DEPLETED URANIUM AND CANADIAN VETERANS

A Review of Potential Exposure and Health Effects

A Report Prepared for the Minister of Veterans Affairs

by the
Scientific Advisory Committee on Veterans' Health

January 2013

ACKNOWLEDGMENTS

The Committee wishes to thank the many individuals who have contributed in different ways to this report.

In particular, we wish to thank Jacinta Keough for the inestimable secretarial and organizational support that she has given throughout, and Dr. Jim Thompson for his diligence in searching out and providing the reference material we required to accomplish our task.

We also wish to thank the Veterans who have taken the time to communicate with us, suggest material for our consideration and appear before the Committee.

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Note 1: *Dr. Morisset is the current Colonel Commandant of the Canadian Forces Medical Branch. The incumbent of this honorary position advises the Surgeon General on matters relating to history, heritage and esprit de corps. He is not involved in administrative or operational matters.*

Note 2: *The views expressed in this report are those of the members of this Committee and are not intended to reflect the position or policy of the organizations with which they are associated.*

ABOUT THE REVIEWERS

An earlier draft of this report was reviewed by three internationally recognized scientists. They were specifically asked to tell us, frankly and objectively, if they considered the report to be clear, accurate, coherent and complete and to make suggestions for how the report might be strengthened.

To the extent possible, their recommendations were incorporated into the report; however, they were not provided with this revised version prior to its release.

We wish to express our gratitude to the following for their valuable contributions:

Dr. Eric Daxon: Battelle Memorial Institute (USA)

Dr. Dominique Laurier: Institute for Radiological Protection and Nuclear Safety (France)

Dr. Nicholas Priest: Atomic Energy of Canada Limited

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SUMMARY

Although extensive research conducted to date suggests that exposure to Depleted Uranium (DU) does not present a significant health risk, some Canadian Veterans nevertheless remain concerned. For this reason, the Minister of Veterans Affairs Canada asked the independent Scientific Advisory Committee on Veterans' Health to conduct a thorough review of the scientific literature on DU, with a view to assessing the likelihood of Canadian military personnel being at risk of developing adverse health effects which could be attributed to DU.

Uranium (U) is a radioactive element which exists in different forms (isotopes). It is naturally present in our food and water at levels which are not considered harmful to our health. DU is a by-product of the enrichment process, whereby natural uranium is made suitable for the production of nuclear power. Unlike the enriched portion, it is not fissile, is much less radioactive and is much denser. This latter property makes it useful for civilian (ballast) and military (armour and penetrating rounds) applications.

DU rounds easily penetrate hard targets (tanks and armoured vehicles) as demonstrated in the Gulf War and Balkans conflict. Canada has not used DU rounds in battle. As it penetrates its target, DU creates small particles that can be inhaled or ingested by soldiers in close proximity. In addition, larger fragments can be embedded in their body. Once inside, the DU can potentially create a rapid onset toxicological effect (mostly on the kidneys) and a more slowly-evolving radiological effect (mostly in the lungs and adjoining lymph nodes).

Before any adverse health effect can be attributed to DU, one must first confirm that an individual has in fact been exposed to DU. Unfortunately, it is not possible presently, to accurately measure the amount of DU that a soldier might have been exposed to on the battlefield. The one exception is a cohort of US soldiers involved in friendly fire incidents during the Gulf War, who still have DU shrapnel in their bodies, and who have since been closely monitored.

The Committee examined the deployment scenarios of Canadian military personnel in theatres where DU weapons were used. The only documented situation in which Canadian soldiers could have been at risk of significant exposure to DU, is the Camp Doha fire in 1991.

Exposure, however, can be estimated by indirect means, such as measuring levels in urine, an approach that has been widely used by Canada and its allies. Live-fire simulations (by the US, UK and France) and modelling have also proven to be reliable methods of estimating exposure.

To better understand the adverse health effects of DU, the Committee examined the numerous studies of civilians (miners and uranium processing workers) who had been occupationally exposed to U for long periods. While these exposures were to U and not DU, they nevertheless provide good substitute measures, since the route of exposure

(inhalation) is similar, as is the toxicological effect. Any radiological effect would, if anything, be overestimated given DU's 40% lower radioactivity.

Mortality and cancer incidence studies conducted by several NATO countries on their military personnel deployed to areas where DU weapons were used, were also carefully examined.

Having completed its thorough reviews, consultations and deliberations, the Committee arrived at the following conclusions:

1) Depleted uranium (DU) is potentially harmful to human health by virtue of its chemical and radiological effects.

2) Within a military setting, the highest risk of exposure to depleted uranium is in those who were: in, on or near vehicles hit with friendly fire; entering or near these burning vehicles; near fires involving DU munitions; salvaging damaged vehicles; or involved in clean up operations of contaminated sites.

3) It is unlikely that Canadian soldiers have been exposed to levels of depleted uranium which could be harmful to their health.

4) There is no consistent evidence from military cohort studies of adverse health effects that could be attributed to depleted uranium.

5) There is no strong evidence of adverse health effects reported in larger civilian studies with longer follow-up periods of populations with increased exposure to uranium (e.g. uranium production and fabrication workers).

6) Our finding that exposure to uranium is not associated with a large or frequent health effect is in agreement with the conclusions of other expert bodies.

7) There are many Veterans suffering from persistent symptoms following deployment or military conflict which, although not linked to specific exposures such as DU, can cause considerable suffering and can be effectively treated.

I. INTRODUCTION

Background

First used militarily during the Gulf War in 1991 and, thereafter, in the Balkans conflict and Iraq, depleted uranium (DU) is alleged by some to be responsible for a number of symptoms and illnesses that later appeared in Veterans of these conflicts.

Although extensive research has been conducted in many countries and by many international agencies on the possible health effects of uranium (U), and more recently of DU, controversy remains. As some Canadian Veterans continue to be concerned that they may have adverse health effects following exposure to DU, the Minister of Veterans Affairs tasked his independent Scientific Advisory Committee on Veterans' Health to:

> (a) Review and summarize the published scientific literature on the human health effects of depleted uranium and evaluate the strength of the evidence for causal relationships.
>
> (b) Assess the information concerning the potential exposures of Canadian military personnel to depleted uranium.

Uranium has been part of our planet's crust since it was formed, and is present in variable amounts in its rock, soil, air and water. Having entered our bodies via the air that we breathe, the water we drink, and the food we eat, its presence can be detected in all humans. It does not play a metabolic role in the human body.

Natural U is a weakly radioactive element which exists in more than one form, called isotopes, each having different radiological characteristics but the same chemical properties. For example, ^{238}U, the most abundant (over 99%), is the least radioactive by virtue of its longest half life which is calculated in millions of years. ^{235}U, unlike the other isotopes of U, is fissile, which means that it can be made to release tremendous amounts of energy for use in nuclear plants and weapons. Because so little ^{235}U is present in natural U (less than 1%), its proportion must be increased when used for energy (except for a few reactors such as the CANDU which use natural uranium) or nuclear weaponry. Enrichment, as the process is called, is accomplished by various centrifugation techniques which results in U that now contains 3% in its fissile form, a concentration suitable for use in nuclear plants. "Weapons grade" U requires a much higher (upwards of 70%) proportion of the fissile form. As the proportion of ^{235}U increases during the enrichment process, that of ^{238}U decreases correspondingly. The U that remains after the enriched fraction has been removed is called DU. It is so named because it has been depleted of its fissile component. Accordingly it cannot be used to produce either nuclear energy or weapons. Furthermore, DU is 40% less radioactive than natural U, which is itself categorized as being weakly radioactive by international standards.

Because DU is one of the densest materials known, it has found many civilian applications including radiation shielding in medicine, drilling equipment, and aviation and nautical ballast. It has two main military applications - defensively as armour plating in fighting vehicles such as tanks, and offensively in armour penetrating munitions. DU is used in a type of anti-armour munition known as long-rod penetrators. Shaped much like an arrow, these long rods are fired at a very high velocity and penetrate armoured vehicles by virtue of their kinetic energy and mass. For DU munitions, the rod is solid DU. DU is far more effective than other materials because of its high density and a property that causes the DU rod to self-sharpen as it penetrates armour. Penetrators made of other materials become blunted as they penetrate. The penetration process generates very fine particles of DU that self-ignite and cool to generate particles that contain DU.

These DU rounds should not be confused with what are generally referred to as 'nuclear warheads'. In fact, DU rounds, unlike conventional rounds, carry no explosive charge. That is not to say, however, that the DU particles released following the penetration of these rounds are innocuous.

Approach to the Study

The Committee, whose members collectively have expertise in scientific, medical and military matters, adopted three guiding principles from the onset: open mindedness, comprehensiveness and clarity in communication.

Accordingly, it has encouraged the input of Veterans via a special e-mail address which allowed any Veteran to freely express his or her concerns. These were taken into account during the review. Furthermore, those Veterans who expressed a desire to appear before the Committee were invited to do so at no personal expense, accompanied by an expert of their choice, if they so wished.

Secondly, the inclusion/exclusion criteria for our literature review were liberal and complemented those used in previous large and comprehensive reviews. In addition to peer-reviewed published articles on human (but not animal) studies, we also examined other material which we felt would further our understanding. These included, for example, reports of the Department of National Defence (DND) Ombudsman, the Canadian Croatia Board of Inquiry, and other reports produced by the Surgeon General. We also examined other documentation such as that produced by the North Atlantic Treaty Organization (NATO), the International Commission on Radiation Protection (ICRP), the European Union, the World Health Organization (WHO), the United Nations (UN), the Agency for Toxic Substance and Disease Registry (ATSDR) and Biological Effects of Ionization Radiation reports (BEIR). Individuals with particular expertise in key areas were also invited to appear before the committee.

Thirdly, our short self-written and independently reviewed report, uses language that, while scientifically sound, can be easily understood by interested, but not necessarily

scientific, readers. We chose not to use the same categories of association that were used in some previous reports, preferring instead to express our conclusions in clear unambiguous terms.

II. HEALTH EFFECTS OF URANIUM AND DEPLETED URANIUM

How Uranium and Depleted Uranium Get into the Human Body

As noted in the Introduction, uranium (U) is widely but unevenly distributed in the environment. It is found in trace amounts in many foods, particularly root vegetables, and there is about 1.5 micrograms (µgs) in each litre of water (ICRP 1975). The estimated average amount consumed on a daily basis by members of the public is 1-2 µgs in food (ICRP 1975), but the amount of U consumed varies considerably depending on where a person lives; for example, people who get their drinking water from wells that derive their water from fissures in bedrock are likely to ingest somewhat more U than those whose water comes from surface sources such as lakes (IOM 2000). On average, individuals have a total amount of 56 µg of U in their bodies, with the skeleton accounting for the largest share at 32 µg or 56%, followed by muscle tissue (11 µg), fat (9 µg), blood (2 µg) and lung, liver and kidney each with less than 1 µg of U (Roth et al. 2001). Only about 2% of the ingested amount is actually transferred from the gastrointestinal tract into the systemic circulation where it is later excreted in the urine. The remainder passes through the gastrointestinal tract without being absorbed and is excreted with feces within a few days (Roth et al. 2001). Consequently, everyone has a measurable amount of U in her/his blood and urine at all times and its excretion can be used to detect incorporated U at an individual level (Roth et al. 2001).

U miners and workers in U processing plants, as a consequence of their employment, are exposed to higher levels of U in the form of U-laden dust than the average person. If these workers inhale the dust, or less commonly, if they inadvertently ingest the dust through hand-to-mouth transfers, U is carried into their bodies. Over time, the technology in mines and processing plants has improved significantly, reducing the amount of dust to which the workers are exposed (IOM 2000). The Canadian Nuclear Safety Commission (CNSC) sets industry standards that dictate the level of exposure that Canadian workers cannot exceed. These standards are derived from the examination of a range of sources of radiological data, for example, animal studies, physiologic human models and studies of the Japanese A-bomb cohort, to determine the tolerable dose limit. The agreed occupational dose limit is one sievert (Sv) over a life time while not exceeding 20 mSv averaged annually over five years and never exceeding 50 mSv in a single year. In contrast, the tolerable dose limit for the public is more conservative. Based on what are considered the attributes of detriment of radiation exposure, the limit for civilian populations was set at 1 mSv per year above which protective action needs to be taken (Butler and Cool 2010).

In underground U mines, the largest health risk is attributed to the inhalation of radon, a radioactive, colourless, odourless, noble gas that occurs naturally as an indirect decay

product of uranium. While U is only weakly radioactive, radon is not because its half-life is much shorter than that of U. Exposure to radon and its progeny has resulted in higher lung cancer rates in miners and these were mistakenly attributed to U in earlier studies. Control of dust and improvements in ventilation in both mines and U processing facilities have removed much of the danger (IOM 2000).

Considerable research has been conducted on the health effects of U on miners and processing plant workers. This is reviewed in another section of the report.

How Uranium & DU Affect Health

The toxicity of U and DU has both a radiation and a chemical dimension. DU is less radioactive than U but from a chemical perspective, the two are equal. There are four factors that influence the probability of harm from U and from DU: the dose; the length of exposure; the solubility of the particles of U/DU that are ingested or inhaled; and in the case of inhalation, respirability. DU can be taken into the body through inhalation, ingestion, wound contamination and injected fragments. Inhalation is the route of concern for Canadian soldiers. The chemical form, the amount inhaled, the size of the DU particles that are inhaled and the site in the respiratory tract where they are deposited are other critical features determining the potential for damage (IOM 2008). Larger particles do not reach the lungs but rather are lodged in the nasal passages or the tracheobronchial area of the throat where mucociliary action transports them to the pharynx where they are then swallowed and excreted in feces. It is the smaller particles that pose a greater threat because they are able to reach the deeper parts of the lungs including the terminal bronchioles and alveoli as well as the lymph nodes (ICRP 1994; IOM 2000). Importantly, research based on U processing plant workers has estimated that only 1-5% of inhaled U particles will actually reach the lungs (Davies 1961).

U occurs in both soluble and insoluble compounds with other elements including oxygen and fluorine. There are three levels of solubility or dissolution: fast (F), medium (M) and slow (S). The most soluble compounds, that is, Type F (uranyl fluoride (UO_2F_2), uranium tetrachloride (UCl_4), uranium hexafluoride (UF6) and uranyl nitrate hexahydrate ($UO_2(NO_3)_2.6H_2O$), are absorbed relatively quickly from the lungs (usually within hours or at most, days) and are also absorbed from the gastrointestinal tract into the blood and then cleared through the kidneys. Type M dissolution compounds including uranium trioxide (UO_3), uranium tetrafluoride (UF_4) and uranyl acetate ($UO_2(CH_3CO_2)_2$), are not as soluble as those noted above and it can take weeks before they dissolve and are absorbed into the blood. The least soluble compounds, Type S, uranium dioxide (UO_2), uranium peroxide (UO_4) and uranium octaoxide (U_3O_8), may take years before they become solubilized and absorbed into the blood (NRC 2008). It has been found that the more soluble compounds are most toxic to the kidneys because they quickly reach higher blood and kidney concentrations, while the less soluble oxides produce a larger radiation dose to the lungs and lymph nodes because of their longer exposure (NRC 2008). Solubility influences the length of exposure. Those that are soluble clear the body quickly while those retained, such as in shrapnel, expose the surrounding tissue over much longer periods and in some cases years (McDiarmid 2012). Respirability

refers to the size of the particles that are inhaled. Larger particles do not reach the lungs but very small dust particles can reach deep into the lungs where they have the capacity to do more damage (Gulf Link 2012).

Radiologic Effects of DU

Radiologically, the DU used for weapons is typically 40% less radioactive than natural U which itself is classed as a weakly radioactive element. Nevertheless, the three isotopes that comprise DU are radioactive with ^{234}U being the most and ^{238}U the least radioactive (see Table 1). In addition to these three isotopes, DU contains trace amounts of ^{236}U and other elements such as plutonium, americium and technetium. These add little to the overall radioactivity of DU and are not regarded as posing a health risk.

Table 1. Isotopic Comparison of Natural and Depleted Uranium

Isotope	Radioactivity	Natural Uranium	Depleted Uranium
	µCi/g	Concentration of Isotopes	Concentration of Isotopes
^{234}U	6200.0	0.0058%	0.001%
^{235}U	2.2	0.72%	0.2%
^{238}U	0.33	99.28%	99.8%
Relative Radioactivity		1	0.6

(Health Canada 2008)

The radiologic threat that U and DU pose to human health comes from the transfer of sufficient energy from ionizing radiation to change the structure of molecules within cells including their DNA. The damage caused can be beyond the cell's capacity to repair itself. These cells may die or the damaged cells may lead to cancer or, if the reproductive cells are involved, to genetic changes (NRC 2008). Isotopes of U and DU emit alpha particles, beta particles and photons. The majority are alpha particles and although they are a form of ionizing radiation, they do not have the capacity to penetrate the outer layer of the skin. Consequently, they only pose a radiation risk when they are taken into the body (NRC 2008). The radiologic risk from inhaled DU is the development of lung cancer as a result of alpha radiation, but it has been estimated that it takes at least 10 years of exposure and perhaps even longer, before this risk is realized (IOM 2000; 2008). Ingested as opposed to inhaled DU does not pose a serious radiological risk by virtue of the fact that it is excreted rapidly (NRC 2008).

The NRC (2006) developed a model to assess the risk of developing cancer from exposure to radiation. The linear no-threshold (LNT) dose response model, which is a mathematical model, proposes that risk increases with increasing dose or exposure to radiation. Interpreting this model leads to the conclusion that no level of exposure is without risk and this risk increases proportionately with exposure. The IOM Committee

on Gulf War and Health (2008) supports this model for determining risk to populations, but has chosen not to apply it when considering individual risk. In contrast to assessing risk for developing cancer, the NRC Committee noted that its model does not apply to non-cancer health effects. While non-cancer diseases including cardiovascular disease have been linked to populations exposed to high doses of radiation such as Japanese survivors of the atomic bomb attacks, there is insufficient evidence to quantify risk, if it exists, at exposure to low doses, that is, doses below 100 mSv (NRC 2006). Exposure to low doses is an under-researched area and there is too little evidence to draw conclusions between health effects and low dose exposures.

Toxicological Effects of DU

As noted earlier, whereas U is more radioactive than DU, there is no difference between them chemically. Like other heavy metals such as lead, mercury and plutonium, U is chemically toxic (Roth et al. 2001) and consequently, so is DU. All three isotopes that comprise U and DU are equally toxic from a chemical perspective (McDiarmid 2012). Whether DU is inhaled or ingested, most ends up being excreted in urine and in feces. As mentioned earlier, the rapidity with which this occurs is dependent largely on the solubility of the compounds involved. The kidney is the organ most at risk for damage because of its role in clearing the U from the blood and excreting it. In the process of doing this, the U accumulates in the epithelium of the renal tubules which, within a few days of heavy exposure, causes the epithelial cells to die and the tubular walls to atrophy. There are also glomerular changes. These changes lead to a decrease in the reabsorption of glucose, sodium and amino acids into the blood resulting in increased glucose levels in the urine and in proteinuria (TRS 2002; IOM 2008). The severity of damage depends on the U level. A single inhalation of 8 mg of soluble U is regarded as the threshold level for transient kidney toxicity, that is, these changes are totally reversible; permanent damage can be caused by 40 mg. (Roth et al. 2001). There is still much to be learned about the link between levels of U in the urine and clinical symptoms despite the fact that many animal studies have been conducted to better understand the mechanisms of kidney injury that U can cause.

Exposure Scenarios

Depleted uranium has a number of uses in civilian and military arenas. In civilian life, these uses are generally outside the purview of most people and there is little name recognition of this metal. It is only in untoward circumstances that the public may become aware of its utilization. One of these circumstances relates to the use of DU as ballast in airplanes. This has no impact at all on human health except for those occasions when an airplane crashes and burns, and the DU burns as part of the conflagration. This occurred outside Amsterdam in October 1992 when a Boeing 747-258F cargo plane crashed into two apartment buildings short of the runway at Schiphol airport (TRS 2002; Bijlsma et al. 2008). The crew and many people in the apartments were killed by the crash and the resulting fire. Firefighters and police officers responded

immediately to fight the fire and rescue victims. Consequently, these workers were at much higher risk to exposure to DU than people residing in the neighbourhood. Subsequently the wreckage was moved to a hangar where it was inspected and catalogued by workers. The plane carried 282 kg of DU as ballast but only 130 kg was recovered (TRS 2002). It was assumed that the remainder was consumed in the fire which created the possibility that uranium oxide particles could have been produced and dispersed in dust and smoke, and subsequently inhaled or ingested. This concerned the rescue and hangar workers and led to a study started in 2000 of the health effects of their participation in the tragedy. A total of 2,499 workers participated and the results showed that the exposed workers did not have significantly higher U concentrations than the non-exposed comparison group, nor did they demonstrate any presence of DU in their bodies (Bijlsma et al. 2008).

Military personnel may encounter DU in the course of their duties. Because of its density, DU is a valuable adjunct to weaponry. Used as armour in some tanks, it serves to protect the occupants from incoming munitions because most cannot penetrate it. It is also used in rounds to increase their capacity to penetrate vehicles such as tanks. Normally it only becomes a threat to military personnel if a DU projectile strikes a sufficiently hard target that causes the DU to fragment, spontaneously ignite and create dust that contains DU particles. This dust may be inhaled or ingested by the soldiers or anyone in close proximity to the impact. The most common forms of U following the firing of DU munitions are uranium oxides (UO_2, UO_3, and U_3O_8). However, it should be noted that aerosols produced by the impact of DU penetrators on armour will contain not only DU but also metals present in the target.

Many countries whose soldiers could have been exposed to DU carried out research subsequent to these deployments to ascertain whether their personnel had sustained any ill effects. This research is described and analyzed in detail later in this report.

Summary

Because of the widespread occurrence of U in soil and water, everyone has some U in her or his system. Although the amounts vary depending on where people live and their diets, in most places they are miniscule and do not affect human health. Beyond the general public, there are groups of individuals who, through their employment, routinely encounter much greater exposures to U. Except in rare circumstances, these long term exposures do not negatively affect their health.

III. ASSESSMENT OF EXPOSURE BY CANADIAN FORCES PERSONNEL

The overall objective of epidemiological research is to determine if exposure to a suspected agent, in this case depleted uranium (DU), is associated with the manifestation of given adverse health effects. For DU to pose a human health risk, DU-contaminated particles must be internalized through inhalation, ingestion or wound

contamination. The resulting adverse radiological and chemical health effects from such exposures are discussed at length in other sections of this report. We will now turn our attention to the exposure side of the equation.

While exposure can be measured accurately in strictly controlled animal experiments, such is not the case with human studies for many reasons, not the least of which are ethical. As imperfect as human epidemiological studies may be, they nevertheless provide scientifically sound approximations of exposure of individuals and groups in non-military occupational settings, such as workers in the U processing industry, populations living in the vicinity of these industries, nuclear plant workers, etc. While the lengthy exposure in these individuals was to U and not DU, the findings can nevertheless be extrapolated to a certain degree, since the chemical effects of both forms are similar. So are the radiological effects, the difference being that they are lessened, because DU is less radioactive than U.

The more immediate concerns that prevail on the battlefield preclude a direct, reliable measurement of exposure, and this has been a frustrating limitation for virtually everyone who has conducted military studies of DU. There is, however, one exception, and that is the cohort of US soldiers who have been, and continue to be, exposed to DU by virtue of having fragments of DU shrapnel embedded in their bodies, the result of friendly-fire during the Gulf War. This group has been extensively followed up since, and this has allowed researchers to draw valuable conclusions about DU's effect in humans. This is discussed in a later section of the report.

Valuable exposure information has also been produced by some NATO Forces through controlled experiments, whereby DU rounds were fired into unoccupied military vehicles thus allowing them to measure the resulting amounts of DU particles under various conditions. (See **Annex A**).

Battlefield exposures have been categorized to provide a standard reference framework. They are:

> Level I: Soldiers either present in or on a vehicle at the moment of impact by a DU penetrator and the first responders entering immediately thereafter.
>
> Level II: Individuals who worked inside these vehicles for lengthy periods well after the impact.
>
> Level III: All others who may have been downwind from impacts or fires, entered contaminated vehicles briefly, or were exposed to resuspended particles from contaminated ground.

Before discussing the risk of Canadian soldiers being exposed to DU, some background information might be useful.

The Canadian Forces do not use DU munitions in their tanks or aircraft. For a brief period however, some ships were so equipped (Phalanx System) but with the exception of the firing of test rounds in the open sea, they have never been used in battle. As confirmed by experts who testified before the Committee, the onboard storage of these rounds was done in a safe manner so as not to present any health risk to the ships' personnel.

None of the enemies facing coalition forces in any of the conflicts where Canadian groups were engaged, had DU weapons.

The actual fighting during the Gulf War took place in January and February of 1991. Canada did not commit ground combat troops to this brief and decisive battle, in which DU rounds were extensively used by US and UK armoured vehicles. Canada's major presence on the ground during the war was a Canadian field hospital which was deployed in support of a UK armoured division. This hospital, however, was well south of the battle, having been set up some 80 kilometres south of the Iraqi border, in Saudi Arabia.

After the war (April 1991), a group of some 290 Canadian combat engineers were deployed as part of a UN mission (UNIKOM) to clear land mines and set up observation posts in the demilitarized zone along the Iraq/Kuwait border. They were stationed at Camp Doha, near Kuwait City, adjacent to a US compound where DU armoured tanks were held ready in case of an Iraqi counterattack. A fire accidentally broke out in the compound, and some Canadian soldiers entered it to render assistance in the early stages. The US Army subsequently completed a comprehensive exposure analysis (Scherpelz et al. 2000) which the Committee has carefully examined. It determined that no DU oxides were released into the air for several hours after the fire had started, since the heat had not built up sufficiently to cause the rounds to ignite. Accordingly, any Canadian soldiers who would have entered the compound at the very beginning, would have been at little risk of contamination by DU. They would, however, have likely been exposed to other fire-related contaminants. The risk of airborne downwind contamination was carefully assessed and it was concluded that given the wind direction and the low level of respirable DU particles that were released into the air, the Canadian soldiers would have had, at most, a level III exposure, a level that has not been shown to be harmful. The highest exposure at Camp Doha (level II) was experienced, not by Canadian soldiers, but by some US personnel who participated in the subsequent clean-up operations of their compound many weeks later.

The only Canadian investigation of the Camp Doha incident, a National Defence Ombudsman Report (CF/DND Ombudsman 2006), did not specifically focus on causes of illness. While it did mention the fact that some of the soldiers who were interviewed were concerned that they may have been exposed to various contaminants, DU is not specifically mentioned. Interestingly enough, the Ombudsman commented on the military's inability "to account with certainty for every person who has served in a particular deployment". Although the exposure of the soldiers at Camp Doha was estimated to be too low to produce any adverse health effects, the Surgeon General's

medical staff nevertheless carefully reviewed their individual medical files in 2001 in response to suggestions in the Canadian media of increased sickness amongst Camp Doha Veterans. Although no abnormal increase in mortality or morbidity was detected during this review, individual letters, signed by the Surgeon General, were sent to every soldier explaining the situation, reassuring them concerning the risk, and also inviting them to 'report any health problem they feel may not have been identified during the review of their health records' to his medical staff. It would appear that no responses were received.

As this constitutes the group of Canadian soldiers having had the highest potential of exposure to DU, the Committee considered the possibility of completing a specific mortality and cancer incidence linkage study of this cohort. However, it decided against it on the advice of other scientists including statisticians from Statistics Canada, because such a study would have had limited scientific validity on account of the small numbers involved and the presence of confounding variables.

Unlike the Gulf conflict, the Balkans war was not a tank war, and no large calibre rounds were fired by coalition forces during this conflict. However, smaller DU rounds were fired by US A-10 aircraft at enemy vehicles and hardened positions. Many of these rounds remained intact, since they either missed their targets or went through the lightly armoured enemy vehicles and lodged deep into the soil.

As NATO kept a record of these A-10 bombing coordinates, one could compare them with the positions of Canadian troops. The Committee deemed that this approach would be of limited value, given the incomplete nature of the NATO information and the inability of precisely locating, in time and place, the Canadian formations, and even less so, of its individual members.

As the enemy had no DU weapons in any theater of operations where Canadian troops were deployed, and because no Canadian troops were ever reported to have been hit by friendly fire, their only other possible exposure would have been through resuspended airborne DU contaminated particles, in much the same manner as the civilian populations may have been. In this respect, extensive post-Balkans conflict environmental studies were conducted by the United Nations Environment Program (UNEP) and its team of international experts in Bosnia and Herzegovina, Serbia and Montenegro, and Kosovo (UNEP 2003; UNEP 2001; UNEP 2002). They all arrived at the same conclusion, that is, with the possible exception of those involved in cleanup operations of heavily contaminated soil or vehicles and children playing in these vehicles for prolonged periods, the civilian population is not exposed to levels of DU which could pose a problem to their health. The European Commission’s Scientific Committee on Health and Environmental Risks (SCHER) arrived at essentially the same conclusions after their 2009 review of DU (SCHER 2010).

A 2002 study that examined uranium levels in the urine of Canadian Forces Veterans of the Gulf and Balkans conflicts (Ough et al. 2002) concluded that their uranium level was comparable to that of the Canadian civilian population exposed to normal and safe

background amounts of uranium. No DU was detected in the urine of any member of the study group. Similar studies have been conducted by many NATO nations on their respective military populations: UK; (UK DUOB 2007; Bland 2007); Germany (Oeh et al. 2007); US (Squibb and McDiarmid 2006; Dorsey 2009); France (Cazoulat et al. 2008); Belgium (Hurtgen 2001); Italy (Ministero della Difesa 2002) and Sweden (Sandström 2001) and they have arrived at the same conclusions. The US studies are interesting in that they include Veterans with historically high levels of documented inhalation exposure and those with retained DU fragments. The only elevated levels of urinary U were amongst those with retained fragments. All others had levels similar to those of the general population.

With respect to more recent conflicts, DU weapons were not used by either side in Afghanistan, where Canadian soldiers were extensively involved for over 10 years. While DU weapons were used in Iraq, Canadian troops were not deployed in that conflict.

Summary

With the exception of the US cohort of friendly fire soldiers from the Gulf War, the Committee found no evidence of any allied soldiers having been directly and specifically exposed to DU. With respect to Canadian military personnel, a few Canadian soldiers may have been exposed to DU during the Camp Doha fire, but this has been estimated to be at levels too low to produce adverse health effects. These soldiers would have also been exposed to other inhalations during this fire, which makes the attribution of any effect to DU specifically, very difficult. Large urinalyses studies designed to retrospectively assess prior exposure to DU have reported levels that were comparable to those of normal civilian populations.

In view of this, the Committee considers that it is unlikely that any Canadian soldiers have been exposed to levels of DU which are deemed to be harmful to their health.

IV. RESEARCH ON THE HEALTH EFFECTS OF URANIUM ON CIVILIAN POPULATIONS

The effect of U on civilian populations of miners and U processing plant and uranium-phosphate fertilizer plant workers has been studied. Summaries, analyses and conclusions of these studies and systematic reviews of sub-groups of studies follow. Our report does not discuss the research on the health effects of uranium in drinking water because this method of ingesting uranium bears little relevance to the possible exposure to DU experienced by Canadian military personnel. This topic, however, has been reviewed by Canu, Laurent et al. (2011).

Research on Uranium Miners and Uranium Processing Plant Workers

A. Miners

A number of epidemiologic studies of the health of U miners have been conducted. In studies in the United States, Canada and Czechoslovakia, the mortality rates of miners from lung cancer were significantly higher than comparison groups of non-miners. For example, a case control study of 9,817 miners from the Colorado Plateau followed from 1960 to 1980, reported a strong positive relationship between U mining and risk of lung cancer; miners with more than 11 years of underground exposure had a relative risk (RR) of 8.5 of developing the disease, that is, they were 8.5 times more likely to develop lung cancer than a population that had not been exposed to U mining (Saccamano et al. 1986). In Canada, studies in Saskatchewan, the Northwest Territories and Ontario reported similar results (IOM 2000).

While much has been done to improve the working conditions of U miners over time, recent studies demonstrate that the risk to these miners of developing cancer continues to be greater than the risk faced by comparative non-U mining populations. Tirmarche et al. (2012) concluded that chronic exposure over 10 years, the age at exposure and the interaction between tobacco smoking and radon contributed to this excess risk. Importantly, the major contributing factor is radiation from radon gas in the mines, while U contributes little to the development of lung cancer.

B. Uranium Processing Plant Workers

In contrast to U miners, U processing plant workers are not exposed to radon gas; for them the risk comes from the inhalation of dust that has U compounds attached. Three systematic reviews have been conducted of epidemiologic studies on the health risks to American, British and Egyptian workers in U processing and enrichment plants, in a nuclear weapons plant and in phosphate-fertilizer production plants in Florida. Most of the U plants processed U ore to produce triuranium octoxide (U_3O_8 or yellow cake) that is shipped to enrichment facilities where it is processed into uranium hexafluoride (UF_6) used to create fuel for nuclear reactors. The fertilizer plant workers are exposed to U because phosphate rock which contains elevated concentrations of natural U and waste solutions containing U from the nuclear fuel industry are used in the production of fertilizers (WISE 2011). These studies are relevant to this examination of the risks of DU because unlike miners, these workers were not exposed to radon so if they suffered negative effects to their health, it is more likely that these effects could be attributed to U. Their type of exposure was inhalation of dusts to which U compounds were attached, which is similar to the exposure of military personnel involved in war zones. Since U and DU are chemically identical, these same effects could be found in populations exposed to DU. Since the studies of uranium plant workers may illuminate potential health threats to military personnel who are exposed to DU, a more extensive review of the research conducted on these workers is presented.

The three systematic reviews have been carried out on subsets of a total of 27 studies conducted on workers in U processing plants, phosphate-fertilizer plants and one nuclear weapons plant. The systematic reviews assess the strengths and weaknesses of the designs of the research, determine the confidence with which the findings can be viewed, and summarize and draw conclusions about what has been learned from examining the totality of the studies. In this section attention is paid to the evaluations of the quality of the studies, the health outcomes included and the conclusions they reached.

The first of the systematic reviews was carried out by the Institute of Medicine Committee on Health Effects Associated with Exposures During the Gulf War (IOM 2000). Twelve American studies of civilians involved in uranium milling were included. (Annex B, studies 1-3, 5-7, 11, 13, 14, 16, 17, 27). This report included detailed descriptions of the nature of the work carried out by the workers in each of the sites, the size of the cohorts involved, the average number of years the workers were employed in the plants, the mean number of years of follow-up where it was available, their exposure to radiation, the analytic methods used, the strengths and limitations of each study and an analysis on a disease-by-disease basis of the strength of the evidence for associations between health outcomes and exposure to U (IOM 2000). These diseases included lung, lymphatic and bone cancer, and non-malignant renal, neurologic and respiratory disease. They examined a range of other diseases but these were based on case reports rather than epidemiologic studies of the populations of workers. This review was the only one to include a case control study (Dupree et al. 1995). The sample for this study overlaps with samples in three other studies in this set (Ritz 1999; Checkoway et al. 1988, Frome et al. 1990) so the results cannot be viewed as independent of these others. The strengths of this case control study are its robust dose response analysis and detailed estimation of individual exposures (IOM 2000).

A second systematic review was undertaken by the Institute of Medicine Committee on Gulf War and Health: Updated Literature Review of Depleted Uranium, and published in 2008. This Committee expanded the number of studies reviewed to 25 (Annex B, 1- 13, 16-27) and included workers in facilities in the US, United Kingdom and Egypt. This review is the most comprehensive of the three in terms of the number of sites, types of cancer and non-malignant diseases assessed and information provided to the reader about the strengths and limitations of each of the studies. The third systematic review, also published in 2008, was conducted by two committees of the National Research Council, the Committee on Toxicologic and Radiologic Effects from Exposure to Depleted Uranium During and After Combat and the Committee on Toxicology. These Committees focused on 14 studies (Annex B, 3-5, 7-8, 11, 14-16, 18-19, 21-22, 25) and all but one were also included in the 2008 IOM Committee review. This review included information on a broad range of cancer types but provided the least information about the quality of the studies included.

Across the three reviews considerable attention was paid to factors that affected the quality of the studies including the critically important *approach to measuring exposure*.

Four methods of measuring exposure in decreasing order of rigour were identified by the 2000 IOM and the 2008 IOM Committees: direct measurement in individual workers using radiation film badges, using work history to model cumulative exposure, classifying workers by maximum exposure and no measurement of exposure. The largest number of studies (10) were those that had access to workers' radiation badges even though for many studies only a portion of the workers had these badges.

A second major factor that influences quality is the *use of comparison groups* (IOM 2000). The majority of cohort studies in this series used standardized mortality ratios (SMRs), that is, death rates of the age-appropriate population of the country in which the study was conducted as the comparator. An SMR is a comparison of the number of the observed deaths in a population with the number of expected deaths. It is expressed as a ratio of observed to expected deaths multiplied by 100. If an SMR equals 100 it implies that the mortality rate of interest is the same as the standard mortality rate. A number higher than 100 implies an excess mortality rate whereas a number below 100 implies a lower than expected mortality. When an SMR is accompanied by a 95% confidence interval (CI) or a p-value equal to or less than .05, it allows the reader to determine the certainty with which the mortality rate is likely to occur within the range. For example, an SMR of 105 with a 95% CI of 80-110 means that 95% of the time, the death rate of the population of interest will lie between 80-110 and therefore, as the SMR falls within it, it is not exceptional and does not differ significantly from the population as a whole.

The IOM (2000) authors point out that the phenomenon of 'the healthy worker effect' must be taken into account when interpreting the results. If the SMR is below 100, the results may be explained by the fact that people who work are likely to be healthier and have lower death rates on the whole than the group with which they are being compared. A preferred method is to compare the cohort of interest to other groups within the same organization that have different levels of exposure, in this case to uranium. The authors of this review point out, however, that even this may not overcome the problem of inadequate comparison groups if other confounding variables such as smoking and length of exposure may differ and have more explanatory power than the exposure differences. An alternative is to calculate a standardized rate ratio (SRR) which uses multivariate analyses levels and takes into account the value of other confounding variables to compare groups that have experienced different exposure levels. Studies by Ritz (1999), Hadjimichael et al. (1983), Dupree et al. (1995), Frome et al. (1990) and Checkoway et al. (1988) used this approach.

The third major factor that contributes to quality is *following up the cohort for an adequate period*, that is, sufficient time must be allowed for the health outcome of interest to occur. Cancer is a primary example of this since the latency period for most cancers is at least 10 years, so cancers that occurred in the cohorts of these studies in less than 10 years should have been eliminated before calculating the SMR to provide a more accurate result (IOM 2000). While some studies provided mean number of years of follow-up, most only described the number of years over which the workers may have been employed and when the follow-up ended so it was not possible to determine the

average length of follow-up for the workers involved. A fourth factor is *sample size*, which means the sample must include enough people followed for adequate lengths of time to have sufficient statistical power to calculate SMRs.

Annex B provides information on the sites where studies were carried out, the studies that were reviewed, the number of workers involved in the analysis, the study design, the radiation dose and the years of follow-up.

Annexes C and D provide results from the studies reviewed, the SMRs and the 95% confidence limits for cancers and for non-malignant diseases respectively. The information in these tables is derived from Tables 8.1-13 of the IOM report (2008, p.190-229) and Tables 5.2 and 6.4 of the NRC (2008, p. 61-62, 78-80) report.

In reviewing Annex B, it is hard not to be impressed by the limited information provided in many of the studies about the radiation dose received by the workers and the years of follow-up, both critical quality criteria. Even when radiation dosage is available through use of dosimeters, it is frequently only available for a portion of the population involved. On the other hand, the number of studies is substantial, the size of the population in many studies is large enough to achieve statistical power and SMRs and their confidence intervals are available for all the cohort studies.

Analysis of cancer outcomes (based on IOM 2008 and NRC 2008)

Lung Cancer:

Twenty-three of the studies examined the relationship between exposure to U and lung cancer. Some of these studies reported statistically increased SMRs while others did not. The strongest studies methodologically did not find an association. The IOM Committee concluded, “there is no consistent evidence of an effect of exposure to natural . . . uranium on lung cancer incidence in the studies reviewed” (IOM 2008, p. 172). They did recommend that monitoring for a possible association between U and lung cancer continue because of the limitations in many of the studies. The Dupree et al. (1995) case control study reported that there was no relationship between a cumulative lung radiation dose up to 25 mSv lagged for 10 years, and lung cancer mortality and that there were too few cases above this level to draw conclusions. Similarly, there was no relationship found between external exposure and cancer deaths except where the workers were 45 years or older when hired. They did note that smoking status was not traceable on all pairs which could influence the results.

Leukemia:

Twenty-two of the 23 studies that examined leukemia reported insignificant increases and decreases in risk associated with exposure to U. The one significant finding (Boice et al. 2003) reported a reduction in leukemia, but there were substantial weaknesses in the study. The Committee (IOM 2008) did not recommend further studies of association between leukemia and U.

Lymphomas (Hodgkin's and non-Hodgkin's):
The 13 studies that assessed the risk of Hodgkin's lymphoma split between reporting increased, no difference or decreased risk (IOM 2008). A total of 24 studies examined the association between non-Hodgkin's lymphoma and U. Most of the results showed either no increased risk or a decrease. The Committee concluded there was a lack of strong and consistent evidence linking U and lymphatic cancers; however, they recommended that further research explore these relationships because U is known to accumulate in lymph nodes (IOM 2008).

Other Cancers: Bone, Renal, Bladder, Brain & CNS, Stomach, Prostate, Testicular:
An analysis was done on the association between U and each of these types of cancers across the studies that comprised the IOM (2008) systematic review. The number of studies included in each assessment of association ranged from 12 to 20. In each cancer type, the IOM Committee reached the conclusion that there was little consistent evidence pointing to an increased risk as a result of exposure to U. In all but two cancers the Committee did not recommend further study. One of the exceptions is brain and central nervous system cancer because there was a fairly even division in increased and decreased risk in the results of the 14 studies included in the review. This led to the recommendation that further study would be useful in trying to reach a more definitive conclusion. The other exception is testicular cancer. There was no consistent evidence of a relationship between testicular cancer and U but because this type of cancer is of particular interest to American Gulf War Veterans, the IOM Committee (2008) recommended further study. Neither of these recommendations was assigned a high priority.

Non-Cancer Outcomes (based on IOM 2008)

Non-malignant Renal Disease:
Fourteen studies assessed the risk of renal disease associated with exposure to U. Four noted an excess in mortality in studies in the US and the UK, and in different facilities in those countries. In no study was this increase statistically significant. Furthermore, alternate explanations for the increased risk were posited. Three other studies reported significantly fewer deaths and one reported no difference. A major limitation in most of these reports was the inability of the researchers to isolate the effects of U from that of other heavy metals and chemicals to which the workers were exposed. The IOM Committee (2008) concluded that the results from these studies did not demonstrate substantial evidence of an association between U and "important clinical renal effects in humans" (IOM 2008, p.182); however, the Committee also determined that it could not rule out renal effects after exposure of any magnitude. The Committee, therefore, recommended that further studies be conducted to explore the association between U and non-malignant renal disease.

Other Non-Malignant Outcomes: Respiratory Disease, Neurologic Effects, Cardiovascular Effects

Respiratory Disease:

Fourteen studies included the outcome of non-malignant respiratory disease. Three studies (Pinkerton et al. 2004; Waxweiler et al. 1983; Frome et al. 1990) reported a significant excess of deaths of workers on the Colorado Plateau and Oak Ridge, Tenn. but these findings reflected the experience of workers prior to 1955 when they were exposed to more dust, silica and vanadium (IOM 2008). A later study by Ritz et al., (1999) demonstrated a significant decrease in deaths. The Committee (IOM 2008) concluded that there was support for employment in uranium-processing plants having an effect on non-malignant respiratory disease but these results are confounded by the "concomitant coexposure of such workers to other respiratory toxicants (such as silica, asbestos, and vanadium)" (IOM 2008, p. 184). Consequently, they recommend more studies be undertaken to better understand the relationship between U and non-malignant respiratory disease.

Neurologic Effects and Cardiovascular Effects:

The eight studies of neurologic disease in uranium processing plant workers did not demonstrate any excess in mortality nor did the four studies that tracked the association between U and cardiovascular effects. Indeed, all four reported fewer deaths from cardiovascular disease which the IOM Committee (2008) attributed to the healthy worker effect.

The IOM (2008) report was the basis for the outcomes reported here, but the recommendations are consistent with the results and conclusions reached independently by the NRC (2008) committees.

A further systematic review by Canu et al. (2008) of 18 cohort and five nested case control studies whose objective was to examine the link between internal irradiation and cancer, was hampered, like many other studies, by three factors: limited statistical power, relatively low radiation doses and inaccurate exposure assessment. Canu and her colleagues concluded that lung cancer was not significantly increased but at some of the U plant sites there were some increases of cancer in lymphatic and hematopoietic tissues, and in the upper aero-digestive tract associated with increased internal exposure. These findings were consistent with results from an earlier study which suggested that cancer was associated with the isotopic composition of the U and its solubility. Slow solubility was associated with increased risk (Canu et al. 2011).

Summary

Studies of U miners conducted over the last half century demonstrate high mortality, mainly from lung cancer. These excess death rates are attributed to the miners' exposure to radon as opposed to U. Based on the results from 27 studies of U plant workers and similar occupations included in at least one of three systematic reviews by

the IOM and NRC, it was concluded that there is no consistent evidence that exposure to U resulted in excess lung, lymphatic, bone, renal, bladder, brain/CNS, testicular or prostate cancer, or leukemia. Among non-malignant diseases, no excess mortality was found for cardiac or neurologic disease but there was some increase in respiratory disease although it is unclear to what it might be attributed. The IOM Committee (2008) concluded that for the health outcomes included in its review, exposure to U is not associated with a large or frequent effect. A fourth systematic review (Canu et al. 2008) supported the conclusion that no currently available evidence links lung cancer and internal exposure to U but there is limited evidence suggesting an association between internal exposure and increased risk for lymphatic and hematopoietic cancer and upper aero-digestive tract cancer.

V. SUMMARY OF THE EVIDENCE OF HEALTH EFFECTS OF DEPLOYMENT IN THEATRES WHERE DEPLETED URANIUM WAS USED

Several expert consensus reports have been published over the past decade regarding the potential health effects of depleted uranium (DU) in military personnel. These include a detailed review and synthesis of the existing evidence by the Institute of Medicine (2000, 2008), the National Research Council (2008), the Royal Society (2001, 2002), the UK Depleted Uranium Oversight Board (UK DUOB 2007), the World Health Organization (WHO 2001) and RAND (Harley 1999). Collectively, these independent scientific groups have concluded that there is insufficient evidence to establish a link between exposure to DU and adverse human health effects. Our committee independently reviewed the primary epidemiological cohort studies carried out among the Veterans of the Gulf and Balkans conflicts. This review is described in detail below.

This review of the evidence concerning the health effects of deployment in the Gulf or Balkans wars is drawn from 16 epidemiological mortality or incidence studies. In addition, we include three epidemiological studies of a specific cancer such as testicular cancer, (Knoke et al. 1998; Levine et al. 2005), and hospitalizations under broad diagnostic categories (Kang et al. 2009). All these studies used a retrospective cohort design. The literature search approach was based on that of a recent review of epidemiological cancer studies in Veterans from the Gulf and Balkans wars (Kang et al. 2009). Search results from the latter were replicated and updated for references after 2007.

Our review excluded case reports, cross-sectional studies and clinical studies of hospitalized Veterans, whatever the outcomes. The review does not include studies of Veterans voluntarily presenting for surveillance with the exception of a summary of findings from the medical surveillance program conducted by the US Department of Veterans Affairs.

(A) US Studies - Gulf War

The US studies show results for all cause and cause-specific mortality including cancer (Kang et al. 1996; Kang et al, 2001; Bullman et al. 2005; Young et al. 2010; Gray et al. 1996; Knoke et al. 1998; Levine et al. 2005;). Some report cancer incidence (Young et al 2010; Knoke et al 2010; Levine et al 2005.). One study from this group used hospitalizations for broad diagnostic categories of diseases as an outcome (Knoke et al 1998). Two of the studies (Kang et al. 2001; Bullman et al. 2005) focused on the effects of exposure to nerve agents in Khamisiyah (Iraq). Testicular cancer was the focus of another study (Levine et al. 2005). The first study was published in 1996 (Kang et al. 1996) and reported on follow-up from the Gulf War up to September 1993; the latest date for follow-up was December 2006 (Young et al. 2010).

Most outcome comparisons were made between Veterans deployed to the Persian Gulf between August 1990 and April 1991, and a random sample of active duty military in the National Guard and in the military reserves, serving between September 1990 and April 1991 but who did not go to the Persian Gulf. Each group included, depending on the study, approximately 600,000 - 700,000 personnel. In some reports from this same base study, only those on active duty were included in the control group (Knoke et al. 1998; Levine et al. 2005). The US population (with appropriate rates for adjustments) was also used as a comparison group.

Results did not indicate elevated rates for all-cause mortality, cancer mortality or cancer incidence among deployed Veterans. At the same time, there were some findings suggesting an increased risk (although not statistically significant). In an internal comparison of deployed Gulf War Veterans (GWV), Bullman et al. (2005) reported an elevated brain cancer risk among those exposed to chemical munition destruction (adjusted hazard rate ratio (HRR)=1.94 (95% confidence interval (95% CI)1.12-3.34), and a risk increasing with exposure duration (3.26; 95% CI 1.33-7.96) for 2 or more days of exposure. Young et al. (2010) reported an increase in lung cancer incidence; comparing GWV to other Veterans, the proportional incidence ratio (PIR) was 1.15 (95% CI 1.03-1.29) and comparing GWV to the US general population, the standardized incidence ratio (SIR) for lung cancer was 1.09 (0.98-1.20). There were inconsistent findings reported for male genital system cancers. Gray et al. (1996) reported an increase for hospitalizations for incident testicular cancer (HRR=2.12 (1.11-4.02) among GWV compared to other Veterans while Knoke et al. (1998) using a longer follow-up period did not report an elevated risk for testicular cancer among GWV. Finally, Levine et al. (2005), with an even longer follow-up (up to 1999), reported a PIR for testicular cancer that was 1.42 for GWV in comparison with Surveillance, Epidemiology and End Results (SEER) data, whereas this risk among other Veterans was below 1 (0.84) (no CI provided). Although of marginal statistical significance, these findings warrant further research.

These are the largest studies carried out among Veterans of the Gulf War and they were mostly very well done. Loss to follow-up was approximately 11% and was not different between the GWV and other Veterans not deployed. Although comparisons were not

fully adjusted for all possible confounders, the main ones (e.g., age, gender, and others) were taken into consideration. Comparisons between Veterans (GWV and other Veterans not deployed) or internal comparisons (between exposed and not exposed) are more informative than those with the general population and much less susceptible to confounding. Some results showing increased risks, such as for testicular cancer, were not consistent from one analysis to the other.

(B) UK Studies - Gulf War

A retrospective cohort study was carried out on all UK armed forces personnel who served in the Gulf at some time between September 1990 and June 1991 (the "Gulf" cohort) (Macfarlane et al. 2000). A comparison group of the same number of armed forces personnel was identified (the "Era" cohort) who did not serve in the Gulf. Selection among the latter was random and stratified to match the Gulf cohort on age, sex, service and rank. There were some 53,000 military personnel in each group.

Mortality from disease-related and external causes was ascertained with follow-up up to 1999 in the first report (Macfarlane et al. 2000) and up to June 2004 in the second (Macfarlane et al. 2005). A third study ascertained cancer incidence up to 2002 (Macfarlane et al. 2003). In the later reports (Macfarlane et al. 2005; Macfarlane et al. 2003) self-reported information on Gulf War experiences and lifestyle factors was available from surveys conducted between 1997 and 2001 in the two cohorts. Approximately 47% of GWV and 36% of the Era cohort participated in these surveys. Among the survey participants the mortality experience was compared and then, within the Gulf cohort, the relationship between self-reported experiences in the Gulf and future mortality was analyzed.

A small increase in mortality from all causes, comparing the two cohorts, was reported in the early study (Macfarlane et al. 2000) (Mortality Rate Ratio [MRR]: 1.05 (95% CI 0.91-1.21). The second report with follow-up to 2004 (Macfarlane et al. 2005) found a similar small elevation in the MRR. Comparing GWV who reported exposure to DU to those who did not report such an exposure, the overall disease-related MRR was 1.99 (95% CI 0.98-4.04) with most deaths being cancer-related. The non-disease (e.g., accidents) related MRR was 0.78 (95% CI 0.24-2.51). With respect to incidence of cancer, there were non-significant increases in certain subgroups of the GWV in comparison with the Era veterans as well as in the surveyed groups (1.12; 95% CI 0.86-1.36). Within the GWV cohort, there was no difference in cancer incidence between those reporting DU exposure and those not reporting exposure.

These are generally well-done studies with negligible loss to follow-up. Although the use of survey information is valuable, the rate of participation in these surveys was not higher than 50%. The association of cancer incidence and mortality risk with self-reported DU exposure was not consistent. Overall there were no strong signs of increased deaths or increased cancer rates in the GW cohort, but the results did suggest possible increases in subgroups.

(C) Italian Studies - Balkans

An initial report was published by the Italian government in 2002 (Ministero della Difesa 2002), estimating cancer incidence among 58,413 Italian Army soldiers deployed in Bosnia-Kosovo between December 1995 and January 2001. Events and time at risk were counted from the date of the first mission. The comparison group was the male population covered by the Italian tumour registries. In two later reports (Peragallo et al. 2010; Peragallo et al. 2011) methods and outcome (cancer incidence) were the same with longer follow-up periods and with the addition of a comparison group composed of Army personnel not deployed during the same time period. The number of this group varied from 130,275 subjects in 1996 to 40,967 in 2007.

With two exceptions, there were no consistent findings of elevated cancer risk among the deployed cohort. First, thyroid cancer showed an increased risk among those who were deployed in Bosnia (1.60; 95% CI 0.87-2.68) in comparison with the Italian male population (Peragallo et al. 2010). A later study published in 2011 in the same population reported a thyroid SIR of 1.83 (95% CI 1.04-2.97) for those deployed to Bosnia, but there was also an increase in those not deployed (1.55, 95% CI 1.12-2.10) (Peragallo et al. 2011). Second, there was also evidence of an elevated risk of Hodgkin's lymphoma in the deployed cohort over the years 1996–2001; the SIR was 2.36 (95% CI 1.22–4.13). However, this excess risk was not reported in the later publications (Peragallo et al. 2010; Peragallo et al. 2011).

These studies have some weaknesses: there were inconsistencies in reporting results between studies and the selection of the reference population is not completely clear. The increased risk for thyroid cancer warrants further research to determine if it is related to military occupational exposures.

(D) Nordic Studies - Sweden and Denmark-Balkans

The two Nordic studies used a retrospective cohort approach to study cancer incidence based on population cancer registries. The general population was used as a reference to estimate SIR.

In the Swedish study (Gustavsson et al. 2004) the cohort included all Swedish military and rescue service personnel involved in UN missions in the Balkans (Bosnia and Kosovo) from 1989 to 1999 (8,750 men and 438 women). Follow-up was almost complete. Person-time at risk was accumulated from the start of the first mission up to December 1999. In the entire group, the all-site cancer SIR was 1.2 (95% CI 0.8-1.8), whereas among those engaged in outdoor operations over large areas, with transport by convoy, the SIR was 3.0 (95% CI 1.0-7.0). The entire group SIR for testicular cancer was 1.9 (95% CI 0.8-3.7) with convoy military having an SIR of 5.9 (95% CI 0.7-21).

The Danish study (Storm et al. 2006) included military personnel (13,552 men and 460 women) without known cancer at first deployment between January 1992 to December

2001 to the Balkans. Follow-up was through December 2002. Date of first deployment was the starting point for person-years accrual. In men the overall SIR was not increased but there were increases for some cancers: testis (1.2; 95% CI 0.8-1.8); bladder (2.2; 95% CI 0.9-4.5); and bone cancer (6.0; 95% CI 1.6-15.3). In women, the overall cancer SIR was 1.7 (95% CI 0.9-3.0).

These studies were well done with excellent cohort enumeration and follow-up. Cancer registries in the Nordic countries are very complete. Further research with extended follow-up is warranted for specific cancers with reported elevated risk.

(E) Netherlands Studies - Balkans

The National Institute for Public Health and the Environment of the Netherlands published a report in 2011 (National Institute for Public Health and the Environment 2011) on cancer incidence and cause-specific mortality in the military following Balkans deployment. Balkans deployment started in 1991, with deployment records available from 1993 onwards. Military personnel in ground mission service between January 1, 1993 and March 1, 2001 were identified from several registers of the Dutch Armed Forces. Ground military personnel who were not deployed formed the comparison group. There were also comparisons between the two military groups and the Dutch population. Cancer incidence and mortality data were collected for the years 1993-2008 obtained from linkage to the Netherlands Cancer Registry.

Approximately 19,000 Balkans-deployed and 135,000 non-Balkans-deployed military personnel were included in the study.

With respect to the incidence of cancer, results indicated no differences between Balkans-deployed military and their peers (Rate Ratio =0.83 (95% CI 0.69-1.00). Comparing the cancer incidence in the deployed personnel to that in the Dutch population (with the usual adjustments) showed a SIR of 0.85 (95% CI 0.73-0.99).

With respect to mortality, the total mortality rate of Balkans-deployed military personnel was lower than the mortality rate of non-Balkans-deployed military personnel (Rate Ratio=0.62 95% CI 0.52-0.75). The risk of death from cancer was also lower among Balkans- deployed military personnel (Rate Ratio=0.66 (95% CI 0.46-0.97). Finally, in comparison with the Dutch population, the overall mortality was lower in the deployed SMR=0.67 (95% CI 0.57-0.78) and the cancer mortality SMR was 0.61 (95% CI 0.43-0.82). Non-deployed military personnel compared to the Dutch population also had an SMR below unity.

This is a well done study with a careful analysis.

(F) The Canadian Persian Gulf Cohort Study

The main objective of the Canadian Persian Gulf Cohort Study was to determine if military personnel deployed to the Persian Gulf between August 24, 1990 and September 30, 1991 were at a higher risk of death or of developing cancer after their return to Canada, than either other members of the military who were not deployed to the Persian Gulf or the general Canadian public. In the Gulf and Kuwait War of 1990-1991 Canada deployed about 5,000 military personnel (soldiers, sailors and airmen) with contributions consisting of one headquarters, a naval task force, an air task group, a field hospital, two infantry companies and a platoon that provided security. The Canadian Persian Gulf Cohort Study was conducted by Statistics Canada (2005) with oversight provided by the Gulf War Veterans Cohort Study Advisory Committee.

Two cohorts were established. The final deployed cohort consisted of 5,117 Canadian Forces (CF) members sent to the Gulf between August 1990 and October 1991. The comparison cohort consisted of 6,093 members of the CF who were eligible for deployment at the time of the 1990/91 Gulf and Kuwait War but who were not deployed. Record linkage methods were used to identify deaths and incident cases of cancer in the two cohorts. In total, there were 96 deaths during the nine-year follow-up and 71 new cases of cancer during the seven-year follow-up. Indirect standardization methods were used to compare the cohort mortality and cancer incidence to the general Canadian population. The study had the statistical power to detect a 60% increase in overall mortality and a 75% increase in overall cancer incidence.

There was no significant difference in the overall risk of death between the deployed and non-deployed cohorts. For both the deployed and the non-deployed cohort, there was a statistically significant lower risk of death from all causes of about 50% compared to the general population. There was no significant difference in the risk of being diagnosed with cancer in the two military cohorts. In total, there were 71 cancer cases, 29 in the deployed cohort and 42 in the non-deployed cohort and the rate of cancer in both the deployed and non-deployed cohorts was not significantly different from the rate in the general population.

(G) Depleted Uranium Follow-up Program US Department of Veterans Affairs

In 1993, the US Department of Veterans Affairs established a medical surveillance program to monitor the health of Gulf War Veterans who were exposed to depleted uranium as a consequence of 'friendly fire' incidents over a 48-hour period in February 1991 during the first Gulf War. There were 11 fatalities and approximately 50 casualties among the 115 armoured vehicle crew members involved in these incidents. There was substantial potential for wound contamination, inhalation and ingestion exposure to DU dust among these armoured vehicle crew members.

A biennial schedule of medical surveillance commenced in late 1993 for the approximately 100 survivors of the Gulf War friendly fire events. Veterans' participation

in the surveillance program has been voluntary. To date, 79 soldiers in the 'DU-exposed' cohort have been evaluated at least once in the surveillance program and 15 cohort members have been found to have embedded DU fragments. In 1997, the surveillance program enrolled a group of 38 Gulf War soldiers with no known exposure to depleted uranium as a comparison group.

The objective of the DU Follow-up Program was to provide medical surveillance of DU-exposed Veterans to identify potential adverse health effects associated with inhalation and ingestion exposures to DU oxides or exposures resulting from DU fragments embedded in tissue (McDiarmid, Albertini et al. 2011, McDiarmid, Engelhart et al. 2011). The focus of the surveillance program was to conduct sensitive assessments of uranium exposure and monitor target organ function using a broad range of biomarkers. Biological monitoring initially focused on renal function and bone metabolism. The monitoring protocol was expanded in 1997 to include surveillance of neuroendocrine, immunologic and reproductive function, as well as renal markers and measures of genotoxicity.

The DU Follow-Up Program has conducted extensive assessments of uranium exposure among cohort members. Whole body radiation exposure measurements have been conducted. In addition, urine uranium concentrations, a measure of uranium excretion, has been assessed at two year intervals. A majority of DU-exposed cohort members have been found to have urinary uranium concentrations below the 95th percentile observed for adults in the US population. However, 43% of the cohort has elevated urinary uranium levels. Of this group with higher urinary uranium levels, 88% have retained embedded DU fragments.

In addition to the longitudinal monitoring of the small cohort of Veterans who were involved in the DU friendly fire incidents in 1991, the DU Follow-Up Program has also provided an exposure assessment protocol for Veterans concerned about possible exposure to DU. As of December 2010, a total of 3,246 Veterans have submitted a urine sample for assessment. Four of these assessments were positive for DU based on the uranium isotopic signature of their samples and a service history has determined exposure to friendly fire incidents (Squibb et al. 2012).

Over the 18 years of the surveillance program, health outcome measures have been compared between the low exposed and high exposed cohort members. Monitoring includes nine hematologic parameters, five neuroendocrine measures, 13 measures of renal function, nine measures of semen characteristics, three measures of genotoxicity and seven measures of bone metabolism. Over the 18 year period, no consistent, clinically significant differences in health outcomes have been observed (Squibb et al. 2012; McDiarmid, Albertini et al. 2011).

The DU Follow-Up Program is the most detailed medical surveillance study documenting exposure status and health status among Veterans with a known history of exposure to DU in combat. Although a small cohort, it is distinguished by the long duration of follow-up. Findings to date from the DU Follow-Up Program do not indicate

that exposure to DU is associated with short term effects on health. Given the established evidence that U accumulates over time in two primary tissues (kidney and bone) and concerns arising from the radiological toxicity of U, continued biological monitoring in this cohort is prudent.

Summary

We have found, after assessing the mortality and cancer incidence cohort studies conducted by several countries, that there is limited evidence, at the moment, to suggest an association between being involved in the Gulf and Balkans conflicts, and an increased risk of cancer or mortality. The comprehensive follow-up surveillance program of US Gulf War Veterans with embedded DU fragments has not detected, after 18 years, any significant adverse health effects in this unique group that is chronically exposed to DU.

VI. CONCLUSIONS

Having carefully and critically reviewed the scientific literature and other pertinent material, the Committee considers that, based on current knowledge, the following conclusions can be drawn:

1) Depleted uranium (DU) is potentially harmful to human health by virtue of its chemical and radiological effects.

2) Within a military setting, the highest risk of exposure to depleted uranium is in those who were: in, on or near vehicles hit with friendly fire; entering or near these burning vehicles; near fires involving DU munitions; salvaging damaged vehicles; or involved in clean up operations of contaminated sites.

3) It is unlikely that Canadian soldiers have been exposed to levels of depleted uranium which could be harmful to their health.

4) There is no consistent evidence from military cohort studies of adverse health effects that could be attributed to depleted uranium.

5) There is no strong evidence of adverse health effects reported in larger civilian studies with longer follow-up periods of populations with increased exposure to uranium (e.g. uranium production and fabrication workers).

6) Our finding that exposure to uranium is not associated with a large or frequent health effect is in agreement with the conclusions of other expert bodies.

7) There are many Veterans suffering from persistent symptoms following deployment or military conflict which, although not linked to specific exposures such as DU, can cause considerable suffering and can be effectively treated. **(Annex F)**

REFERENCES

Archer VE, Wagoner JK, Lundin FE Jr. Cancer mortality among uranium mill workers. J Occup Med. 1973;15(1):11–14.

Bailey MR, Phipps AW. Application of ICRP Biokinetic Models to DU. In: DU; Properties, Uses & Health Consequences. Edited by AC Miller CRC Press 2007;183-228.

Beral V, Fraser P, Carpenter L, Booth M, Brown A, Rose, G. Mortality of employees of the atomic weapons establishment 1951-82. BMJ. 1988;297(6651):757-770.

Bijlsma JA, Slottje P, Huizink AC, Twisk JW, van der Voet GB, de Wolff FA et al. Urinary uranium and kidney function parameters in professional assistance workers in the Epidemiological Study Air Disaster in Amsterdam (ESADA). Nephrol. Dial. Transplant. Jan. 2008;23(1):249-255.

Bland DJ, Rona RJ, Coggon D, Anderson J, Greenberg N, Hull L, Wessely S. Urinary isotopic analysis in the UK Armed Forces: no evidence of depleted uranium absorption in combat and other personnel in Iraq. Occup Environ Med. 2007;64(12):834-38.

Boiano JM, Moss CE, Burr GA. Health hazard evaluation report HETA 83-144-2001, feed materials production center. Fernald, OH: Westinghouse Materials Company of Ohio. 1989.

Boice JD, Cohen CC, Mumma MT, Dupree-Ellis E, Eckerman KF, Leggett RW, Boecker BB, Brill AB, Henderson BE. Mortality among radiation workers at Rocketdyne (Atomics International), 1948-1999. Radiation Research. 2006;166(1Pt 1):98-115.

Brown DP, Bloom T. Mortality among uranium enrichment workers. Cincinnati, OH: National Institute of Occupational Safety and Health. 1987.

Bullman TA, Mahan CM, Kang HK, Page WF. Mortality in US Army Gulf War veterans exposed to 1991 Khamisiyah chemical munitions destruction. Am J Public Health.2005;95:1382–1388.

Butler KM, Cool D. What is the basis for the ICRP limit for a member of the public of 1 mSv/y and of 20 mSv/y for the occupational radiation worker? Answer to Question #8900 Submitted to "Ask the Experts". McLean, VA: Health Physics Society. 25 March 2010. Retrieved from http://hps.org/publicinformation/ate/q8900.html.

Canadian Nuclear Safety Commission (n.d.). Radiation Protection Regulations SOR/2000-203. Ottawa, ON. Retrieved from laws-lois.justice.gc.ca/eng/regulations/sor-2000-203/page-4.html#docCont.

Canu IG, Ellis ED, Tirmarche M. (2008). Cancer risk in nuclear workers occupationally exposed to uranium – emphasis on internal exposure. Health Physics 2008; 94(1):1-17.

Canu IG, Jacob S, Cardis E, Wild P, Caer S, Auriol B et al. Uranium carcinogenicity in humans might depend on the physical and chemical nature of uranium and its isotopic composition: Results from pilot epidemiological study of French nuclear workers. Cancer Causes Control 2011; 22(11).1563-1573.

Canu IG, Laurent O, Pires N, Laurier D, Dublineau I. Health effects of naturally radioactive water ingestion: The need for enhanced studies. Envir Health Perspect. 2011/;149(12):1676-1680.

Cazoulat A, Lecompte Y, Bohand S, Castagnet X, Laroche P. Urinary uranium analysis results on Gulf war or Balkans conflict veterans. Pathol Biol (Paris) 2008;56(2):77-83.

CF/DND Ombudsman. Heroism Exposed - An Investigation into the Treatment of 1 Combat Engineer Regiment Kuwait Veterans (1991). Ottawa, ON: Ombudsman, National Defence and Canadian Forces. Special Report to the Minister of National Defence. October 2006. Available from: http://www.ombudsman.forces.gc.ca/rep-rap/sr-rs/kuw-kow/doc/kuwait-kowait-eng.pdf

Chazal V, Gerasimo P, Dabouis V, Laroche P, Paquet F. Characteristics and dissolution of depleted uranium aerosols produced during impacts of kinetic energy penetrators against a tank. Radiation Protection Dosimetry. 2003;105(1-4):163-6.

Checkoway HN, Pearce N, Crawford-Brown DJ Cragle DL. Radiation doses and cause-specific mortality among workers at a nuclear materials fabrication plant. American Journal of Epidemiology. 1988;127(2):255-266.

Cragle DL, McLain RW, Qualters, JR, Wilkinson, GS, Tankersley WG, Lushbaugh CC. Mortality among workers at a nuclear fuels production facility. American Journal of Industrial Medicine. 1988;12: 379-401.

Davies CN. *Inhaled particles and Vapours*, Vol.1, Oxford, UK: Pergamon Press. 1961. As reported in IOM. Washington, DC: Institute of Medicine. Gulf War and Health: Updated literature review of depleted uranium. Institute of Medicine. 2008.

Davis M. Gulf war illnesses and recognizing new diseases. In: Fulco, CE, Liverman CT, Sox HC (ed), *Gulf War and Health: Volume 1. Depleted Uranium, Pyridostigmine Bromide, Sarin, and Vaccines*. Washington DC: Committee on Health Effects Associated with Exposures During the Gulf War, Institute of Medicine, National Academy of Sciences. 2000.

Donta ST, Clauw DJ, Engel CC, Guarino P, Peduzzi P, Williams DA, Skinner JS, et al. Cognitive behavioral therapy and aerobic exercise for Gulf War veterans' illnesses:a randomized controlled trial. JAMA. 2003;289:1396-1404.

Dorsey CD, Engelhardt SM, Squibb KS, McDiarmid MA. Biological monitoring for depleted uranium exposure in U.S. Veterans. Environ Health Perspect. 2009 Jun;117(6):953-6.

Dupree EA, Cragle DL, McLain RW, Crawford-Brown DJ, Teta MJ. Mortality among workers at a uranium processing facility, the Linde Air Products Company Ceramics Plant, 1943–1949. Scand J Work Environ Health. 1987;13(2):100–107.

Dupree EA, Watkins JP, Ingle JN, Wallace PW, West CM, Tankersley WG. Uranium dust exposure and lung cancer risk in four uranium processing operations. Epidemiology. 1995;6(4):370–375.

Dupree-Ellis E., Watkins J., Ingle J.N, Phillips J. External radiation exposure and mortality in a cohort of uranium processing workers. American Journal of Epidemiology. 2000;152(1):91-95.

Frome EL, Cragle DL, McLain RW. Poisson regression analysis of the mortality among a cohort of World War II nuclear industry workers. Radiat Res. 1990;123(2):138–152.

Frome EL, Cragle DL, Watkins JP, Wing S, Shy CM, Tankersley WG, West CM. A mortality study of employees of the nuclear industry in Oak Ridge, Tennessee. Radiation Research. 1997;148(1):64-80.

Gardner JW, Gibbons RV, Hooper TI, Cunnion SO, Kroenke K, Gackstetter GD. Identifying new diseases and their causes: the dilemma of illnesses in Gulf War veterans. Milit Med. 2003;168:186-193.

Gilroy G. Health Study of Canadian Forces Personnel Involved in the 1991 Conflict in the Persian Gulf, Volume 1. Ottawa, ON: Goss Gilroy Inc. Report prepared for the Gulf War Illness Advisory Committee, Department of National Defence. 1998.

Gilroy G. Health Study of Canadian Forces Personnel Involved in the 1991 Conflict in the Persian Gulf, Volume 2. Ottawa, ON: Goss Gilroy Inc. Report prepared for the Gulf War Illness Advisory Committee, Department of National Defence. 1998.

Gray GC, Coate BD, Anderson CM, Kang HK, Berg SW, Wignall FS, et al. The postwar hospitalization experience of US veterans of the Persian Gulf War. N Engl J Med. 1996;335:1505–1513.

Gulf Link. (n.d.). Health Effects. Retrieved from http://gulflink.osd.mil/library/randrep/du/mr1018.7chap2.html

Gustavsson P, Talbäck M, Lundin A Lagercrantz B, Gyllestad PE, Fornell L. Incidence of cancer among Swedish military and civil personnel involved in UN missions in the Balkans 1989- 99. Occup Environ Med 2004; 61(2): 171-73.

Hadjimichael OC, Ostfeld AM, D'Atri DA, Brubaker RE. Mortality and cancer incidence experience of employees in a nuclear fuels fabrication plant. J Occup Med. 1983;25(1):48–61.

Harley, N, Foulkes E, Lee H. Hilborne, AH and Anthony CR. A Review of the Scientific Literature As It Pertains to Gulf War Illnesses: Volume 7: Depleted Uranium. Santa Monica, CA: RAND Corporation. 1999. http://www.rand.org/pubs/monograph_reports/MR1018z7.

Health Canada. Fact sheet: Information about Depleted Uranium. Ottawa, ON: Health Canada. 2008. Retrieved from www.hc-sc.gc.ca/ewh-semt/pubs/radiation/uranium-eng.php.

Hurtgen C. Suivi de la contamination de l'uranium par son dosage dans les urines, l'expérience Belge. Société Française de Radioprotection: l'uranium sous forme appauvrie. Paris, 27 novembre 2001.

Hyams KC, Wignall FS, Roswell R. War syndromes and their evaluation: from the US Civil War to the Persian Gulf War. Ann Intern Med. 1996;125:398-405.

ICRP. Age-dependent doses to members of the public from radionuclides: Part 3, ingestion dose coefficients. International Commission on Radiological Protection. ICRP Publication 69. Ann. ICRP 1995;25(1).

ICRP. Human respiratory tract model for radiological protection. International Commission on Radiological Protection. ICRP Publication No. 66. Ann. ICRP 1994;24(1-3).

ICRP. Report of the task group on reference man. International Commission on Radiological Protection. ICRP Publication 23. Ann. ICRP 1975.

IOM. Institute of Medicine. An Evaluation of Radiation Exposure Guidance for Military Operations. Washington, DC: Institute of Medicine. 1967.

IOM. Gulf War and Health: Updated literature review of depleted uranium. Washington, DC: Institute of Medicine. 2008.

IOM. Gulf War and Health: Update of Health Effects of Serving in the Gulf War. Committee on Gulf War and Health: Health Effects of Serving in the Gulf War, Update 2009. Washington, DC: Board of the Health of Select Populations, Institute of Medicine. 2010.

IOM. Gulf War and Health: Volume 1: Depleted Uranium, Pyridostigmine Bromide, Sarin, and Vaccines. Washington, DC: Institute of Medicine. 2000.

IOM. Gulf War and Health: Volume 4. Health Effects of Serving in the Gulf War and Health: A Review of the Medical Literature relative to the Gulf War Veterans' Health. Washington, DC: Institute of Medicine. 2006.

Kang HK, Bullman TA. Mortality among U.S. veterans of the Persian Gulf War. N Engl J Med 1996; 335(20):1498-1504.

Kang HK, Bullman TA. Mortality among US veterans of the Persian Gulf War: 7-year followup. Am J Epidemiol. 2001;154:399–405.

Kang HK, Li B, Mahan CM, Eisen SA, Engel CC. Health of US veterans of 1991 Gulf War: A follow-up survey in 10 years. J Occup Environ Med. 2009;51:401–410.

Knoke JD, Gray GC, Garland FC. Testicular cancer and Persian Gulf War service. Epidemiology. 1998;9:648–653.

Kroenke K, Koslowe P, Roy M. Symptoms in 18,495 Persian Gulf War veterans: latency of onset and lack of association with self-reported exposures. J Occup Environ Med. 1998;40:520-528.

Kroenke K, Rosmalen JGM. Symptoms, syndromes and the value of psychiatric diagnostics in patients with functional somatic disorders. Med Clin N Am 2006;90:603-626.

Kurttio P, Komulainen H, Leino A, Salonen L, Auvinen A, Saha H. Bone as a possible target of chemical toxicity of natural uranium in drinking water. Environmental Health Perspectives. 2005;113(1):68-72.

Levine PH, Young HA, Simmens SJ, Rentz D, Kofie V, Mahan CM, et al. Is testicular cancer related to Gulf War deployment? Evidence from a pilot population-based study of Gulf War era veterans and cancer registries. Mil Med. 2005;170:149–153.

Loomis DP, Wolfe SH. Mortality of workers at a nuclear materials production plant at Oak Ridge, Tennessee, 1947-1990. American Journal of Industrial Medicine. 1996;29(2):131-141.

Macfarlane GJ, Biggs A, Maconochie N, Hotopf M, Doyle P, Lunt M. Incidence of lung cancer among UK Gulf War veterans: Cohort Study. BMJ. 2003;327:1373-1378.

Macfarlane GJ, Hotopf M, Maconochie N, Blatchley N, Richards A, Lunt M, Long-term mortality amongst Gulf War veterans: is there a relationship with experiences during deployment and subsequent morbidity? Int J Epidemiol. 2005;34(6):1403-1408.

Macfarlane GJ, Thomas EF, Cherry N. Mortality among United Kingdom Gulf War veterans. Lancet. 2000;356:17-21.

Marshall AC. An analysis of uranium dispersal and health effects using a Gulf War case study. Albuquerque, NM: Sandia National Laboratories. SAND2005–4331 July 2005.

Marshall AC. Gulf War depleted uranium risks. Journal of Exposure Science and Environmental Epidemiology. 2008;18:95-108.

McDiarmid MA, Albertini RJ, Tucker JD, Vacek PM, Carter EW, Bakhmutsky MV, Oliver MS, Engelhardt SM, Squibb KS. Measures of genotoxicity in Gulf war I veterans exposed to depleted uranium. Environ Mol Mutagen. Aug 2011;52(7):569-8.

McDiarmid MA, Engelhardt SM, Dorsey CD, Oliver M, Gucer P, Gaitens JM, Kane R, Cernich A, Kaup B, Hoover D, Gaspari AA, Shvartsbeyn M, Brown L, Squibb KS. Longitudinal health surveillance in a cohort of Gulf War veterans 18 years after first exposure to depleted uranium. J Toxicol Environ Health A. 2011;74(10):678-91.

McDiarmid MA. Meeting with Minister of Veterans Affairs Scientific Advisory Committee on Veterans Health. Ottawa, ON. 2012.

McGeoghegan D, Binks K. The mortality and cancer morbidity experience of workers at the Capenhurst uranium enrichment facility 1946-95. Journal of Radiological Protection. 2000a ;20(4):381-401.

McGeoghegan D. The mortality and cancer morbidity experience of employees at the Chapelcross plant of British Nuclear Fuels PLC, 1955-95. Journal of Radiological Protection. 2001;21(3):221-250.

McGeoghegan D. The mortality and cancer morbidity experience of workers at the Springfields uranium production facility, 1946-95. Journal of Radiological Protection. 2000b; 20(2):111-137.

Ministero della Difesa. Relazione Finale della Commissione istituita dal Ministro della Difesa sull'incidenza di neoplasie maligne tra i militari impiegati in Bosnia e Kosovo. Rome; 11 June 2002. Retrieved from http://www.difesa.it/NR/rdonlyres/ 6DA4D27E-A75D-4C2D-AA46-8E8071EFAE06/0/relazione_finale.pdf

National Institute for Public Health and the Environment. Cancer incidence and cause specific mortality following Balkan deployment. The Hague, NL: National Institute for Public Health and the Environment (RIVM). RIVM Report 630450001. 2011.

NRC. Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII - Phase 2. Washington, DC: Committee to Assess Low Levels of Ionizing Radiation, National Research Council. 2006

NRC. Review of the Toxicologic and Radiologic Risks to Military Personnel from Exposures to Depleted Uranium during and After Combat.: Washington, DC: Committee on Toxicology, National Research Council. 2008.

Oeh U, Priest ND, Roth P, Ragnarsdottir KV, Li WB, Hoellriegl V, et al. Measurements of daily uranium excretion in German peacekeeping personnel and residents of the Kosovo region to assess potential intakes of depleted uranium (DU). Sci Total Environ 2007;381(1-3):77-87.

Ough E, Lewis BM, Andrews WS, Bennett LG, Hancock RC, Scott K. An examination of uranium levels in Canadian Forces personnel who served in the Gulf War and Kosovo. Health Phys 2002;82(4):527-532.

Parkhurst MA, Guilmette RA. Conclusions of the Capstone depleted uranium aerosol characterization and risk assessment study. Health Phys. 2009;96(3):393-409.

Peragallo MS, Lista F, Sarnicola G, Marmo F, Vecchione A. Cancer surveillance in Italian army peacekeeping troops deployed in Bosnia and Kosovo, 1996–2007: Preliminary results Cancer Epidemiology 34 (2010) 47–54.

Peragallo MS, Urbano F, Sarnicola G, Lista,F, Vecchione A. Condizione militare e morbosità per cancro: il punto della situazione (Cancer incidence in the military: an update) Epidemiol Prev 2011; 35 (5-6): 339-345.

Pinkerton, L E, Bloom TF, Hein MJ, Ward EM. Mortality among a cohort of uranium mill workers: An update. Occupational and Environmental Medicine. 2004;61(1):57-64.

Polednak AP, Frome EL. Mortality among men employed between 1943 and 1947 at a uranium-processing plant. Journal of Occupational Medicine. 1981;23(3):169-178.

Richardson DB, Wing S. Lung cancer mortality among workers at a nuclear materials fabrication plant. American Journal of Industrial Medicine. 2006;49(2):102-111.

Ritz B, Morgenstern H, Crawford-Brown D, and Young, B. The effects of internal radiation exposure on cancer mortality in nuclear workers at Rocketdyne/Atomics International. Environmental Health Perspectives. 2000;108(8):743-751.

Ritz, B. Radiation exposure and cancer mortality in uranium processing workers. Epidemiology. 1999;10(5):531-538.

Roth P, Werner E, Paretzke HG. A study of uranium excreted in urine. An assessment of protective measures taken by the German Army KFOR Contingent. (Report for the Federal Ministry of Defense). Neuherberg, Germany: GSF-National Research Centre for Environment & Health, Institute for Radiation Protection. 2001.

Roy MJ, Koslowe PA, Kroenke K, Magruder C. Signs, symptoms and ill-defined conditions in Persian Gulf War veterans: Findings from the Comprehensive Clinical Evaluation Program. Psychosom Med. 1998;60:663-668.

Saccomanno G, Yale C, Dixon W, Auerbach O, Huth GC. An epidemiological analysis of the relationship between exposure to Rn progeny, smoking and bronchogenic carcinoma in the U-mining population of the Colorado Plateau: 1960–1980. 1986; Health Physics. 50(5):605–618.

Sandström B. Levels of uranium in urine from Swedish personnel that have been or will serve in the Swedish KFOR contingent. FOI - Swedish Defense Research Agency. Report no. FOI-R-0165-SE August 2001.

SCHER. Opinion on the Environmental and Health Risks Posed by Depleted Uranium. European Commission, Scientific Committee on Health and Environmental Risks, Report to the European Union. 18 May 2010.

Scherpelz RI, Traub RJ, Droppo JG, Parkhurst MA. Depleted Uranium Exposures to Personnel Following the Camp Doha Fire, Kuwait, July 1991. Report prepared for the US Army Center for Health Promotion and Preventive Medicine by Pacific Northwest National Laboratory, Richland, WA. June 2000.

Shawky S, Amer HA, Hussein MI, el-Mahdy Z, Mustafa M. Uranium bioassay and radioactive dust measurements at some uranium processing sites in Egypt—health effects. Journal of Environmental Monitoring. 2002;4(4):588-591.

Squibb KS, Gaitens JM, Engelhardt S, Centeno JA, Xu H, Gray P, McDiarmid MA,. Surveillance for long-term health effects associated with depleted uranium exposure and retained embedded fragments in US veterans. J Occup Environ Med. 2012 June: 54(6): 724-32.

Squibb KS, McDiarmid MA. Depleted uranium exposure and health effects in Gulf War veterans. Philos.Trans.R.Soc.Lond.B.Biol.Sci. 2006 Apr 29;361(1468):639-648.

Squibb, KS, McDiarmid, MA. Exposure and Health Surveillance in Gulf War Veterans Exposed To Depleted Uranium. Chapter 7 in: Depleted Uranium: Properties, Uses, and Health Consequences, Miller, A., ed. CRC Press, Boca Raton, FL. 2007.

Statistics Canada. Canadian Persian Gulf Cohort Study: Summary Report. Ottawa, ON: Statistics Canada, Catalogue no. 82-580-XIE. 2005. Retrieved from http://publications.gc.ca/Collection/Statcan/82-580-X/82-580-XIE2005001.pdf

Statistics Canada. The Canadian Persian Gulf Cohort Study: Detailed Report. Ottawa, ON: Statistics Canada, prepared for the Gulf War Veterans Cohort Study Advisory Committee. 02 November 2005. Retrieved from http://www.veterans.gc.ca/pdf/pro_research/gulf-war-linkage-project.pdf.

Stayner LT, Meinhardt T, Lemen R, Bayliss D, Herrick R, Reeve GR, Smith AB, Halperin W. A retrospective cohort mortality study of a phosphate fertilizer production facility. Arch Environ Health. 1985;40(13):133–138.

Storm HH, Jørgensen HO, Kejs AMT, Engholm G. Depleted uranium and cancer in Danish Balkan veterans deployed 1992-2001. Eur J Cancer 2006; 42(14): 2355-58.

The Royal Society. The health hazards of depleted uranium munitions: Part 1. Policy document 7/01. The Royal Society. London, England. 2001

The Royal Society. The health hazards of depleted uranium munitions: Part II. The Royal Society. London, England. 2002

Tirmarche M, Harrison J, Laurier D, Blanchardon E, Paquet F, Marsh J. Risk of lung cancer from radon exposure, contribution of recently published studies of uranium miners. Ann ICRP. 2012; 41(3-4):368-377.

UK DUOB. Final report of the depleted uranium oversight board. London, England: Depleted Uranium Oversight Board. Submitted to the Undersecretary of State for Defence. 2007.

UNEP. Depleted Uranium in Bosnia and Herzegovina. Post-Conflict Environmental Assessment. United Nations Environment Programme. March 2003.

UNEP. Depleted uranium in Serbia and Montenegro: Post-Conflict Environmental Assessment in the Federal Republic of Yugoslavia. United Nations Environment Programme. 2002.

UNEP. UNEP Final Report: Depleted Uranium in Kosovo. Post-Conflict Environmental Assessment, United Nations Environment Programme. 2001.

United Nations. Effects of Ionizing Radiation. Volume I: Report to the General Assembly, Scientific Annexes A. United Nations Scientific Committee on the Effects of Atomic Radiation, UNSCEAR 2006 Report.

United Nations. Sources and Effects of Ionizing Radiation. Volume 1: Report to the General Assembly, Scientific Annexes. United Nations Scientific Committee on the Effects of Atomic Radiation, UNSCEAR 2000 Report.

Wagoner JK, Archer VE, Carroll BE, Holaday DA, Lawrence PA. Cancer mortality patterns among US uranium miners and millers, 1950 through 1962. Journal of the National Cancer Institute. 1964;32(4):787-801.

Waxweiler R J, Archer VE, Roscoe RJ, Watanabe A, Thun MJ. Mortality patterns among a retrospective cohort of uranium mill workers. *In:* Epidemiology Applied to

Health Physics, Proceedings of the Sixteenth Midyear Topical Meeting of the Health Physics Society, Albuquerque, New Mexico, January 9-13, 1983. 1983;428-435.

WHO. Guidance on exposure to depleted uranium for medical officers and programme administrators. Geneva, Switzerland: World Health Organization. 2001.

WISE. World Information Service on Energy Uranium Project (Internet web page last updated 13 September, 2011). Retrieved from www.wise-uranium.org/ufert.html#LIT

Young HA, Maillard JD, Levine PH, Simmens SS, Mahan CM, Kang HK. Investigating the Risk of Cancer in 1990–1991 US Gulf War Veterans with the use of State Cancer Registry Data. Ann Epidemiol 2010;20:265–272.

ANNEX A: RISK ASSESSMENT AND MODELLING

One of the limitations in determining the degree to which depleted uranium (DU) might affect the health of Veterans is, with few exceptions, the lack of direct exposure information. To bridge this gap, the US (Parkhurst and Guilmette 2009), the UK (The Royal Society Report 2001), and France (Chazal et al. 2003) have conducted controlled experiments whereby DU munitions were fired into the same type of armoured vehicles as those used in combat.

The most comprehensive of these was commissioned by the US Army and is commonly known as the Capstone Study. Air samples were collected and analyzed to determine air concentrations of DU and particle size amongst other things. Different scenarios were developed (e.g., inside/outside the vehicle, ventilation system on/off, time spent in and around vehicles, etc.). It was thus possible to better estimate the amount of DU that the soldiers might have realistically inhaled or ingested in those situations. The methodology and findings were independently analyzed and validated (Marshall 2005; NRC 2008).

To determine what radiological effect these internalized particles might have once inside the body, one must use models. Modelling, a proven and universally-used approach, integrates scientific information from many sources and expresses it in mathematical equations. In the case of biokinetic models, they allow one to predict how particles of a given element are distributed and redistributed inside the human body and its organs. It thus makes it possible to determine the amount of radiation received by individual organs over time, and predict the potential harm that may ensue. Models can also be used in reverse, that is to say, to estimate the original intake based on the amount presently detected in the body, as in urine testing for uranium (Bailey and Phipps 2007).

The International Commission on Radiological Protection (ICRP) has developed many sophisticated, scientifically sound and internationally-recognized models. Their Human Respiratory Tract and their GI Tract models are key to the understanding of DU's behaviour in the human body. They take into consideration a number of parameters, such as the activity of the material itself, particle size, dissolution in the lung fluid, absorption into the blood and distribution/redistribution in the body, and eventually excretion.

Ultimately, an estimation of the risk of an adverse effect due to radiation can be made. This is based on animal experiments and preferably human studies when available. “In the case of uranium, the IRCP was fortunate in being able to draw on a number of good studies; this is not the case for many other elements. In particular, there are data from the so-called Boston Subjects, a group of terminally ill patients who were injected with uranium in the 1950's" (Bailey and Phipps 2007).

The ICRP updates its models continuously as new scientific information becomes available. While they may not be perfect, they “provide the only valid approach to obtaining a scientifically rigorous assessment of the course of future events where

experimental data relating to such events are not yet available” (The Royal Society 2002, p. 29).

ANNEX B: URANIUM WORKERS AND PHOSPHATE FERTILIZER PRODUCTION WORKERS: EPIDEMIOLOGIC STUDIES

Sites & References	Design	Population	Years Studied	Years Follow-up	Radiation Dose
Colorado Plateau U Millers					
1. Wagoner et al., 1964	Cohort	611	1950-1953	1950-1962	N/R
2. Archer et al., 1973	Cohort	662	1950-1953	1950-1953 14 yrs*	N/R
3. Waxweiler et al., 1983	Cohort	2,002	1940-1977	1940-1977	N/R
4. Pinkerton et al., 2004	Cohort	1,485	1940-1988	1940-1998	N/R
Tennessee Eastman Corp. Oak Ridge, Tenn. (TEC)					
5. Polednak & Frome, 1981	Cohort	18,869	1943-1947	1943-1977 27 yrs*	25-300 µg/m3
6. Frome et al., 1990	Cohort	28,008	1943-1947	1950-1979	N/R
Uranium-Materials Fabrication Plant (Y12) Oak Ridge, Tenn.					
7. Checkoway et al., 1988	Cohort	6,781 men	1947-1974	1947-1979 20.6 yrs*	29%>10 rem Internal dose
8. Loomis & Wolfe, 1996	Cohort	6,591 + 1,764 w men 922 + 562 w women 449 + 85 b men 149 + 69 b women	1947-1990	1947-1989	29%>10 rem Internal dose
9. Richardson & Wing, 2006	Cohort Nested case control	3,864	1947-74	1947-1990 >16 yrs*	10-100+ mSv Internal dose
10. Frome et al., 1997	Cohort	106,020	1943-1985	1950-1979	N/R
Fernald Feed-Materials Production Centre, Ohio					
11. Ritz, 1999	Cohort	4,014	1951-1989	1951-1990	8.2%> 10 rem internal dose
12. Boiano et al., 1989	Cross Sectional	146	Nov-Dec 1984	1985	13µg/l 109 >5µg/l
Portsmouth Uranium-enrichment Facility, Ohio					
13. Brown & Bloom, 1987	Cohort	5,773	1954-1982	1954-1982	N/R
Linde Air Products, Buffalo, NY					
14. Dupree et al., 1987	Cohort	995	1943-1949	1943-1979 30 yrs*	33.9%> 10 rem/yr internal dose
15. Teta & Ott, 1988	Cohort	995	1943-1949	1943-1981 32 yrs*	N/R

Sites & References	Design	Population	Years Studied	Years Follow-up	Radiation Dose
United Nuclear Corp., Conn					
16. Hadjimichael et al., 1983	Retrospective Cohort	4,106	1956-1978	1956-1978	0.5%>rem cumulative dose
Florida Phosphate-Fertilizer Production , Fl.					
17. Stayner et al., 1985	Retrospective Cohort	3,199	1953-1979	1953-1979	Exceeded occupational standards
Mallinckrodt Chemical Works, St. Louis, MO					
18. Dupree-Ellis et al., 2000	Cohort	2,514	1942-1966	1942-1993	17.8 mSv mean exposure
United Kingdom					
British Nuclear Fuels, Springfields Plant					
19. McGeoghegan & Binks, 2000b	Cohort	19,454	1946-1996	1946-1995	22.8mSv mean external dose
British Nuclear Fuels, Chapelcross Plant					
20. McGeoghegan & Binks, 2001	Cohort	2,628	1955-1995	1955-1995	83.6 mSv mean external dose
British Nuclear Fuels, Capenhurst Plant					
21. McGeoghegan & Binks, 2000a	Cohort	12,543	1946-1996	1946-1995	9.85 mSv mean external dose
Atomic Weapons Est. UK					
22. Beral. et al., 1988	Retrospective Cohort	22,552	1951-1982	1951-1982	7.8 mSv whole body 14.4 mSv surface
Rocketdyne Atomics International					
23. Ritz et al. 2000	Retrospective Cohort	2,297	1950-1993	1950-1954	2.1 mSv est. lung dose
24. Boice et al., 2006	Retrospective Cohort	5,801	1948-1999	1948-1999	13.5 mSv mean external radiation 19.0 mSv mean lung dose
Savannah River Plant GA					
25. Cragle et al., 1988	Retrospective Cohort	9,860	1952-1981	1952-1980	Average exposure 13 yrs
Egyptian Processors					
26. Shawky et al., 2002	Cross-sectional	86	N/R	N/R	1-80 mSv

Sites & References	Design	Population	Years Studied	Years Follow-up	Radiation Dose
4 US Processing Facilities					
TEC Y12 Mallinckrodt Fernald Feed Materials Dupree et al.,1995	Pooled 787 lung cancer cases 1:1 matched controls		N/R	26 yrs mean	

* mean number of years follow-up per worker
w men/women = white men/women
b men/women = black men/women
N/R = Not reported

ANNEX C: URANIUM WORKERS AND PHOSPHATE FERTILIZER PRODUCTION WORKERS: MALIGNANT DISEASES

	CANCER SMRs (95% CIs) or p values				
Sites & References	**Lung**	**Leukemia**	**Hodgkin Disease**	**Non-Hodgkin Lymphoma**	**Bone**
Colorado Plateau U Millers					
1. Wagoner et al., 1964	0 (NS)	-	-	-	-
2. Archer et al., 1973	94 (-3 to 191)**	127 (NS)	-	392 (p<0.05)	-
3. Waxweiler et al., 1983	83 (54-121)	0 (NS)	231 (48-675)	91 (NS)	-
4. Pinkerton et al., 2004	113 (89-141)	66 (21-153)	330 (90-843)	122 (NS)	-
Tennessee Eastman Corp. Oak Ridge, Tenn. (TEC)					
5. Polednak & Frome, 1981	109 (97-122)	92 (66-125)	55 (NS)	67 (NS)	90 (33-196)
Corrected	122 (110-136)	102 (74-137)	-	-	100 (40-206)
6. Frome et al., 1990	127 (p<0.01)	113 (NS)	-	85 (NS)	106 (NS)
Uranium-Materials Fabrication Plant (Y12) Oak Ridge, Tenn.					
7. Checkoway et al., 1988	136 (109-1670)	50 (14-128)	87 (18-254)	62 (13-181)	-
8. Loomis & Wolfe, 1966 All	117 (101-134)	60 (3-107)	62 (13-183)	50 (14-129)	62 (1-345)
White men	120 (104-138)	-	-	-	-
9. Richardson & Wing, 2006	1.4 (.65-3.01)	-	-	-	-
10. Frome et al., 1997	118 (NS)	98 (NS)	77 (NS)	91 (NS)	119 (NS)
Fernald Feed-Materials Production Centre, Ohio					
11. Ritz, 1999	101 (83-121)	116 (62-198)	204 (74-443)	167 (72-329)	0 (0-370)
12. Boiano et al., 1989	-	-	-	-	-

Sites & References	CANCER SMRs (95% CIs) or p values Lung	Leukemia	Hodgkin Disease	Non-Hodgkin Lymphoma	Bone
Portsmouth Uranium-enrichment Facility, Ohio					
13. Brown & Bloom, 1987	88 (65-117)	-	-	146 (NS)	-
Linde Air Products, Buffalo, NY					
14. Dupree et al., 1987	0.97 (.60-198)	-	-	-	-
15. Teta & Ott, 1988	-	-	-	-	-
United Nuclear Corp., Conn					
16. Hadjimichael et al., 1983	95 (52-160)	113 (13-409)	-	65 (7-234)	206 (3-1140)
Florida Phosphate-Fertilizer Production , Fl.					
17. Stayner et al., 1985	113 (61-192)	-	-	53 (9-167)	-
Mallinckrodt Chemical Works, St. Louis, MO					
18. Dupree-Ellis et al., 2000	102 (83-124)	111 (57-189)	92 (15-283)	28 (1-156)	120 (7-526)
United Kingdom					
British Nuclear Fuels, Springfields Plant					
19. McGeoghegan & Binks, 2000b	85 (p<0.01)	100 (NS)	124 (NS)	60 (NS)	67 (NS)
SIR***	75 (<0.001)	79 (NS)	139 (NS)	79 (NS)	0 (NS)
British Nuclear Fuels, Chapelcross Plant					
20. McGeoghegan & Binks, 2001	-	-	-	-	-
British Nuclear Fuels, Capenhurst Plant					
21. McGeoghegan & Binks, 2000a	89 (NS)	69 (NS)	177 (NS)	109 (NS)	0 (NS)
SIR	84 (NS)	74 (NS)	65 (NS)	58 (NS)	0 (NS)
Atomic Weapons Est. UK					
22. Beral. Et al., 1988	64 (p<0,01)	44 (NS)	56 (NS)	49 (NS)	74 (NS)
Rocketdyne (Atomics International)					
23. Ritz et al. 2000	81 (59-108)	146 (63-288)	-	45 (NS)	-

Sites & References	CANCER SMRs (95% CIs) or p values Lung	Leukemia	Hodgkin Disease	Non-Hodgkin Lymphoma	Bone
24. Boice et al., 2006	89 (76-105)	133 (86-197)	199 (65-463)	98 (59-152)	0 (0-352)
Savannah River Plant GA					
25. Cragle et al., 1988	85 (NS)	163 (NS)	-	95 (NS)	0 (NS)
Egyptian Processors					
26. Shawky et al., 2002	-			-	-

**These values reported in IOM 2000, 2008
RR=Relative Risk
SIR***=Standardized Incidence Ratio

Sites & References	CANCER SMRs (95% CI) or P value Renal	Bladder	CNS	Stomach	Prostate	Testicular
Colorado Plateau U Millers			-			
1. Wagoner et al., 1964	-	-	-	-	-	-
2. Archer et al., 1973	-	-	-	-	-	-
3. Waxweiler et al., 1983	112(23-325)	-	-	40 (8-117)	71 (26-154)	-
4. Pinkerton et al., 2004	81 (22-206)	-		-	-	76 (43-126)
Tennessee Eastman Corp. Oak Ridge, Tenn. (TEC)						
6. Frome et al., 1990	84 (NS)	82 (NS)	116 (NS)	78 (NS)	106 (NS)	73 (NS)
Uranium-Materials Fabrication Plant (Y12) Oak Ridge, Tenn.						
7. Checkoway et al., 1988	122 (45-266)	72 (15-210)	180 (98-302)	57 (19-133)	92 (37-190)	-
8. Loomis & Wolfe, 1966	130 (74-211)	72 (31-142)	129 (79-200)	64(33-112)	131 (91-181)	0 (0-159)
9. Richardson & Wing, 2006	-	-				-
10. Frome et al., 1997	92 (NS)	76 (NS)	109 (NS)	73 (NS)	101 (NS)	72 (NS)
Fernald Feed-Materials Production Centre, Ohio						
11. Ritz, 1999	63 (20-146)	115 (50-227)	124 (64-217)	134 (75-221)	144 (93-212)	67 (1-374)

Sites & References	CANCER SMRs (95% CI) or P value					
	Renal	**Bladder**	**CNS**	**Stomach**	**Prostate**	**Testicular**
12. Boiano et al., 1989	-	-	-			
Portsmouth Uranium-enrichment Facility, Ohio						
13. Brown & Bloom, 1987	-	-	-	169 (NS)	-	-
Linde Air Products, Buffalo, NY						
14. Dupree et al., 1987	-	-	-	165 (66-339)	-	-
15. Teta & Ott, 1988	-	-	-	-	-	-
United Nuclear Corp., Conn						
16. Hadjimichael et al., 1983	-	0.52 (1-292)	240 (65-615)	-	-	-
Florida Phosphate-Fertilizer Production , Fl.						
17. Stayner et al., 1985	-	-	-	-	-	-
Mallinckrodt Chemical Works, St. Louis, MO						
18. Dupree-Ellis et al., 2000	117 (54-218)	116 (48-236)	157 (84-264)	38 (12-89)	115 (74-170)	93 (5-408)
United Kingdom						
British Nuclear Fuels, Springfields Plant						
19. McGeoghegan & Binks, 2000b	60 (NS)	92 (NS)	67 (NS)	92 (NS)	89 (NS)	61 (NS)
SIR	63 (NS)	76 p<.05	64 (NS)	76 p<.05)	77 p<.05	92 (NS)
British Nuclear Fuels, Chapelcross Plant						
20. McGeoghegan & Binks, 2001	-	-	-	-	-	-
British Nuclear Fuels, Capenhurst Plant						
21. McGeoghegan & Binks, 2000a	49 (NS)	104 (NS)	139 (NS)	90 (NS)	79 (NS)	0 (NS)
SIR	45 (NS)	96 (NS)	103 NS	93 (NS)	54 (NS)	96 (NS)
Atomic Weapons Est. UK						
22. Beral. Et al., 1988	188 (NS)	51 (NS)	32 p<0.05	67 p<.05	139 (NS)	58 (NS)

	CANCER SMRs (95% CI) or P value					
Sites & References	**Renal**	**Bladder**	**CNS**	**Stomach**	**Prostate**	**Testicular**
Rocketdyne Atomics International						
23. Ritz et al. 2000	126 (41-294)	89 (18-259)	131 (48-284)	118(43-257)	73 (29-150)	-
24. Boice et al., 2006	94 (49-164)	65 (8-129)	115 (67-183)	117 (73-179)	93 (66-129)	69 (2-382)
Savannah River Plant GA						
25. Cragle et al., 1988	40 (NS)	60 (NS)	23 p<0.05	68 (NS)	60 (NS)	-
Egyptian Processors						
26. Shawky et al., 2002	-	-	-	-	-	-

ANNEX D: URANIUM WORKERS AND PHOSPHATE FERTILIZER PRODUCTION WORKERS: NON-MALIGNANT DISEASES

Sites & References	Renal	Respiratory	Neurologic
Colorado Plateau U Millers			
1. Wagoner et al., 1964	-	-	-
2. Archer et al., 1973	-	-	-
3. Waxweiler et al., 1983	167 (60-353)	163 (123-212)	-
4. Pinkerton et al., 2004	135 (58-267)	143 (116-173)	-
Tennessee Eastman Corp. Oak Ridge, Tennessee (TEC)			
5. Polednak & Frome, 1981	77 (45-109)	122 (110-136)	77 (49-105)
6. Frome et al., 1990	99 (71-126)	125 (117-133)	93 (71-115)
Uranium-Materials Fabrication Plant (Y12) Oak Ridge, Tennessee			
7. Checkoway et al., 1988	72 (31-142)	76 (53-104)	-
8. Loomis & Wolfe, 1966	-	-	-
9. Richardson & Wing, 2006	-	-	-
10. Frome et al., 1997	83 (NS)	112 (NS)	70 (NS)
Fernald Feed-Materials Production Centre, Ohio			
11. Ritz, 1999	21 (4-129)	66 (50-87)	-
12. Boiano et al., 1989	-	-	-
Portsmouth Uranium-enrichment Facility, Ohio			
13. Brown & Bloom, 1987	-	-	-
Linde Air Products, Buffalo, NY			
14. Dupree et al., 1987	-	-	-
15. Teta & Ott, 1988	-	-	-
United Nuclear Corp., Conn			
16. Hadjimichael et al., 1983	-	-	-
Florida Phosphate-Fertilizer Production , Fl.			
17. Stayner et al., 1985	-	-	-
Mallinckrodt Chemical Works, St. Louis, MO			
18. Dupree-Ellis et al., 2000	188 (75-381)	80 (62-101)	82 (43-141)
United Kingdom			
British Nuclear Fuels, Springfields Plant			
19. McGeooghegan & Binks, 2001, 2000b	57 ($p<0.01$)	79 ($p = 0.02$)	69 ($p<0.05$)
British Nuclear Fuels, Chapelcross Plant			
20. McGeoghegan & Binks, 2001	108 (NS)	-	71 (NS)
British Nuclear Fuels, Capenhurst Plant			
21. McGeoghegan & Binks, 2000a	98 (NS)	70 ($p = 0.008$)	98 (NS)
Atomic Weapons Est. UK			
22. Beral. Et al., 1988	-	-	-
Rocketdyne (Atomics International)			
23. Ritz et al. 2000	78 (25-181)	75 (50-106)	-
24. Boice et al., 2006	118 (61-206)	67 (52-84)	96 (65-137)
Savannah River Plant GA			
25. Cragle et al., 1988	39 (10-96)	41 (24-66)	81 (NS)
Egyptian Processors			
26. Shawky et al., 2002	-	-	-

ANNEX E: COMPARATIVE RADIATION DOSES AND HUMAN LIMITS

Doses in mSv	DESCRIPTION
1000	Dose which may cause radiation sickness if received within 24 hours
100	Lowest dose known to cause cancer (UNSCEAR 2006)
60	Committed dose received over 50 years from worst-case level I-exposed soldiers involved in friendly fire tank accidents (Squibb and McDiarmid 2007)
50	Annual dose limit for nuclear energy workers
15	Diagnostic myocardial perfusion imaging test
12	CAT scan of the abdomen
2.4	Average background radiation received annually by worldwide population of which 1.2 mSv comes from radon (UNSCEAR 2000)
1.0	Annual radiation dose limit for the general public in addition to background radiation (ICRP 1995)
0.7	Mammography
0.55	Committed dose over one year received by soldiers in tanks hit by DU rounds (Chazal et al. 2003)
0.03	Worst-case level III exposure within a contaminated vehicle (The Royal Society 2001)
$4.1X\ 10^{-6}$	Committed dose received over 50 years by Iraqi civilians downwind of a battle zone (Marshall 2008)

ANNEX F: CHRONIC SYMPTOM-BASED ILLNESSES FOLLOWING WARS

A condition frequently reported after military conflicts is characterized by persistent symptoms for which physical examination and laboratory testing is often unrevealing. This has been best studied in Veterans returning from the Gulf War in the early 1990's (IOM 2010; IOM 2006) who experienced a chronic multi-symptom illness which could not be attributed to a specific cause (IOM 2000). However, other illnesses manifested by persistent symptoms date back at least as far as the American Civil War (Hyams 1996). One category of symptoms is physical (somatic), with pain (e.g., low back and other types of musculoskeletal pain, headache), fatigue, sleep disturbances and gastrointestinal symptoms being especially prominent. The symptom cluster of pain, fatigue, and impaired sleep bears a strong resemblance to somatic syndromes like fibromyalgia and chronic fatigue syndrome. A second category of symptoms reflects psychological conditions, the most common being post traumatic stress disorder (PTSD) and depression. Chronic physical and psychological symptoms frequently co-occur, causing reciprocal adverse effects in terms of suffering, health-related quality of life, disability, and response to treatment. Studies in Canadian Force (CF) members have been similar. A survey of 3,113 CF Gulf and Kuwait War Veterans and 3,439 active CF members who were non-deployed indicated that deployed Veterans had a higher prevalence of self-reported health problems including diseases of bones and joints, digestive system, skin, and respiratory system (Gilroy 1998). They also had a higher prevalence of chronic fatigue symptoms, cognitive dysfunction, major depression, posttraumatic stress disorder, anxiety and fibromyalgia. However, long-term follow-up of CF deployed Veterans has not revealed an increased risk of mortality or cancer (Statistics Canada 2005).

These findings are not unique to military populations but are true of patients seen in civilian practices where common symptoms are highly prevalent, often co-occur with one other, are "medically unexplained" (i.e., symptom-only diagnoses) a third to half of the time, become chronic in 20% of those who experience symptoms, and cause substantial impairment in health-related quality of life. Moreover, symptom reporting is increased in a number of stressful circumstances, including: the aftermath of natural or manmade disasters; civilians in war-torn nations; immigrant populations who have fled distressing situations and enter unfamiliar cultures; and individuals after major losses (e.g., bereavement; unemployment; breakup of relationships; severe illnesses; catastrophic events; financial crises).

Other terms that may appear in the literature include: 1) *functional somatic syndromes* (typically applied to conditions like fibromyalgia, irritable bowel syndrome, and chronic fatigue syndrome); 2) *somatoform disorders* or somatization (often implying some psychological mechanisms); or 3) *medically unexplained symptoms (MUS)*. There is overlap between all of these constructs; each has some inherent problems; and an ideal classification system or nomenclature has not yet been developed or agreed upon (Kroenke 2006). This is highlighted by the 780-799 section of ICD (commonly used in

Gulf War Veterans with persistent symptoms) called symptoms, signs and ill-defined conditions (Roy 1998).

The most extensively investigated instance of symptoms following military deployment occurred after the Gulf War in the early 1990s which to date has not been linked to any specific exposures (e.g., pyridostigmine, sarin, pesticides, vaccinations, oil fires or fumes, depleted uranium, other biological or chemical agents, etc.). Also, no new unique disease has emerged (Davis 2000; Gardner 2003). However, effective treatments are available including cognitive-behavioral therapy for chronic multi-symptom illness, exercise, medications targeting specific symptoms (e.g., pain, mood, gastrointestinal symptoms), and symptom-based behavioural interventions (Donta 2003). It is also important to address barriers to treatment and rehabilitation such as inadequate physician education about these types of conditions, perceived stigma related to chronic poorly-understood symptoms, and concerns about disability and health care.

The Institute of Medicine (IOM) is completing an expert consensus report on *Gulf War and Health: Treatment of Chronic Multisymptom Illness*, targeted for release in early 2013. Information about the work the committee was asked to undertake can be found at http://www.iom.edu/Activities/Veterans/GulfWarMultisymptom.aspx

ACRONYMS & DEFINITIONS

ATSDR	Agency for Toxic Substance and Disease Registry (US)
BEIR	Biological Effects of Ionizing Radiation. It is a committee of the NRC (US).
BIOMARKER	A measurable characteristic or indicator of organ function or the presence or severity of a disease
CANDU	Canadian Deuterium Uranium Reactor
CF	Canadian Forces
CNSC	Canadian Nuclear Safety Commission
Cohort Study	Follows a group of people over time to understand the relationship between an exposure (for example to an environmental pollutant) and the subsequent development of a disease or illness. One cohort study design, a retrospective cohort study, will use information available from administrative sources to look back in time to understand the relationship between exposure and the development of disease.
Committed Dose	The effective dose that is expected to be received in a given period after the intake (usually in 50 years for workers and in 70 years for the general population)
Cross-sectional Study	Describes the relationship between population characteristics and the prevalence of disease at one point in time
Depleted Uranium	Natural uranium whose isotopic mix contains a higher proportion of the non-fissile and less radioactive isotope ^{238}U
DND	Department of National Defence (Canada)
DU	Depleted uranium
Effective Dose	A measure of the risk of harm, from irradiation, to a whole person, which takes into account the different types of radiation and the different doses to different organs in the body. Radiation protection limits are expressed as effective doses.
Enriched Uranium	Natural uranium which has been modified so that it has higher percentage of the fissile isotope ^{235}U. Only enriched uranium is

	suitable for use in nuclear reactors and bombs.
Fissile	A material's ability to disintegrate and sustain a chain reaction, thus releasing large amounts of energy
Genotoxic	A chemical or other agent that is damaging to DNA, thereby causing mutations which can result in cancer
GWV	Gulf War Veteran
Half-life	The time that an initial quantity of radioactive material takes to decay to half of its original amount. In general, the longer its half-life, the less radioactive that element is. For example, ^{238}U, a weakly radioactive isotope of uranium, has a half-life of 4.5 billion years. Radon, a known lung carcinogen, has a half-life of 3.82 days.
HRR	Hazard Rate Ratio: a statistical method for determining the chance of events occurring in the treatment arm of a research trial as a ratio of the chance of events occurring in the control arm
ICRP	International Commission on Radiation Protection
IOM	Institute of Medicine (of the National Academies (US))
Ionization	The process by which a neutral atom or molecule acquires a positive or negative charge
Ionizing Radiation	A type of radiation which has sufficient energy to displace electrons from molecules
Isotope	The atoms of the same element that have different numbers of neutrons
Low-level Ionizing Radiation	Radiation below 100 mSv
MRR	Mortality Rate Ratio: the mortality rate (deaths divided by persons alive over a defined period of time) in one group of a population as a ratio of the mortality rate in a second group in a population. It is conceptually similar to the incidence ratio. The mortality rate ratio is based on deaths, whereas the incidence ratio is based on new cases of disease.
NRC	National Research Council (United States)

PIR	Proportional Incidence Ratio: a statistical method for comparing data sets where a standard set of age-specific proportions is available and can be compared with the data set of interest
Radioactivity	The spontaneous nuclear transformations that result in the formation of new elements
Radon	A radioactive, colourless, odourless, noble gas that occurs naturally as an indirect decay product of uranium
Respirable	The fraction of an aerosol that is inhaled and reaches the deep sections of the lung where gas exchange with blood takes place
RR	Relative Risk: the ratio of the probability of disease occurring in an exposed group versus a non-exposed group
SCHER	Scientific Committee on Health and Environmental Risks (European Union)
SEER	Surveillance, Epidemiology and End Results: a national registry for cancers commissioned by the National Cancer Institute (US)
Sievert	A measure of radiation energy deposited in tissues. The mSv or 1/1000th of a sievert is the measure most often used in this report.
SIR	Standardized Incidence Ratio: compares the morbidity experience between the population of interest and the experience of that population, had they had the same morbidity experience of a comparison population
SMR	Standardized Mortality Ratio: the ratio of observed deaths in a study group to expected deaths in the general population adjusted for age differences between the two populations
U	Uranium
UNEP	United Nations Environment Program
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation
VAC	Veterans Affairs Canada
WHO	World Health Organization