ANNEX A - STATEMENT OF WORK (SOW)

TITLE	Study on the impact of occupational radon exposure on lung cancer and cardiovascular disease mortality risk.
OBJECTIVE	The objective of this project is to examine the impact of occupational radon exposure on lung cancer and cardiovascular disease mortality risk by providing a final analysis of a cohort of radon-exposed fluorspar miners in Canada, extending the follow-up by 14 years (from 2001 to 2015).
BACKGROUND	The Newfoundland Fluorspar Cohort comprises a group of approximately 1,700 underground miners exposed to radon progeny, and an additional 300 surface miners with minimal exposure. The Canadian Nuclear Safety Commission (CNSC) has supported previous mortality updates (2001) of this cohort in order to provide objective scientific information on the health effects of radon. Radon is the second leading cause of lung cancer in Canada after tobacco smoking, and is the number one cause of lung cancer in non-smokers (1). This information comes largely from epidemiological studies of radon-exposed miners, including this study, and extrapolations from high radon exposures have been made to estimate risk at lower radon exposures. In recent years, an increasing number of mining cohorts have provided insights on the relationship between lower radon exposures and the risk of lung cancer (2-5). While these studies demonstrated variations in the excess relative risk per working level month across studies, they consistently found increased risks of lung cancer. The Newfoundland Fluorspar cohort is unique, since miners were not exposed to other forms of radiation (i.e., gamma) that could confound the radon-lung cancer relationship, as exposure was result of underground water sources that carried the radon gas. It is also unique because of its extensive tobacco smoking information over three different time periods, and captures both intensity and duration of smoking. In the most recent mortality analyses (1950-2001), underground miners had a significantly higher mortality from lung cancer than similarly-aged Newfoundland males and lung cancer death rates increased dramatically with increasing radon exposure. The analyses also found statistically significant variations in the excess relative risk per working level month (ERR/WLM) of exposure based on the effect modifiers: attained age, time since last exposure, and calendar period. There was also an inverse-exposure rate effect. However, the analyses were limited by small numbers, especially those that sought to look at the combined impacts of more than one variable. A strategy to overcome this is to extend the follow-up of this cohort. The

	youngest men in the cohort were born in 1956, and the mean birth year in the underground miners was 1927. In the last follow-up, approximately half of the workers had died, and so this number will have increased substantially by 2012 (or most recent year available). This will increase the statistical power to improve the understanding of the joint impacts of tobacco smoking and radon exposure (for example). Perhaps more important, it will provide an enhanced opportunity to look at the impacts of lower radon exposures as a result of the introduction of ventilation into the mine in 1968 (2). Extending the mortality follow-up up the cohort would be expected to identify lung cancers among workers who worked during this time, while past record linkages were more likely to identify lung cancers among those who began working as early as 1928. The identification of additional lung cancer deaths will provide an increased ability to discriminate between additive and multiplicative models so as to better understand the joint impacts of radon and cigarette smoking on lung cancer risk. Changes in the prevalence of smoking are also valuable to better understand the smoking patterns in current miners.
SCOPE	The Contractor must provide an analysis team composed of at least one (1) senior resource to complete the three (3) main components: <u>1. Reconstruction of the Newfoundland fluorspar cohort linkage files:</u> The Newfoundland fluorspar cohort has been followed in terms of their lung cancer mortality experience until 2001. The current analysis will lengthen that follow-up nearly to the end of 2012. The cohort comprises 1,742 underground miners and 328 mill workers who worked on the surface (unexposed group). Complete radon exposure assessment by year, mine, and occupation from 1933–1978 are available. Histological information on the types of lung cancer and detailed tobacco smoking behaviours are available. Approximately 200 lung cancers deaths had been identified by 2001; the extended follow-up will identify at least 40 more lung cancers. Since the linkage files submitted to Statistics Canada for the last study of this cohort have been destroyed, they will need to be reconstructed by the analysis team. These files include surname, data of birth, smoking information, place of last known residence, vital status, and underlying cause of death and occupational work histories. <u>2. Creation of a new linked file:</u> The updated linkage file defining the cohort will be provided to Statistics Canada to conduct a deterministic record linkage and validation. This linkage must include mortality data and cancer histopathology as well as incident lung cancer data (available from the Canadian Cancer Registry). The analysis team will be required to make the necessary arrangements

	with Statistics Canada including payment for their services. The analysis team will be compensated for the cost of Statistics Canada's services at actual cost. 3. Analysis: Both external and internal cohort analyses will be conducted. An external cohort analysis will compare the fluorspar miners with the general Newfoundland male population from 1950–2014. This will be done by obtaining cause-specific mortality rates in 5-year age groups and 10-year calendar periods. Standardized Mortality Ratios (SMRs) and their 95% confidence intervals will be estimated. An internal cohort analysis will incorporate Poisson regression to fit Excess Relative Risk (ERR) models for lung cancer, using Epicure software. Relative risks (RR) will first be estimated for each cumulative radon exposure category, adjusting for attained age and calendar year period. Further analyses will examine whether the Excess Relative Risk/Working Level Month (ERR/WLM) vary by different effect modifiers. Importantly, incident and mortality cases of lung cancer from 2002–2014 will occur predominantly among those who worked in the mine after 1960. The association between low-levels of radon exposure and lung cancer will be compared with past analyses. The impact of tobacco smoking on the radon-lung cancer ERRs will also be examined as both a confounder and an effect modifier. The ERRs by histological type of lung cancer will also be examined although may have a limited sample size. Finally, similar analyses will be pursued using cardiovascular mortality outcomes.
TASKS	The analysis team must perform the following tasks: 1. Attend a start-up meeting with the Technical Authority to discuss the objectives and requirement. 2. Prepare information for the linkage of the Newfoundland Fluorspar Miners' Cohort with Statistics Canada mortality and cancer incidence data. This includes the reconstruction of the cohort from historical information and preparation of any supporting documentation required to make the linkage with Statistics Canada databases. 3. Meet with Statistics Canada staff to discuss the arrangements for completing the linkage of the Newfoundland Fluorspar Miners' Cohort at Statistics Canada premises and creating the linked file

for further analysis by the contractor.

4. Conduct record linkage of the Newfoundland Fluorspar Miners' Cohort at Statistics Canada facilities in Ottawa. The linked data will include mortality and cancer incidence data provided by Statistics Canada.

5. Conduct analyses for both external and internal cohorts and report. Analyses must include:

   5.1 For lung cancer:

      5.1.1 Descriptive analyses;

      5.1.2 External cohort analyses including estimation of SMRs;

      5.1.3 Internal cohort analyses:

         5.1.3.1 ERR/WLM modelling by age at first exposure, time since last exposure, smoking status, histological types;

         5.1.3.2 Applying Biological Effects of Ionizing Radiation (BEIR) modifier models including time windows;

         5.1.3.3 Fitting mixture models to look at joint relationship between smoking and radon;

         5.1.3.4 Further analysis of absolute excess risk models.

   5.2 For cardiovascular disease:

      5.2.1 Conduct the following internal cohort analyses:

         5.2.1.1 ERR\WLM;
         5.2.1.2 Absolute excess risk models.

6. Finalize analysis through discussions with Technical Authority.

7. Prepare two (2) papers suitable for publication in an epidemiological journal:

   7.1 Lung cancer analyses from the updated Newfoundland Fluorspar Miners' cohort ; and

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<tr><td></td><td>7.2 Cardiovascular disease analyses from the updated Newfoundland Fluorspar Miners' cohort.

8. Prepare a Draft Report on the project findings. Format and content to be as final report.

9. Present the project findings, conclusions and recommendations as documented in the Draft Report to CNSC staff at 280 Slater.

10. Prepare and deliver Final Report on the impact of occupational radon exposure on lung cancer and cardiovascular disease mortality risk to the CNSC's Technical Authority. The report must include:

• Title page with the report number, RSP 222.2
• Table of contents;
• An Executive Summary

Any spreadsheets or graphics embedded in the report are also to be provided as separate files.</td></tr>
<tr><td>TECHNICAL ENVIRONMENT</td><td>MS Office Suite and other software for profession epidemiological analysis such as Epicure or equivalent.</td></tr>
<tr><td>CLIENT SUPPORT</td><td>The contractor will need to make an arrangement with Statistics Canada to complete the linkage of the Newfoundland Fluorspar Miners' Cohort with Statistics Canada data. Payment for Statistics Canada services will be at cost and charged back to the CNSC through this contract.</td></tr>
<tr><td>DELIVERABLES AND SCHEDULE</td><td>The analysis team must provide the following deliverables:

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<tr><th>Deliverables</th><th>Schedule</th></tr>
<tr><td>Start-up meeting at the CNSC Head Office</td><td>Within 7 days of the Contract award</td></tr>
<tr><td>Linkage files for Statistics Canada, to be provided to the Technical Authority in an agreed format via email.

Refer to tasks 2 and 3 for instructions.</td><td>By February 28, 2018</td></tr>
<tr><td>Progress Report which includes:
• Status on creation of cohort
• Status of discussions with Statistics Canada

To be provided to the Technical Authority via email.</td><td>By March 15, 2018</td></tr>
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	Linkage files provided to Statistics Canada and Linked data file(s) created by Statistics Canada complete with format descriptions. To be provided to the Technical Authority. Refer to task 4 for instructions.	By May 1, 2018
	Initial Findings Report to be provided to the Technical Authority via email. The report will include the initial statistical analysis of the revised cohort and initial observations.	By June 30, 2018
	Draft Report to be provided to the Technical Authority via email. Format and contents to be the same as the final report.	By September 1, 2018
	Presentation of the Project findings, conclusions and recommendations documented in the draft report. The presentation to CNSC staff will be held at the CNSC Head Office.	By October 15, 2018
	Final Report to be provided to the Technical Authority via email. Refer to the task 10 for instructions.	By November 30, 2018
	Scientific papers (2) to be provided to the Technical Authority via email in a format suitable for journal publication. Refer to the task 7 for instructions	By December 31, 2018
	Progress meetings with the Technical Authority to assess the degree to which the agreed project objectives are being achieved as planned and thus to facilitate timely adjustments (if necessary) to ensure the project success. The meetings will be held at the CNSC Head Office or via Telephone.	As requested by either party
ACCEPTANCE CRITERIA	Electronic copies of reports must be readable using Microsoft Word. Any electronic files that cannot be read or require major formatting changes when opened will not be accepted and will be returned to the analysis team for correction. Data files must be readable using Microsoft Suite and	

	be accompanied by a description of their format. All deliverables are subject to review and acceptance by the Technical Authority. The analysis team will be required to remedy any errors, omissions or revisions identified by the Technical Authority within ten (10) business days of being notified.
LANGUAGE OF WORK	The proposed resource will be required to perform the work in English. Every individual proposed in its bid must be fluent in English and must be able to communicate orally and in writing without any assistance and with minimal errors. http://www.international.gc.ca/ifait-iaeci/test_levels-niveaux.aspx?lang=eng#b
LOCATION OF WORK AND TRAVEL REQUIREMENTS	The Contractor will need to liaise with Statistics Canada and visit their facility in Ottawa in order to complete the linkage of the Newfoundland Fluorspar Miners' Cohort.
REPORTING AND COMMUNICATION	It is the responsibility of the analysis team to facilitate and maintain regular communication with the Technical Authority. Status updates, verbal or written, may be requested by the Technical Authority over the course of the contract. Communication is defined as all reasonable effort to inform all parties of plans, decisions, proposed approaches, implementation, and results of work, to ensure that the project is progressing well and in accordance with expectations. Communication may include: phone calls; electronic mail; faxes; and meetings. In addition, the analysis team is to immediately notify the Technical Authority of any issues, problems or areas of concern in relation to any work completed under the contract, as they arise.