measured 25 by 25 yards and the sampling team collected 15 to 20 sub-samples to make the composite samples.

In 1996, USACHPPM evaluated environmental quality near the proposed site of a new US Army garrison. In addition, USACHPPM also collected soil samples at Camp Doha, the Iraqi Tank Yard, and the existing garrison of US Army Forces Central Command-Kuwait. The sampling team collected discrete samples, following the 1993 soil sampling methodology.

USACHPPM summarized its 1991, 1993, 1994, and 1996 sampling survey findings in "Final Soil Report, Depleted Uranium and Isotopic Uranium Analysis Results." In these surveys USACHPPM analyzed 298 soil samples for total and depleted uranium using Inductively Coupled Plasma-Mass Spectrometry. All the samples collected during the four sampling trips were substantially below the Nuclear Regulatory Commission's maximum permissible contamination limit of 35 picocuries of depleted uranium per gram of soil (pCi/g) for radioactively contaminated soils, structures, and equipment released for unrestricted public use. The highest amount of total uranium measured was 7.81 pCi/g from the Iraqi Tank Yard, which is less than one fourth of the NRC's guideline for unrestricted public access. All other samples were less than 2.1 pCi/g total uranium. By comparison, the Agency for Toxic Substances and Disease Registry reports the typical natural concentration of uranium in soil is 2 pCi/g. Isotopic analysis of these same samples detected DU in only five of the 298 soil samples -- two from the Iraqi Tank Yard in both 1994 and 1996 and one from Camp Doha in 1996. Though not addressing battlefield contamination near DU-struck tanks, these surveys reassured the safety and health communities there was no DU contamination of concern to health in those areas of troop concentrations.

In addition to the soil samples collected at the Iraqi Tank Yard (also called the "boneyard," Figure 9) in 1994 and 1996, the team collected samples from vehicles destroyed by DU munitions to evaluate the radiological hazards associated with the boneyard. To determine which vehicles DU rounds hit, the team measured the radioactivity levels at the penetration holes. The team took wipe samples near these holes to determine whether the contamination was "fixed" (in the form, for instance, of hardened molten splatters) or "removable" (in the form of oxides or residues that could be wiped away). The team ascertained the remaining contamination was fixed. To assess personnel exposures at the site, the team collected soil samples on-site in drainage pathways and used lapel-mounted "personal breathing zone" samplers. The report concluded: "[N]o measurements significantly exceeded any applicable regulatory or consensus radiation protection exposure limit values used for assessing radiological health risk. In addition, these results indicate no DU exposure hazard to military personnel working outside the Iraqi boneyard but still within its immediate vicinity as long as there are no ongoing operations within the boneyard."
USACHPPM also radiologically analyzed 216 air samples collected at various military facilities throughout Kuwait and Saudi Arabia in 1991 to determine airborne contaminant levels caused by the Kuwait oil well fires. The report concluded that the airborne concentrations of uranium were not a health concern, stating, "Any dose assessments calculated using the measured radionuclide concentrations from air filter samples are well below US regulatory limits for the general public." [127]

To further evaluate environmental conditions US personnel encountered in Kuwait and Saudi Arabia, the US Army Central Command deployed the 520th Theater Army Medical Laboratory to Camp Doha in early March 1998, supplementing the already-deployed Theater Medical Surveillance Team. These personnel conducted environmental surveillance during the spring and early summer, collecting a total of 22 additional soil samples from areas US forces were occupying or about to occupy, including 4 samples each from the Udari Test Range (a live fire range located near Camp Doha, Kuwait) and Iraqi Tank Yard in Kuwait. The team suspected DU might contaminate both. They slightly modified the soil sampling methodology of USACHPPM's previous efforts by collecting the composite samples in a grid measuring 15 by 15 meters. Each composite sample consisted of 5 to 15 sub-samples. The team analyzed the samples for total uranium and its specific isotopes. Of the samples, 21 contained fewer than 1.34 micrograms total uranium per gram of soil (µg/g). One sample collected at the Iraqi Tank Yard contained 33.0 µg/g total uranium (0.53 µg natural uranium/g of soil and 32.47 µg DU/g). This translates to a total radioactivity of 12.1 pCi/g (0.4 pCi natural uranium/g + 11.7 pCi DU/g), which, although higher than the 7.81 pCi/g total uranium previously measured, is still less than the 35 pCi/g MPCL screening guideline for unrestricted public access. [128]

In addition, the US Air Force has rotated Theater Medical Surveillance Teams to the Gulf since 1996. Between December 1997 and January 1998, one of the teams collected a total of 6 swipe samples, 8 water samples, and 37 soil samples from 3 Air Force bases for radiological analysis. All the samples' radioactivity was below minimum detectable levels or within normal background levels. [129]

Finally, an independent study by Firyal Bou-Rabee, a professor in the Department of Geology at Kuwait University, reported on air, tap water, and soil sampling for ambient uranium at various Kuwait locations. Bou-Rabee found the tap water uranium was very low, which he attributes to the fact Kuwait produces its tap water from desalinated seawater. Although the report did not specify where the study sampled the ambient air, Bou-Rabee concluded, "...these uranium concentrations in the surface air do not represent any substantial radiological hazard for the Kuwait population." The study reported that the total annual intake of uranium by inhalation in Kuwait was less than 0.2 percent of the recommended annual intake limit for the general population. [130]

B. Post-Gulf War Developmental Testing and Evaluation of DU Munitions

The only new DU munition the US has fielded since the Gulf War is the M919 25mm APFSDS-T cartridge, which entered service in 1995 for use in Bradley Fighting Vehicles. The M919 hazard classification testing produced data consistent with those from hazard-testing other DU munitions. The testing report concluded, "There was no indication that any measurable DU became airborne as a result of the External Fire Stack Test." [131] During hard impact testing, less than 10 percent of the DU penetrator was aerosolized. Less than 0.1 percent of the initial mass of the penetrator was in the respirable range. Of the oxide formed, 83 percent was insoluble. [132]
To evaluate the actual hazards of a fire in a fully loaded Bradley Fighting Vehicle, in 1994 the Army also conducted a burn test on a Bradley loaded with tube-launched, optically-tracked, wire-guided (TOW) anti-tank missiles and 1,125 M919 25mm DU cartridges. The fire completely engulfed the Bradley, which burned vigorously for about an hour. After subsiding, the fire continued to emit a plume over the next five hours (with smoldering hot spots) into the next day. The Army testers found 625 of the 1,125 DU penetrators, including 9 live rounds which were found within a few meters of the test pad. The test report indicated a large percentage of the missing 500 rounds was trapped within the melted remains in the vehicle and a significant amount of DU oxide mixed with the ash and settled inside and around the vehicle's hull. Although the fire and subsequent explosions released a small amount of DU oxide, the testers detected only trace amounts on the air monitoring filters placed at various distances from the Bradley during the 29 hours of air sampling. The major difference between the Bradley burn test and previous stack test burns was that testers discovered six readily accessible piles of DU oxide in the Bradley's burned-out remains. This was the first burn test to actually involve a vehicle fire (testers had used metal and wooden storage crates in previous burn tests), making the Bradley test more closely resemble actual battlefield conditions.

The Army also conducted DU hard-impact aerosolization tests on various foreign armored vehicles in June 1995 at the US Army Research Lab Test Facility, located at the Department of Energy's Nevada test site. Several technical and procedural difficulties, e.g., sampler failure, seriously affected the data and limited the conclusions that could be drawn from these tests. Nevertheless, the Army found:

- A DU penetrator's impact against an armored vehicle generates DU aerosols containing particles of respirable sizes inside the vehicle. The concentration of DU aerosol decreases with time, but measurable concentrations of respirable particles remain suspended inside the vehicle hours later;
- Measurable quantities of DU oxide particles can resuspend when individuals re-enter the vehicle; the resuspended aerosols contain particles of respirable sizes.

C. DoD and VA Medical Surveillance Programs for Gulf War Veterans

The Baltimore VA and DoD have conducted a DU medical follow-up program for friendly fire victims since 1993. This Section reviews the key aspects of this DU medical follow-up program, which demonstrates to date that those veterans in the US vehicles hit by DU munitions during the Gulf War have experienced no adverse clinical outcomes attributable to DU since their initial traumatic injuries. (A more detailed description is in Tab P.)

In 1993, the Office of the Army Surgeon General gave the VA Maryland Health Care System-Baltimore Division (VAMHCS-BT, formerly the Baltimore Veterans Affairs Medical Center) a list of 68 persons wounded by friendly-fire incidents in the Gulf War. The VA was able to locate and contact 48 of these veterans and invited them to participate in a DU medical follow-up program; 33 agreed to do so. VAMHCS-BT gave them a comprehensive medical and psychological evaluation in late 1993 or 1994. In 1995, this same group submitted a urine sample. Since then, the VA has invited members of this group back in 1997 and most recently 1999 for a similar battery of tests. Additionally, in 1997 the VA gave 38 non-DU-exposed Gulf War veterans a comprehensive evaluation for comparison with the DU-exposed group.

Many of the veterans participating in the initial Baltimore VA program received significant wartime injuries, including severe burns, traumatic amputations, fractures, and concussions. Of the 33 initial participants, 15 had scattered in their muscles and soft tissues several tiny DU fragments.
be surgically removed without extensively damaging the surrounding tissues. The estimated annual committed effective radiation dose produced by the uranium released by the embedded DU fragments for these veterans is lower than the estimated background exposure for the US population (0.360 rem); only one person receives a higher radiation dose than the Nuclear Regulatory Commission's annual exposure guideline for the general population (0.1 rem per year). Additionally, VAMHCS-BT did not observe any significant localized effects from the DU fragments.

Everyone has some amount of uranium in their urine and body due to small intakes of natural uranium in air, food and water. In 1993-1994, VAMHCS-BT measured the average urine uranium concentration in the 15 veterans who retained fragments and found it was about 150 times higher than the average uranium concentration of the 18 veterans with no fragments. The 18 veterans without DU fragments are believed to have had short-term inhalation exposure to DU in the first minutes after impact and possibly sustained wound contamination from DU oxides. However, their average urine uranium was similar to the average concentrations in civilian populations in previous studies. Urine uranium results for 1995 were very similar to those measured in 1993-1994, indicating "mobilization of DU from shrapnel is occurring on a slow but ongoing steady basis."

Baltimore VA doctors performed a series of clinical laboratory tests and evaluations specifically designed to determine if program participants' DU exposures were affecting their health. High exposure to uranium in laboratory animals has resulted in specific types of kidney damage. No significant relationship was found between kidney function and urine uranium values in the program participants. No uranium-related cancer has been found. The latency period for the onset of cancers from environmental exposure varies from 2-5 years for leukemia to 10-20 years or more for other cancers, so continued medical follow-up is appropriate. Since cancer naturally occurs in about 40 percent of the US population, a significant portion of the test group can be expected to develop cancer over their remaining lifetime. Doctors must continue to evaluate laboratory findings, physical examination results, patients' complaints, and clinical testing results to conclude if the DU exposure is creating adverse health effects.

Studies of other populations with heavy metal (arsenic) exposures showed arsenic in semen, so Baltimore VA doctors measured semen uranium in 22 of the DU medical follow-up program participants in 1997. They detected uranium (0.44 to 2.18 ng/g) in the semen of five participants, all from the DU-exposed group, and in none of five non-exposed veterans tested. Since the DU Follow-up Program's analysis of uranium in Gulf War veterans' semen is the first published analysis of uranium in semen, its clinical significance is uncertain. The uranium exposure apparently did not affect the semen's characteristics. While stating further study is required to fully assess DU exposure's effects on reproductive health, VAMHCS-BT notes, "...no known birth defects in the approximately 20 pregnancies fathered by the DU-exposed group since their return (1991-present) from the Gulf." Elevated urine uranium values were associated with high normal to slightly elevated prolactin levels. Progesterone's role in men is uncertain, although extremely elevated levels are associated with hypogonadism. In women prolactin is associated with lactation.

In 1994 and 1997 the DU-exposed group underwent neurocognitive testing to measure mental functions such as attention, memory, and problem solving. Program participants performed normally on standard,
validated "pen-and-paper" neurocognitive tests. However, VAMHCS-BT found a statistical relationship
between elevated urine uranium and poorer performance on computerized neurocognitive tests[155] with
no deterioration of performance over time. The Baltimore VA doctors stated, "The principal caveat of
the assessment was that the number of individuals with elevated uranium values was small and it
appeared that a few veterans with complex histories may have contributed appreciably to the observed
variance."[156] While it is important to continue studying neurocognitive effects, it is too early to draw
any conclusions from these findings.

VAMHCS-BT medical evaluators report that while these veterans have definite medical afflictions
resulting from their wartime injuries, they exhibit none of the known clinical manifestations seen in
other (civilian) exposed groups from uranium's chemical or radiological toxicity. To date, VA has seen
no adverse effects in kidney function and only subtle irregularities in the reproductive and central
nervous systems of veterans with retained DU fragments and elevated concentrations of urinary
uranium. This study's veterans without retained DU fragments generally have not shown abnormal
amounts of uranium in their urine or any other medical effects from uranium. The 1997 follow-up tests
showed most DU-exposed veterans without fragments continued to have normal urinary uranium values
and those with fragments continue to excrete elevated amounts.[157] The evaluation of the 1999 data
continues.[158]

In the summer of 1998, the VA and DoD collaborated to expand the DU medical follow-up program to
evaluate all veterans who were in or on vehicles struck by friendly fire and those who worked around
DU-struck vehicles or burned vehicles containing DU. The purpose of this expanded follow-up exam,
accomplished in either military treatment facilities or VA hospitals, was to measure the uranium in
participating veterans' urine. While their DU exposures were not expected to cause health effects, DoD
and VA wanted to verify that these veterans had normal amounts of uranium in their bodies. The
program guidelines called for OSAGWI to notify these veterans of their exposures and offer a medical
evaluation. OSAGWI's efforts to identify and contact all individuals in, on, or near vehicles when they
were struck by DU rounds increased the number of veterans in the Baltimore DU medical follow-up
program. In addition to 21 of the original 33 follow-up participants who agreed to participate in the 1999
evaluations, 30 new friendly-fire victims were added to the Baltimore program, including 4 with known
or suspected embedded DU fragments.[159] We have identified all 104 survivors in or on vehicles when
penetrated by DU munitions, of whom 99 are participating in either the expanded DU follow-up
program or Baltimore program.[160] In total, this office has notified 219 Level I and Level II veterans of
the expanded DU medical follow-up program.[161] Level III veterans concerned about their possible DU
exposure can obtain a DU medical evaluation from a DoD or VA physician at their nearest appropriate
facility. Thus far, approximately 400 veterans have taken advantage of this opportunity.[162] In addition
to the standard Gulf War physical, patients in this expanded program submitted a urine sample, which
the researchers evaluated for uranium. For amounts higher than the specified 50 nanograms of uranium
per gram of creatinine, the facility retested the veteran.[163]

As of September 2000, of the 309 veterans who have completed the testing program, 11 veterans
initially tested higher than the screening guidelines. Seven veterans have submitted follow-up samples
and four have either not resubmitted samples for analysis or their results are pending.[164] Three of the
seven retested samples were elevated a second time. The VA is following up with these individuals.
In 1992 the Boston VAMC initiated another DU medical evaluation program examining the 144th Service and Supply Company, New Jersey Army National Guard, which worked in the damaged equipment yard at King Khalid Military City. Approximately 27 members of this unit were exposed to DU for several weeks before learning some of the equipment in the yard was contaminated. Of 12 volunteers from the 144th, 8 underwent urine testing and whole-body radiation counting, while the other 4 underwent only whole-body radiation counting. Although these veterans potentially were exposed to DU dust on and off over several weeks, the tests showed no residual uranium above background. In 1993, 13 members of the 144th provided urine samples to the US Army Center for Health Promotion and Preventive Medicine (USACHPPM), including 7 of the 12 members the Boston VAMC had evaluated. Both USACHPPM and the Environmental Measurements Laboratory of New York analyzed these samples. Their results were consistent with the Boston VA test results -- urine uranium values were within normal background ranges. (Tab P discusses DU medical follow-up programs in more detail.)

D. Medical Testing by Other Laboratories

During the past year, various media reports have cited claims of elevated uranium in urine samples from veterans in the United States, the United Kingdom, and Canada based on unpublished, non-peer reviewed data from US and Canadian researchers who based their conclusions on measurements of uranium isotopes using nuclear techniques. Discussions with scientists have indicated that measuring uranium-238 with these techniques can be subject to considerable error.

Not surprisingly, the discrepancies between the government's and outside laboratories' test results concern veterans. Although standard analytical methods for uranium in urine have been in use for many years, no national or international board certifies analytical laboratories in using these methods. Therefore, to help resolve the issue, we initiated a laboratory assessment study of approximately 10 laboratories that have analyzed Gulf War participants' urine. In April 2000, a non-governmental, independent laboratory started an eight-month study of these laboratories' measuring techniques and findings. All the laboratories participating volunteered to do so.

E. Postwar Research and Literature Reviews

1. Embedded Fragment Research

While there is an extensive database on the chemical and radiological hazards associated with uranium, the Gulf War produced a new medical problem that had not been previously evaluated -- friendly-fire casualties with DU fragments embedded in their bodies. Traditionally, physicians leave metal fragments in a patient unless there is a high risk they will cause further damage, because surgery to remove them may be more harmful than leaving the fragments in place. Because of this standard medical practice, physicians caring for wounded Gulf War veterans left most DU fragments in place but decided to monitor these soldiers carefully with a series of medical evaluations.

In addition to patient follow-up, DoD also funded a series of studies by the Armed Forces Radiobiology Research Institute (AFRRI) and Lovelace Respiratory Research Institute in an attempt to answer theoretical questions about the medical significance of embedded DU fragments. These studies are summarized below.

One study in rats assessed whether DU migrated from implanted pellets and where in the body it moved...
Sprague-Dawley rats were surgically implanted with low, medium and high doses of DU to bracket the estimated amounts in Gulf War friendly fire victims with embedded fragments. Results showed that it moved from the pellet and accumulated in different amounts in the kidneys, muscle, liver, spleen, lymph nodes, testicles, heart, lungs, brain, and bone. DU excretion in the urine was present at the third day (first day measured) and the concentration reached a maximum at six months. While scientists might have expected the amount of DU found in the kidney at six months to poison the kidney, these organs remained normal both microscopically and biochemically, indicating the kidneys may have the ability to adapt to gradually increasing DU concentrations. The fact that DU continued to accumulate in the bone after six months might be because rat bones continue to grow far into adulthood and thus continuously provide new sites for DU deposition. As with other heavy metals, the study also indicated that DU crossed the blood-brain barrier.

Another study in rats with implanted DU or inert metal (tantalum) pellets evaluated the possibility of neurotoxicity (effects on the brain). Here again, Sprague-Dawley rats were surgically implanted with low, medium and high doses of DU to bracket the estimated amounts in Gulf War friendly fire victims with embedded fragments. Because the hippocampus is the region involved in cognition (knowing or perceiving) and learning, researchers chose to examine it, focusing on its electrical properties, after 6, 12, and 18 months. Data from individual experiments in such studies are complex, but the combination of results can be summarized in straightforward terms: the presence of DU in the hippocampal region of the brain changes normal electrical activity there. Changes were related to the length of time the pellets had been implanted. Six months after implantation, the "excitability" of the neurons (that is, the ease of triggering a nerve impulse) in the DU-implanted rats was statistically different from the rats receiving only tantalum. Twelve months after implantation, both the "synaptic signal" (the event that relays the signal between neurons) and the excitability of the neurons were different from the tantalum-implanted animals. These changes did not progress further in DU-implanted rats over the next six months. Eighteen months after implantation, the tantalum-implanted rats showed the normal effects of aging on their electrical activity in the hippocampus and were then no longer different from the DU-implanted rats. It appeared as if the changes associated with aging occurred earlier in the DU-implanted rats.

AFRRI performed a third study to see if the urine or serum of animals with implanted DU pellets contained any substances that can cause mutations. The test was conducted by implanting DU pellets in the leg muscle of rats and inert metal pellets in other rats. Researchers then tested blood serum and urine from each group of rats on a laboratory strain of bacteria that need a mutagen (a substance causing mutations) present to grow. The blood serum from the DU rats and the inert metal rats did not cause mutations. The urine from the DU rats caused mutations in the laboratory bacteria, while the urine from the inert metal rats did not. The higher the DU concentration in the urine, the greater the rate of mutations in the bacteria. The ability of the urine from DU rats to cause mutations is apparently due to the presence of DU in the urine. The kidneys in all the DU rats functioned normally during this entire experiment.

Researchers performed a fourth study to see if DU can make cells in tissue culture transform (change) to start behaving like tumor cells. They put a soluble form of DU, uranyl chloride, in growth medium with bone cells for 24 hours, then removed the cells and put them in new growth medium. Control cells (no heavy metal present) showed transformations in 4 of every 10,000 cells; lead-exposed cells showed 21 per 10,000; nickel-exposed cells showed 28 per 10,000; and DU-exposed cells showed 42 per 10,000. Researchers then injected these transformed cells into a special strain of mice that forms tumors easily. No tumors formed in mice injected with transformed cells from the control cells, while 1 of 10 mice...
injected with lead-transformed cells formed tumors, as did 4 of 12 mice injected with nickel-transformed cells and 8 of 19 mice injected with DU transformed cells. Finally researchers measured how much sister chromatid exchange (SCE) was found in cells exposed to DU. Measuring SCEs is one way to detect abnormal DNA behavior. Lead-exposed cells showed slightly elevated numbers of SCEs; nickel-exposed cells had SCEs similar to the control cells, while DU-exposed cells had twice the number of SCEs as cells not exposed to heavy metals. These studies suggest that DU in tissue culture may be genotoxic (damages genetic material). However, further studies in animals are required to determine if this applies to humans.

A fifth study conducted by Lovelace Respiratory Research Institute evaluated DU's carcinogenic potential in male Sprague-Dawley rats. The studies used three sizes of DU/0.75% titanium (DU/Ti) fragments, a nonradioactive metal (tantalum), and injections of radioactive Thorotrast. The researchers noted that a fibrous capsule developed around the implanted metals, but not around the site of the injected Thorotrast. The capsules around DU implants were thicker. Tumors developed around the Thorotrast injections (positive control) and around some of the capsules of the two largest DU/Ti implants, but not the smallest. Study results indicate DU in sufficient dosage reduced weight gain, caused local tissue reactions, and, for the two largest implants, caused local tumors. Compounds and materials carcinogenic in rats frequently are carcinogenic in humans. However, there are exceptions, particularly when an unusual or peculiar carcinogenic mechanism is involved. For example, many materials are carcinogenic when inserted in rats' subcutis (connective tissue beneath the skin). This phenomenon, "foreign body or solid state carcinogenesis," stimulated much study in the 1960's and 1970's because of the concern about implanted medical devices. Subsequent experience has shown that implanted medical devices have a very low risk of cancer in humans. Thus, further study is needed to clarify the risk of local cancer from embedded DU fragments in humans.

Though these studies do not answer every question about the possible effects of exposure to DU fragments, they justify the need for continued medical surveillance of friendly-fire victims through the Baltimore VA DU Medical Follow-up Program and for further animal studies. In particular, the relevance of the tumors in rats compared to humans needs further studies because of problems in extrapolating studies of solid state-caused cancers in rats to humans. In February 2000, DoD solicited "proposals for studies on biological effects of heavy metals currently used or contemplated for use in armor and as armor penetrators." DoD cited a special interest in research proposals to identify injury mechanisms to heart, liver, kidney, and nervous systems from particulate and solubilized forms and local soft tissue responses produced by embedded fragments." Funding for the research projects will total approximately $5 million.

Although ongoing research will provide further insight into DU's radiological and chemical toxicity effects, the most important medical consideration is the friendly-fire victims' current state of health. While these current studies have indicated subtle changes in reproductive and central nervous systems, to date, the Baltimore DU Medical Follow-up Study has attributed no illness or other harmful effects to DU in the evaluated veterans.

2. Literature Reviews

Three major scientific reviews of the toxicology of uranium and depleted uranium have been published since our initial report was published. The first was the RAND Corporation's "A Review of the Scientific Literature As It Pertains to Gulf War Illness, Volume 7 Depleted Uranium." The study is one of eight the Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses commissioned
from RAND's National Defense Research Institute. The second review, dated September 1999, was the Toxicological Profile for Uranium published by the Department of Health and Human Services' Agency for Toxic Substances and Disease Registry (ATSDR). This document was the final version of the September 1997 Draft Toxicological Profile for Uranium cited in our 1998 report with minor updates. Both the RAND the ATSDR reports have been cited throughout our report.

The findings of these two reports were recently supplemented by a third review. The Department of Veterans Affairs (VA) funded a series of independent investigations by the Institute of Medicine (IOM) to evaluate potentially harmful chemical, biological and environmental agents that may have affected Gulf War veterans. On September 14, 2000, IOM released its first report evaluating four agents: depleted uranium, chemical warfare agents (sarin and cyclosarin), pyridostigmine bromide, and vaccines (anthrax and botulinum toxoid). The IOM researchers considered only published, peer-reviewed, scientific literature and did not collect original data or perform any secondary data analysis. The committee then classified the evidence for association between exposure to a specific agent and a health outcome into one of these five categories:

- **Sufficient Evidence of a Casual Relationship.** Evidence is sufficient to conclude that a causal relationship exists between the exposure to a specific agent and a health outcome in humans. The evidence fulfills the criteria for sufficient evidence of an association (below) and satisfies several of the criteria used to assess causality: strength of association, dose-response relationship, consistency of association, temporal relationship, specificity of association, and biological plausibility.
- **Sufficient Evidence of an Association.** Evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between an exposure to a specific agent and a health outcome in human studies in which chance, bias, and confounding could be ruled out with reasonable confidence.
- **Limited/Suggestive Evidence of an Association.** Evidence is suggestive of an association between exposure to a specific agent and a health outcome in humans, but is limited because chance, bias, and confounding could not be ruled out with confidence.
- **Inadequate/Insufficient Evidence to Determine Whether an Association Does or Does Not Exist.** The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association between an exposure to a specific agent and a health outcome in humans.
- **Limited/Suggestive Evidence of No Association.** There are several adequate studies covering the full range of levels of exposures that humans are known to encounter that are mutually consistent in not showing a positive association between exposure to a specific agent and a health outcome at any level of exposure. A conclusion of no association is inevitably limited to the conditions, levels of exposure, and length of observation covered by the available studies. In addition, the possibility of a very small elevation in risk at the levels of exposure studied can never be excluded.

As previously noted, the primary concerns associated with uranium exposure are its chemical toxicity, primarily associated with renal (kidney) dysfunction attributable to soluble uranium, and lung cancer, potentially attributable to ionizing radiation from the insoluble uranium retained in the deep pulmonary region of the lung. IOM surveyed the literature to assess the current understanding of both these concerns. To understand IOM's conclusions and recommendations, it is important to understand their criteria and the limitations of their available data. For example, IOM stated that little information existed on actual exposure levels for Gulf War veterans for the four agents (depleted uranium, sarin, pyridostigmine bromide, and vaccines) they investigated, and that the amount of exposure is a vital factor when assessing possible health effects. For that reason the committee said it could not draw
specific conclusions about the Gulf War veterans' health problems. It had to review the scientific literature for evidence of health effects due to the agents. Except for background purposes, IOM could not consider USACHPPM's Health Risk Assessment of Gulf War DU exposures because the document was not published in peer-reviewed literature, even though the Scientific Peer Advisory and Review Services of the American Institute of Biological Sciences had reviewed it. Still, the committee was able to draw some significant conclusions. For example, its evaluation of the research data on lung cancer indicated, "...limited/suggestive evidence of no association between exposure to uranium and lung cancer at cumulative internal dose levels lower than 200 mSv or 25 cGy. However, there is inadequate evidence to determine whether an association does or does not exist between exposure to uranium and lung cancer at higher levels of cumulative exposure."

It is important to note that estimated exposures for Level II and Level III scenarios were orders of magnitude below 200 mSv (20 rem). Even with the highly conservative assumptions USACHPPM made in its Health Risk Assessment, it is highly unlikely the seven survivors of the two incidents in which two rounds penetrated the crew compartment exceeded 20 rem, because the rounds did not penetrate DU armor, as USACHPPM assumed. Furthermore, we believe all other Level I scenarios were well below 20 rem because they involved either no or only one penetration of the Abrams crew compartment or they involved the lighter-armored Bradley Fighting Vehicles. (Section VI and Tab O contain USACHPPM's exposure estimates.)

As to kidney disease, IOM concluded that there is "limited /suggestive evidence of no association between exposure to uranium and clinically significant renal dysfunction."[183]

Based on the literature, IOM concluded that there was inadequate/insufficient evidence to determine whether an association exists between exposure to uranium and these health outcomes: [184]

- Lung cancer at higher levels of cumulative exposure (greater than 200 mSv or 25 cGy)
- Lymphatic cancer
- Bone cancer
- Nervous system disease
- Nonmalignant respiratory disease
- Other health outcomes (gastrointestinal disease, immune-mediated disease, effects on hematological parameters, reproductive or developmental dysfunction, genotoxic effects, cardiovascular effects, hepatic disease, dermal effects, ocular effects, or musculoskeletal effects).

For most of these health conditions, the incidence rate among uranium workers was just too low for the committee to draw a conclusion. It is important to note that despite the overall absence of final conclusions in the IOM report, it cited many studies showing no discernable impact of exposure. For example, in the case of bone cancer, IOM commented "...the large size of the Oak Ridge cohort (Polednak and Frome, 1981) does provide some evidence that exposure to uranium is not associated with a large excess risk of bone cancer (e.g., a relative risk of 3.0 or greater)."[185]

The IOM panel called for more research on all four agents studied (depleted uranium, sarin, pyridostigmine bromide, and vaccines). DoD and VA continue to promote such research, with 190 studies examining a full range of possible causes of Gulf War illnesses in progress. The Department of Veterans Affairs will continue to monitor the health of servicemembers with the greatest Gulf War DU exposures in case any long term effect does appear.