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HUMAN HEALTH AND THE BIOLOGICAL EFFECTS OF TRITIUM IN DRINKING WATER: PRUDENT POLICY THROUGH SCIENCE – ADDRESSING THE ODWAC NEW RECOMMENDATION

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□ Tritium is a radioactive form of hydrogen and is a by-product of energy production in Canadian Deuterium Uranium (CANDU) reactors. The release of this radioisotope into the environment is carefully managed at CANDU facilities in order to minimize radiation exposure to the public. However, under some circumstances, small accidental releases to the environment can occur. The radiation doses to humans and non-human biota from these releases are low and orders of magnitude less than doses received from naturally occurring radioisotopes or from manmade activities, such as medical imaging and air travel. There is however a renewed interest in the biological consequences of low dose tritium exposures and a new limit for tritium levels in Ontario drinking water has been proposed. The Ontario Drinking Water Advisory Council (ODWAC) issued a formal report in May 2009 in response to a request by the Minister of the Environment, concluding that the Ontario Drinking Water Quality Standard for tritium should be revised from the current 7,000 Bq/L level to a new, lower 20 Bq/L level. In response to this recommendation, an international scientific symposium was held at McMaster University to address the issues surrounding this change in direction and the validity of a new policy. Scientists, regulators, government officials, and industrial stakeholders were present to discuss the potential health risks associated with low level radiation exposure from tritium. The regulatory, economic, and social implications of the new proposed limit were also considered.

The new recommendation assumed a linear-no-threshold model to calculate carcinogenic risk associated with tritium exposure, and considered tritium as a non-threshold chemical carcinogen. Both of these assumptions are highly controversial given that recent research suggests that low dose exposures have thresholds below which there are no observable detrimental effects. Furthermore, mutagenic and carcinogenic risk calculated from tritium exposure at 20 Bq/L would be orders of magnitude less than that from exposure to natural background sources of radiation. The new proposed standard would set the radiation dose limit for drinking water to 0.0003 mSv/year, which is equivalent to approximately three times the dose from naturally occurring tritium in drinking water. This new standard is incongruent with national and international standards for safe levels of radiation exposure, currently set at 1 mSv/year for the general public. Scientific research from leading authorities on the carcinogenic health effects of tritium exposure supports the notion that the current standard of 7,000 Bq/L (annual dose of 0.1 mSv) is a safe standard for human health.

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Policy-making for the purpose of regulating tritium levels in drinking water is a dynamic multi-stage process that is influenced by more than science alone. Ethics, economics, and public perception also play important roles in policy development; however, these factors sometimes undermine the scientific evidence that should form the basis of informed decision making. Consequently, implementing a new standard without a scientific basis may lead the public to perceive that risks from tritium have been historically underestimated. It was concluded that the new recommendation is not supported by any new scientific insight regarding negative consequences of low dose effects, and may be contrary to new data on the potential benefits of low dose effects. Given the lack of cost versus benefit analysis, this type of dramatic policy change could have detrimental effects to society from an ethical, economical, and public perception perspective.

Key Words: Tritium, Health Risk, Carcinogen, Low Dose Radiation, Standard

1. INTRODUCTION

An international scientific symposium was held at McMaster University (Hamilton, Ontario, Canada) on August 26 and 27, 2010, focusing on human health and the biological effects of tritium in drinking water. This meeting and review are timely as both the federal and provincial regulators (Ministry of the Environment (MOE) and Canadian Nuclear Safety Commission (CNSC), respectively) are considering major revisions to current policies. The specific goal of the McMaster University symposium was to address the new recommendation proposed by the Ontario Drinking Water Advisory Council (ODWAC) to lower the limit of tritium in drinking water from its current 7,000 Bq/L to 20 Bq/L. The rationale for the new proposed limit is that the current limit does not adequately protect humans against the carcinogenic risk of tritium exposure. Professionals in radiation science, regulation, government and industry were brought together to discuss; 1) if the proposed limit is supported by modern science, 2) if the methodologies used to develop the recommendation are appropriate, and 3) if the new recommended value will have the benefit of improving human health.

Tritium (^3H) is a radioactive isotope of hydrogen that emits beta particles with a maximum energy of 18 keV (average 5.7 keV) as it decays to helium. It is generated naturally when cosmic radiation interacts with gases in the upper atmosphere of the Earth and is also a by-product of nuclear energy production in CANDU (**Can**ada **D**euterium **U**ranium) reactors. Tritium exists in many forms: in water molecules as tritiated water (HTO), in organic molecules as organically bound tritium (OBT) and in air as tritiated gas (HT). The physical half life of tritium is 12.3 years, however its biological half life depends on its form; OBT has been shown to have a half life of 40 days (Osborne, 2002) whereas gaseous tritiated water is eliminated almost immediately through respiration. Given its low energy beta emission and corresponding short range in air (6 mm), tritium poses a health risk only when ingested, inhaled or absorbed through the skin. Exposure of the general public to extremely low doses of tritium most often occurs through the ingestion of tritiated water. The current annual limit for tritium ingested through drinking water is 7,000 Bq/L (one Becquerel (Bq) is one radioactive decay per second) which translates into an annual effective dose of 0.1 mSv if consumed at a rate of two litres per day for 365 days. The recommended limit (20 Bq/L) translates into an annual effective dose of 0.0003 mSv; a dose reduction of 0.0997 mSv/year. It is scientifically unclear what has prompted revision of the current policy. It might be expected that new evidence exists indicating negative consequences associated with exposure to tritium, even at low doses, which could lead to adverse health effects such as an increased risk of mutation and cancer. However, this is not the case and justification for implementing a new, decreased limit has been predicted using a historical approach of applying a linear no threshold (LNT) model for risk estimation.

2. TRITIUM PRODUCTION, RADIATION DOSIMETRY AND BIODISTRIBUTION (DRS ANTONIAZZI, WAKER, ULSH, AND KRAMER)

Tritium is a by-product of energy production in CANDU reactors, which use heavy water (D2O) and natural uranium oxide fuel. Heavy water is employed in two areas of the CANDU cycle; as a coolant in the primary heat transport system and as a moderator to control the nuclear reaction. Tritium is generated by the interaction of neutrons, emitted during the fission of uranium fuel, with heavy water. Tritium is produced at a rate of 2×10^{12} Bq/MW(e) in the heat transport system, but the majority (97%) comes from the moderator where it is produced at a rate of ~7.2×10^{13} Bq/MW(e) (Wong *et al.*, 1984). As such, an operating 700 MW(e) nuclear power unit can have a tritium inventory exceeding 10^{17} Bq. However, less than 1% of the production rate has ever been lost to the environment because of multiple barriers that are in place to minimize releases (Wong *et al.*, 1984). Controlling tritium release is directly proportional to controlling heavy water leakage from the moderator and primary heat transport systems. Heavy water and tritium losses to the environment are minimized in CANDU reactors through design, usage of components with higher leak-tightness standards, and water recovery systems. Specific methods employed to control emissions to the environment include: detritiation, recovery, confinement of tritiated air, and ventilation control. Among these, detritiation, the extraction of tritium from the heavy water via distillation, is the most effective method of reducing tritium emissions. The management of heavy water is an important aspect of CANDU operations; from the perspective of reducing tritium emissions and also due to the cost of replacing lost heavy water.

Radiation quality and the relative biological effectiveness (RBE) of tritium have been studied extensively over the past 30 years. Energy deposited in a cell is a random variable (stochastic process) and is dependent on radiation dose or quality. At low doses and dose rates, the density of energy deposited along radiation tracks is low; some cells are hit with radiation, others are not. The low dose rate from tritium at 20 Bq/L in drinking water would consequently translate into only a small fraction of the cell population being exposed with the majority of cells never being exposed at all. Energy deposited in a cell or cell nucleus can be determined by using low pressure tissue equivalent gases and a wall-less proportional counter. This approach allows for the measurement of the distribution of energy deposition by single electron interactions for any radiation quality (Eickel and Booz, 1976). From the measured single event spectra, the average energy deposited in a cell or cell nucleus per event or the average number of events for a certain exposure period may be determined (Ellett and Braby, 1972). This technique can be employed to compare the ionization event frequencies for tritium exposure at 20 Bq/L with that of other naturally occurring radionuclides such as potassium-40 which is ingested by humans through the food chain. Potassium-40 also undergoes beta decay like tritium, but produces a higher energy emission. The fraction of cells experiencing an event per year from natural sources such as potassium-40 is about 2 events per 100 cells. On the other hand, events from tritium in drinking water at concentrations of 20 Bq/L would be about 2.5 events per 100,000 cells. Therefore, annually there would be thousands of times more cellular events caused naturally from decay of potassium-40 compared to tritium at 20 Bq/L. DNA damage is one of the most important determinants of the cellular response to radiation but at very low doses, computer modeling is one of the only tools available to estimate single strand or double strand breaks resulting from radiation interactions with DNA. This method was used to establish that a radiation weighting factor (RBE) of 1 is appropriate for tritium beta particles, meaning that tritium is not significantly different in its ability to damage DNA from other sources of energetic electrons (Moiseenko *et al.*, 2001). Calculations using computer modeling predicted no major difference in DNA strand break yields or in the complexity of double-strand breaks between tritium, high energy gamma rays or potassium-40, even though there is a difference between these radiation qualities in the average dose delivered to a hit cell. Overall, evidence indicates that tritium beta particles at low doses do not produce unique DNA lesions and that significantly more DNA interactions would occur from other naturally occurring radioisotopes than from tritium in drinking water at a concentration of 20 Bq/L.

Tritium in drinking water at its current limit of 7,000 Bq/L, and the proposed limit of 20 Bq/L, can be compared with international standards and other sources of radiation exposure. International standards, guidelines, action levels, and limits vary from 100 Bq/L (European Union) to 30,000 Bq/L (Finland). The proposed ODWAC limit is therefore significantly lower than any existing regulatory limit (Canadian Nuclear Safety Commission, 2008). Even the current limit of 7,000 Bq/L in Canada falls below limits imposed by other nations such as Russia, Switzerland, and Australia (Canadian Nuclear Safety Commission, 2008). It is important to note that, regardless of the current regulatory limit of 7,000 Bq/L, good performance by the nuclear industry has kept levels of tritium far below this level. At a concentration of 7,000 Bq/L, the annual effective radiation dose would be 0.1 mSv, and the proposed new limit of 20 Bq/L would result in an annual effective dose of 0.0003 mSv, to a person consuming 2 L of water daily. Both of these annual doses are insignificant relative to the variation in annual background levels of radiation in different geographical locations across Canada. For example, individuals living in Winnipeg receive an annual dose of 4.0 mSv whereas residents of Toronto only receive 1.8 mSv (Canadian Nuclear Safety Commission, 2008). Moreover, routine activities, such as eating (0.3 mSv/year) or watching television (0.3 mSv/year) result in higher annual doses than the dose received from tritium in drinking water, even with the current limit. Based on these facts alone, it could be questioned whether or not the new proposed standards are an effective use of limited public health resources.

The average total effective dose per person in North America is 6.3 mSv/year (National Council on Radiation Protection and Measurements, 1987). Contributing to this exposure, radioactive materials are ingested and inhaled daily such as: uranium (1 Bq for U and each decay product), thorium (0.1 Bq for Th and each decay product), radon (25 - 1000 Bq m^{-3} internal), potassium-40 (4,400 Bq), carbon-14 (3,080 Bq), rubidium-87 (600 Bq) and polonium-210 (37 Bq) (National Council on Radiation Protection and Measurements, 1984; National Council on Radiation Protection and Measurements, 1987). Tritium in drinking water can be compared to levels of natural background radiation exposure and the corresponding cancer risk at low doses can be extrapolated from risk observed at high doses assuming a linear no threshold response (LNT) model. A 1000 mSv acute total body dose increases the average individual's risk of cancer mortality over their lifetime by 5% above the average population risk of 25% (International Commission on Radiological Protection, 1991). Using this information, the LNT model estimates that all radiation doses increase cancer risk, and in the absence of low dose risk data, the model proposes that risk be extrapolated from effects at high doses. This assumption is not universally accepted for doses below 100 mSv and is not supported by recent scientific research. Nonetheless, using this LNT approach, the increase in cancer risk associated with a 0.1 mSv exposure would be predicted to be between 0.00043% to 0.00072% and the increase in cancer risk associated with a 0.0003 mSv exposure would be predicted to be roughly 1 to 2 per million. Given the background cancer mortality rate of 25% (Office for National Statistics, 2009), changing the standard would effectively reduce the overall cancer risk from 25.00043% to 25.00000123% (a factor of 1.00007). Given that the LNT model is widely disputed, the validity of any risk estimates derived from it is debatable. It would be expected that there will be high analytical costs associated with monitoring to lower detection levels. It is also plausible that significant costs will be incurred if there is a need to seek out alternative sources of drinking water or electricity production, should levels approach the new lower regulatory limit.

3. TRITIUM RADIATION PROTECTION AND LINEAR EXTRAPOLATION FROM HIGH DOSES (DRS CHAMBERS AND CALABRESE)

The background tritium concentrations in the Great Lakes of Superior, Huron and Ontario have been stable and below 5 Bq/L since 2002. The 52 week running average tritium levels at water supply plants in cities located on these lakes have been consistently below 10 Bq/L since 2001. The fact that the current limit is much higher than the actual measured levels indicates that current practices for tritium management are effective. The current Health Canada and Ontario Drinking Water guidelines are based on the World Health Organization guidelines (World Health Organization, 2006). These guidelines recommend a reference dose level of 0.1 mSv/year from drinking water; a dose equivalent to 10% of the ICRP's annual limit for public exposure. However, there have been previous attempts to change this policy including the Advisory Committee on Environmental Standards' (ACES) recommendation (Advisory Committee on Environmental Standards, 1994) to lower the tritium standard to 100 Bq/L, to be further decreased to 20 Bq/L within five years. This recommendation lead to a joint Health Canada and Atomic Energy Control Board (AECB) review of ionizing radiation and genotoxic chemical risk assessment and management strategies. Ultimately, it was concluded that the current practices were providing a "high degree of health protection", and the tritium standard was left unchanged at 7,000 Bq/L (Joint Working Group (AECB, Health Canada, and Ontario Ministry of Environment and Energy Staff), 1998). Our understanding of low dose effects has continued to improve since then and no new evidence has appeared to indicate that the current limit should be changed. Using the LNT model, it can be calculated that consuming two liters of water at 20 Bq/L per day over a 75 year span corresponds to a one in a million lifetime cancer risk (using the current ICRP 103 (2008) cancer risk coefficient of approximately 5 % per Sievert). This is the level set by international authorities as the cut-off for acceptable risk. However, this risk calculation and the LNT model incorporate many assumptions that will be discussed below. Nonetheless, changing a standard without good evidence to support the change could create negative public perception issues. Specifically, a drastic decrease in the standard (by a factor of more than 300) may have the consequence of implying that previous standards were inadequate and that risks from tritium exposure have been underestimated.

The rationale for proposing a new standard has been solely based on the LNT model and therefore a historical perspective on the implementation of the linear no threshold dose response curve for ionizing radiation regulations should be reviewed (Calabrese, 2009). The first radiation tolerance dose, set to 1/100 of the dose necessary to cause erythema of the skin, was based on a threshold dose response and was proposed by Mutscheller in 1925 (Mutscheller, 1925). Three years later the ICRP recommended the same tolerance dose, and the National Council of Radiation Protection and Measurement (NCRPM) followed suit using the same logic in 1931. In 1934, the NCRPM introduced the first explicit exposure standard of 0.6 r/month (equivalent to 1/1000 of the erythema dose). In the mean time, Muller (1927) observed that radiation caused sex-linked mutations in fruit flies (Muller, 1927), and based on data collected at high doses postulated that the dose response curve must also be linear at low doses. It seemed that the discovery of high dose radiation-induced mutations in fruit flies and the speculation that the dose response was linear at all doses had monumental influence at the time over the acceptance of a linear response at low doses. In 1956, Muller persuaded the Biological Effects of Atomic Radiation (BEAR I) committee to accept linearity at low doses for gonad irradiation. The following year (1957), Lewis published a controversial paper in which he declared that the relationship between radiation dose and cancer induction was linear (Lewis, 1957). In subsequent years, NCRPM, the US Federal Radiation Council, ICRP, UNSCEAR and other regulatory bodies adopted a precautionary linear no threshold dose response curve since there were insufficient, and inconclusive data in the low dose range. However, as science and technology progressed so did the breakthroughs in our understanding of cellular effects at low doses. Early discoveries included the adaptive response in human lymphocytes, first described by Olivieri *et al.* (1984), where ironically low doses of tritium were used to adapt, stimulate, or prime cells such that they became resistant or tolerant to subsequent DNA damage by high dose radiation. This contrasted the linear model which would predict that the effect of a low dose followed by a high dose would be additive when in actuality, the combination did not cause more damage than the high dose alone. This concept of an adaptive response, which supports the use of a threshold in assessing risk, only emerged after linearity was already thoroughly accepted. Currently there is a multitude of scientific publications demonstrating beneficial effects resulting from low dose exposure. Many terms have been used to describe this phenomenon including adaptive response, inducible tolerance, and hormesis. Hormetic dose response models perform very well in the low dose range. It could be argued based on current knowledge that a hormetic model for risk assessment is valid and that a threshold-based tritium standard or regulation could be supported.

4. RADIATION RISK AND LOW DOSE ADAPTATION PART 1 (DRS MITCHEL, SAKAI AND BROOKS)

The Linear No Threshold (LNT) hypothesis, as it pertains to radiation protection, is based on four assumptions: (1) dose is a surrogate for risk, (2) risk per unit dose is constant, and there is no threshold, (3) dose (risk) is additive and can only increase and (4) with low doses and dose rates, risk is reduced two-fold (a Dose and Dose Rate Effectiveness Factor (DDREF) = 2). These assumptions can be challenged given that many experiments show that cells and animals are able to adapt to radiation, and under certain circumstances may also benefit from an exposure to low doses. When a low dose priming exposure is given, prior to a large challenge dose, the ability to repair DNA damage (measured by the formation of micronuclei) is enhanced and the frequency of formation of micronuclei is decreased. This DNA repair adaptation has been shown in human cells (Broome *et al.*, 2002), deer cells (Ulsh *et al.*, 2004) and frogs *in vivo* (Mitchel, unpublished data). It has also been shown that a low dose priming exposure (100 mGy) can sensitize human lymphocytes to apoptosis induced by a subsequent higher dose (Cregan *et al.*, 1999), potentially eliminating cells harbouring aberrations from the population. *In vivo* experiments using a cancer prone mouse model system show that a low dose exposure alone can increase the latency period of spontaneous lymphoma, and spontaneous spinal osteosarcomas (Mitchel *et al.*, 2003), and when given before a large cancer-inducing challenge dose can increase the latency period of myeloid leukemia in mice (Mitchel *et al.*, 1999). Therefore low doses of radiation can significantly increase lifespan in mouse model systems. It would seem that this risk reducing phenomenon is not unique to radiation induced cancer. Radiation can also provide protection from exposure to other carcinogens. A dose of 0.5 Gy of β-radiation prior to exposing mice to a chemical carcinogen (MNNG) decreased the incidence of skin tumours (Mitchel *et al.*, 1990). There is evidence showing that low doses of radiation have effects which are inconsistent with those caused by higher doses indicating that there is a threshold below which beneficial effects can be seen. Low doses of radiation can also stimulate the human immune system, by activating T-Lymphocyte IL-2 receptors (Xu *et al.*, 1996). Furthermore, any low dose between 1 and 100 mGy has been shown to reduce the spontaneous frequency of malignant transformation in rodent cells by 3-4 fold (Azzam *et al.*, 1996). Recent data shows that low doses of radiation, given at low dose rates reduced serum cholesterol levels and aortic root atherosclerotic lesions, in atherosclerosis prone mice (Apo E -/-) (Mitchel, unpublished data). It can be concluded that the LNT hypothesis is not supported by data and should not be used for radiation risk estimation at low doses below 100 mGy. Adopting new regulatory standards based on the LNT approach is precarious especially since no evidence exists to indicate that current limits are invalid.

Based on the LNT model at high doses from atomic bomb survivors, there is an increase in the variation of solid cancer incidences at doses below 100 mGy, when compared to doses above this threshold (Preston *et al.*, 2007). It can be noted that there is a bio-protective effect from low doses of ionizing radiation, and risk is only increased when a net increase in risk, above a threshold, outweighs this bio-protective effect. Experiments in mice have shown that the risk of developing cancer can change depending on dose rate and not total dose. Mice were exposed to either four acute fractions of 1.8 Gy (2 Gy/min) or irradiated chronically at a dose rate of 1.2 mGy/hr to a total dose of 12.6 Gy. The mice that received the acute doses developed thymic lymphoma beyond 200 days post irradiation, while those that received the chronic dose (a larger total dose of 12.6 Gy) did not develop thymic lymphoma by 500 days (Ina *et al.*, 2005). Epidemiological data on cancer incidence caused by chronic exposures in people living in regions with naturally high background levels of radiation have been reported. In regions such as Yangjiang, China, the average annual effective dose, due to natural background radiation, is as high as 6.4 mSv and there is no significant increase in cancer incidence (Tao *et al.*, 2000). This is over sixty times higher than the dose a person would receive if they were to consume water at the current limit and orders of magnitude higher than the proposed new limit. Similarly, an epidemiological study of cancer incidence in Kerala, India, another region with naturally high levels of background radiation ranging from 4-70 mGy/year, revealed that there is no excess cancer risk associated with this type of chronic exposure, relative to a control population (Nair *et al.*, 2009). These studies do not support the notion that the LNT hypothesis is suitable for radiation risk estimation. Again, it can be argued that a threshold based system, which more carefully considers the effect of dose rate, would be more appropriate for use in radiation risk estimation and protection policy.

It is difficult to appreciate the magnitude of various doses when different measurements and units of dose are compared. A central question is: How much of a biological effect is expected from tritium beta radiation when the concentration is 20 Bq/L? Many studies have compared reference doses of radiation with doses from tritium where toxicological effects have been observed in mice. It has been shown that a total dose of 37,000,000,000 Bq/kg of tritium was required to kill 50% of the animals in 30 days (LD50/30) (Brues *et al.*, 1952), and that a lower high dose of

740,000,000 Bq/kg was required to decrease the survival of reproductive cells (spermatagonia) to 70% (National Council on Radiation Protection & Measurements, 1978). Consumption of water with a tritium concentration of 111,000,000 Bq/L, continuously for 330 days, resulted in a 50% elevation in chromosome aberrations (Brooks *et al.*, 1976) and significantly increased the occurrence of dominant lethal mutations (Carsten and Commerford, 1976). In contrast, a lower but still significantly high concentration of 37,000,000 Bq/L, over the same time, resulted in no detectable cancers in mice (Brooks *et al.*, 1976). This concentration of tritium can be compared to the natural variation in background radiation, at different altitudes, due to changes in cosmic radiation levels. An annual exposure resulting from the consumption of 2 L of water per day, containing tritium at a concentration of 20 Bq/L, would be 0.0003 mSv. An increase in annual dose, as a function of elevation, is approximately 1.0 mSv per 20,000 ft (Phillips *et al.*, 1993). Therefore, based on these estimates, the annual dose from consuming 2 L of water daily, with a tritium concentration of 20 Bq/L, is equivalent to an increase in elevation of about 6 ft annually. Consumption of the same volume of water, containing 7,000 Bq/L, is equivalent to a change in elevation of 2,100 ft annually. It can be concluded that a new recommendation that lowers a limit seven orders of magnitude lower than detectable biological change, and indistinguishable from natural variation in background radiation, is not a reasonable level to establish as a safety regulation.

5. RADIATION RISK AND LOW DOSE ADAPTATION PART 2 (DRS AZZAM, YANCH AND HOWELL)

A number of mechanistic studies have been conducted to provide insight into the adaptive response *in vivo* as well as *in vitro*. Mechanistic studies, especially in the low dose region where the statistical power of human epidemiological studies is limited, are critical for an understanding of biological responses. There are a growing number of research studies demonstrating evidence of protective effects of low dose, low dose rate radiation in various model systems using numerous endpoints. Low dose priming gamma radiation exposures of 10, 50 or 100 mGy significantly reduced the number of micronuclei (DNA damage) induced by a subsequent high dose challenge exposure of 1 Gy. In cultured human cells, this protective effect was observed up to 24 hours after the low dose exposure, and longer in animal models. These low dose exposures have been shown to decrease the spontaneous levels of DNA damage, and spontaneous transformation frequency in different cell lines (Azzam *et al.*, 1996; de Toledo *et al.*, 2006; Redpath and Antoniono, 1998; Redpath *et al.*, 2001). Recently the role of free radicals has been shown to be involved in low dose, low dose-rate, adaptive response mechanisms via oxidative metabolism and DNA repair. Specifically, low dose, low dose-rate gamma radiation up-regulated the antioxidant glutathione in cells, and increased the activity of manganese superoxide dismutase *in vivo*. Protective effects can be correlated with low dose, low-dose rate exposures by demonstrating that such exposures induced the expression of translationally controlled tumour protein (TCTP) (Azzam, unpublished data). Additionally, a decrease in the mitochondrial function of normal cells following an acute low dose radiation exposure has been reported. It has been postulated that the observed decrease may be a protective mechanism used to attenuate the production of reactive oxygen species following radiation stress. Biological responses to low dose and low dose-rate radiation exposures are multifaceted and complex; assuming that these processes can be understood with the simple linear no threshold model conflicts with the complexity of the mechanisms at play in the low dose range. Mechanistic studies are fundamental in risk assessment, and they will enhance and provide insight into epidemiological data enabling a more informed approach to radiation risk estimation and protection policy.

Dose rate and not total dose is critical in risk assessment and it is important to maintain perspective on the dose rates relevant to lifetime exposures from tritium in drinking water. The dose rate from the proposed standard for tritium in drinking water is orders of magnitude smaller than the dose rates encountered from natural background and occupational exposures. Regulatory bodies convert risk from doses incurred at high dose rate to risk from doses of low dose rate radiation by dividing the former by a dose rate effectiveness factor (DREF). In fact, most regulatory bodies use a DREF of 1.5 or 2, based on NCRP report number 64, to make such risk conversions. However, NCRP has acknowledged that, in some instances, low dose, low dose rate radiation can extend longevity (National Council on Radiation Protection & Measurements, 1980). This observation indicates, that as the dose-rate decreases, the DREF should approach infinity and therefore the risk would approach zero. It is important to distinguish between DREFs which have a mean of approximately 4 and protraction factors (PFs) which have a mean of approximately 10 (National Council on Radiation Protection & Measurements, 1980). Briefly, it can be shown that a protracted dose represents a long-term, chronic exposure spanning a long enough time period such that age-dependent changes in susceptibility are important, whereas the dose-rate effects relevant for the DREFs in use are for much shorter exposures. A lifetime consumption of tritium in drinking water can be considered a protracted dose, and thus a PF rather than a DREF is most appropriate for estimating the associated risk. Furthermore, the universal use of DREFs results in an overestimation of the risks from protracted doses. In conclusion, there is a need for more biological data at the dose rates relevant to environmental exposures to further establish accurate protraction factors for risk assessment and subsequent prudent protection policy.

There are well established model systems where cells have been chronically irradiated by particles emitted by radionuclides introduced into the cell such as tritium beta particles. Using these systems, the radiotoxicity of tritium was compared to alpha particles, beta particles, and Auger electron emitters on the basis of absorbed dose to the cell nucleus (mean lethal dose D_{37}). The radiotoxicity of tritiated water was far below that of alpha emitters or DNA-incorporated Auger electron emitters. However, tritium effects were similar to those of acute external beams of ^{137}Cs gamma-rays. To further characterize the nature of the radiobiological damage, the capacity of various radioprotectors to mitigate the lethal effects of these different radionuclides was measured and reported as a dose modifying factor (DMF). The highest DMFs were observed for tritiated water thereby suggesting that, as for other low-LET radiations, indirect effects are the predominant mechanisms of radiation-induced damage (Bishayee *et al.*, 2000; Howell *et al.*, 1991; Howell *et al.*, 1998). Bystander effects are biological changes observed in cells in the vicinity of irradiated cells but that were not directly irradiated themselves. It has been reported that various bystander effects can be induced by radiolabeled cells. These experiments were performed in co-culture conditions where radiolabeled and unlabeled cells were combined in the same culture environment. The results varied depending on endpoint but included bystander effects that were lethal (Bishayee *et al.*, 1999; Bishayee *et al.*, 2001; Persaud *et al.*, 2005; Persaud *et al.*, 2007), mutagenic (Persaud *et al.*, 2007), proliferative (Gerashchenko and Howell, 2004; Gerashchenko and Howell, 2005; Kishikawa *et al.*, 2006) and anti-proliferative (Xue *et al.*, 2002). These bystander effects observed were modulated by several factors such as the ratio of labelled to unlabelled cells, the dose and dose-rate of the labelled cells, the radiochemical used, and the tissue microenvironment (Pinto *et al.*, 2006; Pinto *et al.*, 2010). Based on experiments of this nature, it can be concluded that tritium exposure results in biological effects that are comparable to those resulting from low LET radiation and not to those resulting from high LET radiation.

6. FREE RADICAL BIOLOGY AND LOW DOSE RESPONSES (DRS SPITZ, KNOX AND DUBLINEAU)

The free radical scavenger manganese superoxide dismutase (MnSOD), and the transcription factor nuclear factor-κB (NF-κB) have been shown to be involved in low dose adaptive responses. There is a balance maintained between pro-oxidants and antioxidants, and there is a resulting cellular injury or death when pro-oxidant production exceeds antioxidant capacity. It has been reported that a low dose of radiation (100 mGy) induces NF-κB transcriptional activity and MnSOD immunoreactive protein activity in JB6P+ mouse epidermal cells. It was shown that the NF-κB inhibitor IMD-0354 and siRNA inhibition of

MnSOD, were both able to inhibit low dose radiation induced adaption to subsequent higher doses (Fan *et al.*, 2007). It can be concluded that the low dose radiation-induced adaptive response in JB6P+ cells is at least partly mediated by signaling pathways leading to NF-κB and MnSOD activity.

Low dose radiation and free radical biology also play an important role in non-cancer endpoints including the progression of prion diseases. It has been postulated that the induction of endogenous protective systems by a low dose whole body irradiation could slow or prevent the progression of prion disease. It has been shown that there is a correlation between oxidative stress, as measured by 8-hydroxydeoxyguanosine (8-OHdG) levels in the urine, and disease progression in prion infected mice (Plews *et al.*, 2010). Further, it was found that a dose of 500 mGy reduces oxidative stress and prolongs the symptom free phase of the disease, as well as survival of the animals (Plews *et al.*, 2010). These studies concluded that low dose ionizing radiation can have a protective function in diseases associated with free radical damage.

Low dose effects of chronic ionizing radiation exposure have been studied following internal radionuclide contamination. Experiments have been performed involving chronic exposures to uranium at a concentration of 40 mg/L. This chronic low dose exposure led to several non-cancerous effects on various target systems. Iron accumulation (Donnadieu-Claraz *et al.*, 2007) and modification of iron metabolism in the kidneys was reported (Berradi *et al.*, 2008). It was further shown that modification of cytochrome P450 expression (Souidi *et al.*, 2005) and vitamin D metabolism (Tissandié *et al.*, 2007) occurred in the kidneys and the liver. There were also effects on the nervous system, including increases in paradoxical sleep (Lestaevel *et al.*, 2005), and anxiety, a decrease in short-term memory (Houpert *et al.*, 2005), changes of oxidative defenses (Lestaevel *et al.*, 2009), and modification of cellular density in the intestinal mucosa (Dublineau *et al.*, 2007). However, experiments with external radiation showed that low doses of Cs-137 gamma irradiation resulted in a decrease in arterial pressure (Guéguen *et al.*, 2008). Concerning tritium effects, a review of experimental studies was performed on the topic of chronic ingestion of tritium in drinking water. The review was shown to support the conclusion that there is an absence of data for evaluating biological effects of tritium for levels <1 MBq/L. This is orders of magnitude lower than current limits.

7. PROCESS, PUBLIC PERCEPTION, ETHICS AND NEW POLICY (DRS BRATT, DONEV, SEYMOUR, AND LEMAY)

There is a policy making model that can be used to analyze the Government of Ontario's decision making process over regulating tritium levels in drinking water. There are five stages to this model: 1) problem definition and agenda setting; 2) policy goals; 3) policy options/instruments; 4) policy implementation; and 5) policy evaluation. Knowledge of the decision making process allows opportunities for stakeholders to be actively involved in the development and implementation of various aspects of the intended policy. Using the five stages identified, key issues can be highlighted that impact the priority and social importance of appropriately regulating tritium levels in drinking water. Concerns regarding radiation and "focusing events", such as the National Research Universal (NRU) reactor tritium leaks (Canadian Nuclear Safety Commission, 2009) and Walkerton's past bacterial water contamination (Salvadori *et al.*, 2009), have attracted an abundance of media attention, which can influence policy-making, regardless of the science. Since environment, health and energy are critical election issues, the politics of regulating levels of tritium in drinking water have been at the forefront of debates. Ultimately, regardless of which drinking water tritium levels the Government of Ontario decides to regulate to, the success of the policy that is chosen will depend on its design and implementation. It should be emphasized that issues such as mitigating health risks and associated economic costs need to be evaluated quantitatively to measure the success of a policy. Additionally, it is important to objectively identify the goal of the policy as being either health or public relations oriented in response to "focusing events".

Public perception and attitudes have an important influence over policy decisions concerning nuclear radiation safety regulation. Popular culture plays a role in shaping opinions of radiation and its safety at a political level. In regard to safety policy-making, people not only need to *be* safe, but also *feel* safe; and the insufficiency of the latter is what complicates the policy making process. The need to engage the public about radiation and its safety in a non-condescending manner is essential. People do not change their perception of radiation by being told they are wrong; the change in perception can only take place through educational discussions regarding radiation and its safety.

It is important to consider ethical issues involved in making policy related decisions and this pertains to new limits for tritium levels in drinking water. Different ethical and justice paradigms exist from past philosophers such as Aristotle, Jeremy Bentham and John Stuart Mills. There is always some uncertainty in science and policy-related decision making processes. This universal uncertainty leads to difficulty in predicting the consequences of government policies, as these policies interconnect dimensions of ethics, politics, society, and economics. The precautionary principle is an example of a multidimensional approach that could be used in addressing the potential consequences associated with changing the standard for tritium levels in drinking water. The precautionary principle states that if an action or policy has an associated, suspected risk of causing harm to the public or to the environment, in the absence of a scientific consensus *the burden of proof falls on those taking the action or implementing the policy*. This principle allows policy makers to make discretionary decisions in situations where there are concerns regarding the health of the general public and a consensus amongst the scientific community cannot be reached. Furthermore, the principle implies that there is a social responsibility to protect the public from exposure to harm, when scientific investigation has found a plausible risk. The question needing deliberation is whether or not the current scientific evidence can strongly refute a plausible health risk if the current regulated levels of tritium in drinking water were left unchanged.

The intended purpose of the new regulation is to have a target derived risk level from tritium radiation exposure to the public of one or less new excess cancer occurrences over existing background cancer rates in a million people. It can be argued that is a target that cannot be achieved in any meaningful way. The problem with this approach is that radiation is not like other chemical carcinogens and toxic substances such as mercury and benzene, since radiation is always present and doses increase and decrease continually based on cosmic and terrestrial sources. An interesting analogy of this concept of natural exposure levels and risk combined with some additional exogenous exposures is sodium intake. Regulating tritium levels down to 20 Bq/L in drinking water is like regulating sodium intake in drinking water to a maximum level of 0.3092 mg/day. However, the average Canadian intake for sodium is 3.000 mg/day and therefore such a limit in drinking water would have insignificant health benefit. Nonetheless, using a linear no threshold model to calculate sodium risk based on known risks from high dose exposures, a maximum level of 0.3092 mg/day of sodium in drinking water would theoretically reduce risk of cardiovascular diseases down to one in a million, analogous to the theoretical one in a million risk associated with 20 Bq/L of tritium given that naturally occurring radiation exposures are orders of magnitude higher. Another example would be radioactive intake from milk. The dose from radioactive potassium naturally occurring in milk is 2-3 orders of magnitude higher than the dose from tritium at 20 Bq/L in drinking water. The biological consequences of the tritium beta exposure from drinking water will be insignificant compared to the potassium beta exposure from drinking milk. Implementing misaligned regulations, such as the 20 Bq/L of tritium level in drinking water, cause excessive demands on resources. The concept of *de minimus* risk has been adopted to guard against such excesses.

8. TRITIUM REGULATIONS AND NATIONAL AND INTERNATIONAL REGULATORS (DRS THOMPSON, HART, AND HOOKER)

The Canadian Nuclear Safety Commission's (CNSC) perspective on the regulation of tritium in general was reviewed based on the Tritium Studies Project that was recently undertaken by the CNSC staff. The Tritium Studies report was an extensive information review with the specific aim of producing a series of reports. The reports issued in the Tritium Studies Project were: Tritium Releases and Dose Consequences in Canada (INFO-0793); Standards and Guidelines for Tritium in Drinking Water (INFO-0766); Evaluation of Facilities Handling Tritium (INFO-0796); Investigation of the Environmental Fate of Tritium in the Atmosphere (INFO-0792); Tritium Activity in Garden Produce from Pembroke in 2007 and Dose to Public (INFO-0798); and Health Effects, Dosimetry and Radiological Protection of Tritium (INFO-0799). The details and availability of the reports can be found on the CNSC website (Canadian Nuclear Safety Commission, 2008). The findings and conclusions of the Tritium Studies Project were summarized in the Tritium Studies Project Synthesis Report (INFO-0800). Overall, the conclusions of the Tritium Studies Synthesis Report were that adequate provision had been made through current regulations and procedures to appropriately protect the health and safety of Canadians against tritium exposure. The existing principals, by which tritium releases are controlled are, ALARA (As Low As Reasonably Achievable), social and economical factors taken into consideration) and Action level responses. It was concluded that these principals are being appropriately applied and in fact are effective at protecting human health. It was shown that levels of tritium released from nuclear power plants are already close to the minimum achievable level. The CNSC recommended value of 100 Bq/L was derived from many factors including: 1) the consideration of the health risks associated with exposure to tritium, 2) the levels of tritium measured in drinking water supply plants in the vicinity of nuclear facilities, 3) levels of tritium in groundwater on-site and off-site of nuclear facilities, 4) achievability of the regulation limit, 5) practicality of monitoring the limit, 6) cost effectiveness of enforcing the limit, 7) the linear no threshold model for calculating the risk of developing cancer from a given exposure to a carcinogen, and 8) the risk management frameworks in use for managing chemical carcinogens and exposures to radiation. It was concluded that the recommended value of 100 Bq/L represents an appropriate balance of scientific, practicality, and public policy considerations.

Tritium regulations vary globally and in many countries, tritium has not received the same level of interest as in Canada. Australia has one of the higher regulatory limits for tritium in drinking water. Tritium is not a concern in Australia due to its low abundance (typically <0.5 Bq/L). Historically, tritium concentrations were monitored in rainwater and groundwater to examine the effects of nuclear fall-out on water supplies. There are a number of different guidelines in Australia dependent on the purpose and use of the water, which refer to a range of radionuclide concentrations including tritium. Generally, each state and territory in Australia has their own radiation protection legislation; however, there is a uniform approach outlined by the National Directory for Radiation Protection. Based on recommendations from the International Commission on Radiological Protection (International Commission on Radiological Protection, 1991; International Commission on Radiological Protection, 1999) and Australia's National Health and Medical Research Council Australian Drinking Water Guidelines (Australian Government National Health and Medical Research Council, 2004), the limit for tritium in drinking water is 7,800 Bq/L. This limit is based on a consumption of 2 L of water per day with a committed effective dose of 1 mSv/year from total radionuclides in water. It should be noted that the tritium limit is the same for water used for irrigation and watering livestock. The ANSTO OPAL reactor limit for tritium discharges is up to 195,000 Bq/L, assuming a 25x dilution factor as the discharge mixes with sewage from the treatment plant. Australia's low dose radiobiology research program has demonstrated that there are cellular protective effects following low dose radiation exposure between doses of 0.001 mGy and 10 mGy (Hooker *et al.*, 2004; Zeng *et al.*, 2006). There is a large body of evidence which demonstrates that the linear no threshold model for risk estimation is flawed and yet radiation protection regulation markedly deviates from proven science. Once again it was concluded that regulating tritium levels in drinking water to 20 Bq/L is not only a poor use of resources, but introduces many other problematic issues associated with the implementation and monitoring of, compliance with the new regulation.

9. CONCLUDING POSITION STATEMENTS FROM THE CANADIAN RADIATION PROTECTION ASSOCIATION (CRPA) AND THE CANADIAN NUCLEAR ASSOCIATION (MR TUCKER AND COUPLAND)

The Canadian Radiation Protection Agency (CRPA) "supports the development and implementation of radiation safety programs in industry, medicine, research and the environment through scientific inquiry, public involvement and interaction with local, provincial, federal and international authorities"(Canadian Radiation Protection Association, 2010). A position paper was created by the CRPA in April 2010 in response to the proposed change in drinking water standards (Canadian Radiation Protection Agency, 2010):

> *"The Ontario Drinking Water Advisory Council has recently recommended to the Ontario Minister of the Environment that the Ontario drinking water quality standard for the radionuclide tritium be lowered by a factor of 350. The rec-*

ommendation has not been prompted by a finding of an increase in the risk associated with the ionizing radiation from tritium but from the reliance on the methodology recommended by the US National Academy of Sciences (NAS) for the assessment of risks due to exposure to carcinogenic chemicals. The NAS risk assessment methodology is not generally applied to ionizing radiation nor is it generally applied to situations where exposure is dominated by naturally occurring sources, as is the case with ionizing radiation."

The Canadian Radiation Protection Association opposes the recommended change for four reasons: 1) there is no scientific basis for the proposed decrease; 2) the methodology that led to the recommendation is not appropriate; 3) adoption of the recommended value would not lead to any significant improvement in public safety because environmental levels of radionuclides from man-made sources are already managed through Canadian radiation protection regulations; and 4) such a radical change and implementation of the new value would likely cause unwarranted public concern.

Accordingly, the position of the Canadian Radiation Protection Association is that there is no need for a reduction in the Ontario drinking water quality standard for the radionuclide tritium, and in particular for the reduction from its present value of 7,000 Bq/L to the value of 20 Bq/L recommended by the Ontario Drinking Water Advisory Council.

The Canadian Nuclear Association (CNA) is a "non-profit organization established to represent the nuclear industry in Canada and promote the development and growth of nuclear technologies for peaceful purposes" (Canadian Nuclear Association, 2010). The CNA believes that the standard for drinking water should remain at 7,000 Bq/L and elaborated on key issues behind that decision. The CNA concludes the justification for changing the standard was not science based but rather performance based and that while superior performance should always be encouraged and promoted, as per the ALARA principle, it should not be the basis for changing standards. Changing standards without a scientific basis sets a dangerous precedent that can have implications that reach beyond the nuclear industry. The CNA suggests that if the 20 Bq/L standard proposal becomes a practical operating limit, it may have major impacts on public perception and operating costs for nuclear power plants. Radiological environmental monitoring data confirms that nuclear power plants rarely exceed a 20 Bq/L emission level; however, occasionally there are short-term peaks ("spikes"). With the change in policy, these occurrences will be strictly monitored and widely disseminated resulting in unnecessary public concern. Moreover, in order to attempt to avoid exceeding a 20 Bq/L limit, industry will have to spend significant capital in new technology because current technology is only efficient at removing tritium at high concentrations in low volumes of water and not efficient at low concentrations in high volumes of water.

This would translate into higher energy costs with no significant benefit to human health or protection.

10. CONCLUSION

The McMaster Symposium on Human Health and the Biological Effects of Tritium in Drinking Water attracted radiation scientists, industry representatives, regulators and non-government organizations. There was no new scientific evidence reported to support the recommendation that a new regulatory limit for tritium in drinking water is required to protect people or improve human health. The carcinogenic potential of very low dose radiation exposure from tritium at a concentration of 20 Bq/L was considered insignificant. Much higher levels of exposure to humans, caused by natural radioactivity in the environment, have not been shown to be deleterious. Radiation is not a chemical carcinogen and treating it as a non-threshold chemical carcinogen results in a significant overestimation of cancer risk. Current radiation protection regulations are being appropriately applied and are effective at protecting human health. Levels of tritium released from nuclear power plants are already close to the minimum achievable level. The Canadian Radiation Protection Association does not support the new recommendation, because it is not supported by science. The Canadian Nuclear Association does not support the new recommendation because it is not scientifically based and the industry already protects the environment and humans by keeping tritium emissions as low as reasonably achievable. There is growing evidence to suggest that the LNT model for risk estimation is inadequate and that low dose radiation induces cellular responses that are different than detrimental effects observed at high doses. Overall, the new recommendation does not seem to be justified based on scientific evidence.

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APPENDIX A.

ONTARIO DRINKING WATER ADVISORY COUNCIL RECOMMENDATION

The Ontario Drinking Water Advisory Council (ODWAC) provides advice on drinking water quality standards as a result of direct requests by the Minister of the Environment. In February 2007, the Minister formally requested the Council to provide advice on the Ontario Drinking Water Quality Standard for tritium (Currently at 7,000 Bq/L) subsequent to the issue being raised by the Medical Officer of Health for the City of Toronto.

A working group was created to deal with this issue and a formal report was issued in May 2009 (Ontario Drinking Water Advisory Council, 2009). This report came to six main recommendations as follows:

1. The Ontario Drinking Water Quality Standard for tritium should be revised to 20 Bq/L, recognizing that:
   - 20 Bq/L relates to heath effects from long-term, chronic exposure over a life time of exposure of 70 years;
   - 20 Bq/L is within the range of variations considered by the Council (7 Bq/L to 109 Bq/L), for a 10^{-6} risk level; and
   - 20 Bq/L, based on a running annual average, is achievable in drinking water, without significant cost to the nuclear power industry, according to the Canadian Nuclear Association.
2. The Standard of 20 Bq/L should be applied as the running average of the preceding 52 weekly composite samples. This running annual average is consistent with the current weekly sampling and reporting programs, and should also be used to generate monthly averages and identify trends.
3. The current sampling and monitoring programs, as conducted by the Ministry of Labour and the industry, are appropriate, and should continue. Sampling and reporting should only be required for those drinking water treatment plants that are in the proximity of or under the influence of sources of tritium. As well, the Ministry of the Environment should continue to monitor tritium at drinking water systems as part of the Drinking Water Surveillance Program (DWSP).
4. Monthly reports of weekly test results and running annual averages should be sent to regulatory bodies, local municipalities and health units, local public interest groups, and should also be made available to the general public.

5. It is equally important to monitor trends in the monthly data and if there is an indication of increases (even if they are below the Standard), the province should require the discharger to take appropriate corrective actions, in collaboration with other appropriate authorities.
6. Monitoring and reporting at the point of discharge should be the focus for emergency response in that monitoring at drinking water treatment plants is not an appropriate approach for alerting authorities and the public of significant and / or elevated discharges of tritium. The current program should be enhanced to require the dischargers to report monthly to regulatory authorities and other public bodies on the levels of tritium discharges and immediately in each case where discharges exceed designated notification level(s).

The Council arrived at the conclusion that the Ontario Drinking Water Quality Standard for tritium should be revised to 20 Bq/L, by determining what limit would be "reasonably practicable" within the range of variations considered (7 Bq/L to 109 Bq/L). To address this, the Council turned to two documents received as part of the consultation process:

- The Canadian Nuclear Association noted in a letter to the Council that 20 Bq/L on an annual average basis is achievable in drinking water, without significant cost to the industry (See Appendix 5 of the report).
- The Toronto Medical Officer of Health noted in a letter to the Council that the concern with tritium is chronic exposure, and that an annual average of 20 Bq/L would not be exceeded if Ontario Power Generation did not exceed its current discharge limit of 4,000 Bq/L *(at either Pickering or Darlington Nuclear Power Generating Stations)* (See Appendix 6 of the report).

Based on these two documents, the Council concluded that an Ontario Drinking Water Quality Standard for tritium of 20 Bq/L, applied as a running annual average, would meet the requirements for an appropriate level of risk and public safety, while remaining practicable and achievable by the nuclear power industry. The current data supported this conclusion, in that all of Ontario's nuclear power generators are currently capable of controlling their liquid tritium discharges, to the extent that local water treatment plants should be able to meet the new Standard. The Council further noted that, in applying a test of practicability to this proposed Ontario Drinking Water Quality Standard for tritium, it should not be necessary for the nuclear power industry to alter any of the applicable regulations for occupational or other radiological criteria.

Mr. Jim Merritt, the Chair of Ontario's Advisory Council on Drinking Water Quality and Testing Standards, was in attendance at the McMaster Symposium on Human Health and the Biological Effects of Tritium in Drinking Water to review this report and address questions.

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