PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cancer and non-cancer mortality among French uranium cycle workers: The TRACY cohort
AUTHORS	SAMSON, ERIC; PIOT, Irwin; ZHIVIN, Sergey; Richardson, David; LAROCHE, Pierre; SEROND, Ana Paula; LAURIER, Dominique; LAURENT, Olivier

VERSION 1 - REVIEW

REVIEWER	Doug Brugge Tufts University School of Medicine, USA I have had travel funds from environmental and public health organizations to give presentations on the health effects of uranium and the uranium miner compensation system in the US.
REVIEW RETURNED	10-Nov-2015

GENERAL COMMENTS	This is a nicely presented and clear and clean analysis. I have only a couple of recommendations with regard to framing and interpretation: 1) Uranium exerts its biological effects (including DNA damage) primarily as a chemical toxin, not through radiation. The paper should acknowledge this and indicate whether the follow up of this cohort will address only radiation induced health outcomes or chemical also. I have reviewed uranium health effects, which might be a quick short cut to find the sources for this information: Brugge D, Buchner. Health effects of uranium: new research findings. Reviews on Environmental Health. 2011; 26:231–249. 2) While the industrial processes at the later stage of the nuclear cycle are dealing with pure uranium, the earlier stages (conversion, for example) still have other contaminants from the ore. These include uranium decay products such as radium, thorium, radon as well as non-radioactive toxins such as arsenic. It is important to at least mention this. 3) This is a mortality study, which is fine, but perhaps also a mention, briefly at least, of the health end points short of mortality that are a concern with uranium, including kidney damage, reproductive harm and birth defects. 4) There is a lot more toxicology on brain effects in animals than is listed. Not necessary to cite them all, but maybe pick one of the most recent studies.

REVIEWER	Sharon Silver National Institute for Occupational Safety and Health, U.S.

REVIEW RETURNED	13-Nov-2015

GENERAL COMMENTS	This initial assessment of the French combined internal uranium exposure cohort provides a useful overview comparing the cohort's mortality experience to that of the general population and includes supplemental analyses suggesting a strong healthy worker effect within the cohort. If statistical power permits, the paper might be enhanced by additional analyses of major facility/activity groupings. Methods/results: Exposures differ among and within uranium cycle facilities, such as those included in this study; key differences include levels of exposure and uranium solubility, with the latter leading to differences in organ dose (see Anderson JL et al. Radiation Protection Dosimetry 2015). This manuscript reports SMRs for the combined facilities, an approach that enhances statistical power but may obscure exposure-related risks. The ongoing exposure assessment the authors discuss will facilitate the optimal exposure/dose-response analyses. However, as the exposure assessment is complex and will not be available for some time, supplemental SMR analyses grouping roughly similar activities (similar at the level described in Appendix Table 1) across facilities could, in the interim, be informative. For example, the gaseous diffusion activities could comprise one grouping, and the assembly-support work at the two FBFC facilities another grouping; the two sets of workers would likely have very different summary exposure profiles. Appendix Table 1 does not provide number of workers or person-years by facility/operation. Lack of statistical power would likely hamper evaluation of some groupings; however, where possible, such analyses could provide crude information about possible exposure effects while the exposure assessment and subsequent analyses are pending. These additional analyses could also help address, in part, the issue raised in the discussion of inclusion of unexposed workers in the analyses. Interim analyses considering calendar time periods to reflect changes in exposures and exposure levels may be warranted as well, though calendar time and age at exposure may not be independent in this population. If these analyses are not feasible, expanded discussion of the likely impact of these limitations (inclusion of unexposed workers, exposure diversity, temporal changes in exposures) on the SMR findings would be helpful. Discussion: The discussion could be enhanced by nothing that cohort is young, with an average age of 60 at study end and only 17% of the cohort deceased. In addition to the planned exposure analyses, the authors might consider repeating the SMR analyses when additional follow-up data become available. The significant excess observed was for pleural mesothelioma. Ascertainment of mesothelioma prior to ICD-10 (1999) has been problematic. If this classification issue applies to this cohort, it should be addressed in the discussion. Minor points: Results – some additional detail on reasons for exclusion of >8,000 workers would be informative (how many were short-term workers, contractors, etc.) Discussion:

	Some of the SMRs with non-significant excesses are quite low. For pancreatic cancer, the SMR is 1.05, with CI 0.79-1.38. This finding may not warrant a paragraph in the discussion; if the intent is to compare with other cohorts, then presentation of the magnitude of the findings from the other cohorts would be helpful (likewise for some of the other outcomes).

REVIEWER	Michaela Kreuzer Federal Office for Radiation Protection in Germany
REVIEW RETURNED	20-Nov-2015

GENERAL COMMENTS	This is a very well written, clearly structured and interesting paper. It provides for the first time information on characteristics of the new TRACY cohort of uranium workers and on comparisons of the mortality in the cohort with that of the general population. An improved health risk assessment in relation to internal emitters, and particularly uranium exposure, is a key issue in radiation protection. The cohort is very large and is highly valuable in this field. Specific comments: P3, line 15: Typing error: Instead of "investigation or uranium-related" please correct into "of" P6, line 17-23: If there is an overlap of the TRACY cohort with one of the two addressed French cohorts, the number of cohort members with overlap might be mentioned. P 6, line 37: It is mentioned that complete individual work histories were reconstructed. It would be interesting to know what kind of information this includes. E.g. Annual information on the type of job (how many different jobs), workplace (how many different work places), etc. P7, line 18: It is stated that there was a file-matching with the National Vital Status Registry. Is there any experience about the quality of linkage, meaning how sure it is that the correct person was identified and not a false one (e.g. same name and birth date). The procedure might be explained. How many people of the group of lost to follow-up moved to another country? P7, 21-24: Here file-matching with the French national mortality registry is mentioned. How valid is this information? What type of information was transferred? Only the code of the underlying cause of death based on the certificate of death or also other information (contributing causes of deaths) or even written text of the causes of deaths. P10, line 50: The expression "with more than 20 years of employment" is a little bit misleading. I assume you mean "with more than 20 years since end of employment". P14, line 26: It would be useful to mention the other sources of occupational radiation exposure. Table 2: The table is a little bit confusing. Sometimes the main ICD 10 groups are used and sometimes specific subgroups, which is difficult to identify for the reader. It might be useful to mark the main ICD 10 groups and to indent the subgroups (like e.g. diseases of the

	blood and blood-forming organs). The sum of the number of non-cancer diseases (1012), cancer (912) and external causes (186) is 2110, whereas the total number is 2130. It would be interesting to see the SMR for the leukemia subgroup non-CLL. Table 3: It might be helpful to include the numbers of deaths in each of the categories. I wonder whether the broad group of non-cancer diseases is useful, because it mixes e.g. circulatory diseases and respiratory diseases, which have different etiology and probably latency periods. Appendix Figure 1: In the last two boxes, there is a typing error in the numbers. Instead of 17.712, the correct number is 12.712 and instead of 17649 the correct number is 12649.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Doug Brugge
Tufts University School of Medicine, USA

Please leave your comments for the authors below

This is a nicely presented and clear and clean analysis. I have only a couple of recommendations with regard to framing and interpretation:

1) Uranium exerts its biological effects (including DNA damage) primarily as a chemical toxin, not through radiation. The paper should acknowledge this and indicate whether the follow up of this cohort will address only radiation induced health outcomes or chemical also. I have reviewed uranium health effects, which might be a quick short cut to find the sources for this information:

Brugge D, Buchner. Health effects of uranium: new research findings. Reviews on Environmental Health. 2011; 26:231–249.

Thank you for this pertinent comment. We acknowledge that uranium may exert effects throughout chemical toxicity, and therefore added the following sentences to the Introduction section, where we added a citation for your helpful paper (pages 4-5):

“In addition to its radiological toxicity, uranium may exhibit chemical toxicity, as a heavy metal. This chemical toxicity was demonstrated on kidney and brain,11 and might possibly extend to other organs. Therefore, even if models used to predict radiation-induced health effects from uranium exposure proved strictly adequate, additional data would be needed to characterize the total (i.e.: radiological plus chemical) health effects of uranium exposure in humans. This further justifies the need to directly quantify these effects in exposed populations.”

In addition, we stated more explicitly in the discussion section (page 17) our future plans to investigate both chemical and radiological health effects of uranium exposure, and to disentangle them:

“The calculation of uranium concentrations in the target organs of uranium (e.g.: lungs, kidneys, bones and brain among others) but also of resulting absorbed radiation doses to these same organs, will help disentangling chemical from radiation effects of uranium exposure. This specific investigation will be possible since separate populations of workers have been exposed to uranium of different isotopic compositions, which show contrasted specific activity (e.g.: 0.33 µCi/g for depleted uranium, 0.68 µCi/g for natural uranium and up to 50 µCi/g for enriched uranium). Since depleted uranium has a very low specific activity, an estimate of the relationship between depleted uranium concentrations in organs and health risks will almost purely assess the potential chemical toxicity of uranium. Beside this, workers exposed to a same level of uranium concentration in organs will receive different internal radiation dose from this nuclide, depending on whether they were exposed to depleted, natural or enriched uranium (again, because of their varying specific activities). Comparing risks in workers exposed to uranium of different isotopic compositions will therefore provide an opportunity to isolate and quantify the radiological component of uranium toxicity."

2) While the industrial processes at the later stage of the nuclear cycle are dealing with pure uranium, the earlier stages (conversion, for example) still have other contaminants from the ore. These include uranium decay products such as radium, thorium, radon as well as non-radioactive toxins such as arsenic. It is important to at least mention this.

We agree that uranium is not the only pollutant, radiological or chemical to which workers of the nuclear fuel cycle have been exposed. The TRACY cohort does not include millers who were monitored for radon, long-live radioactive and uranium dust. The first step covered is the purification of the yellow cake (natural uranium with a degree of purity varying between 66 and 89%, average 80%) and for these workers, the monitoring covers only uranium exposure (urinalysis) and external radiation (chest badge) even if exposure to radon and other uranium decay products is also possible. It is also true that exposure to chemicals such as acids, trichloroethylene, perchloroethylene or tributylphosphate could be very high in certain facilities. We have checked for any mention of arsenic on the different Workplace Exposure Sheets reporting all potential exposure. Arsenic exposure was reported only in one company, SOCATRI, in a specific workshop in which activities were not related to uranium (it was a decontamination work for a customer which was not in involved in nuclear activities) involving only 23 workers.

We completed the paragraph about multiple exposures on page 16, by mentioning uranium decay products:

"The reconstruction of the multiple exposures of the workers in the TRACY cohort represents a necessary effort to assess risks according to different levels of exposure to uranium, while taking into account other sources of radiation (external exposure to X and gamma rays, and internal contamination with radionuclides such as for instance uranium decay products, plutonium and tritium) and other potential risk factors, including CMR (Carcinogenic, Mutagenic or Toxic to Reproduction) chemicals, heat, noise and shift work."

And just after:

"Job Exposure Matrices allow estimating exposures not covered by any individual monitoring and better document uranium compounds present at each place of work."

3) This is a mortality study, which is fine, but perhaps also a mention, briefly at least, of the health end points short of mortality that are a concern with uranium, including kidney damage, reproductive harm and birth defects.

We now mention in the discussion section (page 15) that:

"In addition, although the use of mortality data is very informative, it does not allow capturing the full range of possible health effects of uranium exposure, for instance cognitive, reproductive effects or kidney damage.11 More generally, it does not capture adequately the incidence of diseases which are rarely fatal."

4) There is a lot more toxicology on brain effects in animals than is listed. Not necessary to cite them all, but maybe pick one of the most recent studies.

Following our statement "Animal studies have shown that brain is a target organ for uranium effects" in the discussion section (page 14) we cited two more papers in the field, which were recently published:
Dinocourt C, Legrand M, Dublineau I, Lestaevel P. The neurotoxicology of uranium. Toxicology. 2015 Nov 4;337:58-71.
Shaki F, Hosseini MJ, Ghazi-Khansari M, Pourahmad J. Depleted uranium induces disruption of energy homeostasis and oxidative stress in isolated rat brainmitochondria. Metallomics. 2013 Jun;5(6):736-44

Reviewer: 2

Sharon Silver
National Institute for Occupational Safety and Health, U.S.

Please leave your comments for the authors below

This initial assessment of the French combined internal uranium exposure cohort provides a useful overview comparing the cohort's mortality experience to that of the general population and includes supplemental analyses suggesting a strong healthy worker effect within the cohort. If statistical power permits, the paper might be enhanced by additional analyses of major facility/activity groupings.

Methods/results:
Exposures differ among and within uranium cycle facilities, such as those included in this study; key differences include levels of exposure and uranium solubility, with the latter leading to differences in organ dose (see Anderson JL et al. Radiation Protection Dosimetry 2015). This manuscript reports SMRs for the combined facilities, an approach that enhances statistical power but may obscure exposure-related risks. The ongoing exposure assessment the authors discuss will facilitate the optimal exposure/dose-response analyses. However, as the exposure assessment is complex and will not be available for some time, supplemental SMR analyses grouping roughly similar activities (similar at the level described in Appendix Table 1) across facilities could, in the interim, be informative. For example, the gaseous diffusion activities could comprise one grouping, and the assembly-support work at the two FBFC facilities another grouping; the two sets of workers would likely have very different summary exposure profiles. Appendix Table 1 does not provide number of workers or person-years by facility/operation. Lack of statistical power would likely hamper evaluation of some groupings; however, where possible, such analyses could provide crude information about possible exposure effects while the exposure assessment and subsequent analyses are pending. These additional analyses could also help address, in part, the issue raised in the discussion of inclusion of unexposed workers in the analyses. Interim analyses considering calendar time periods to reflect changes in exposures and exposure levels may be warranted as well, though calendar time and age at exposure may not be independent in this population. If these analyses are not feasible, expanded discussion of the likely impact of these limitations (inclusion of unexposed workers, exposure diversity, temporal changes in exposures) on the SMR findings would be helpful.

Although a precise analysis separating workers involved in operations corresponding to different steps of the process is not feasible yet at this stage because assigning all workers to specific activities is part of our ongoing exposure assessment work, we followed on your suggestion and conducted preliminary additional analyses by groupings of companies involved in separate steps, according to the three main steps of the cycle (conversion, enrichment and oxide fuel manufacturing). Results are presented in Appendix Table 5, and we added new related paragraphs in Material and methods, Results and Discussion sections.

In the Material and Methods section (pages 8-9):

“We also conducted supplementary analyses according to groupings of companies involved in the three main steps of the uranium cycle (conversion, enrichment by gaseous diffusion and manufacturing of oxide fuel), in two ways. First, we considered workers involved in only one grouping of companies covering a specific step (therefore not allowing for overlap between population subgroups, by excluding workers who got involved during their careers in several groupings of companies covering different steps) and second, considering workers involved in at least one of these grouping of companies (therefore allowing for overlap between the population groupings analyzed). For conversion, we considered workers employed by Comurhex (Malvési and Pierrelatte plants). For enrichment, we considered a specific sub cohort extract from the TRACY cohort with workers involved in both military and civil enrichment (Zhivin and al, accepted). Workers employed by FBFC (Romans sur Isère and Pierrelatte plants) constituted the oxide fuel manufacturing grouping.”

In the Results section (page 12):

“For all groupings of causes of death considered, we observed no difference in mortality patterns? according to groupings of companies involved in the main 3 steps of the cycle, regardless of the way the groupings were defined (see Appendix Table 5). “

In the Discussion section (page 16):

“However, as a preliminary approach we explored the hypothesis of different health effects according to different parts of the uranium cycle, by conducting a first analysis by groupings of companies involved in the three main steps of the uranium cycle (conversion, enrichment and fuel manufacturing). We failed to demonstrate potential differences, possibly because of the lack of statistical power and of the inclusion of non-exposed workers in each group.”

Because of the limited statistical power available for these analyses, we felt further stratifying results by calendar time and age at exposure was premature. However, we agree that such an analysis would be of interest after further extension of the follow-up (as you soundly suggested below), especially when the detailed exposure assessment will have been completed.

We added the person-years by facility in Appendix Table 1 as you suggested.

Discussion:
The discussion could be enhanced by nothing that cohort is young, with an average age of 60 at study end and only 17% of the cohort deceased. In addition to the planned exposure analyses, the authors might consider repeating the SMR analyses when additional follow-up data become available.

We added this limitation in the Discussion section (page 17):

“The cohort is still young, with an average age of 60 and only 17% of the cohort deceased at the end of follow-up.”

We agree that the SMR analyses will deserve replication when additional follow-up data will become available, in addition to the planned exposure analyses. This will notably allow conducting more subgroup analyses with increased statistical power. We stated more explicitly our plans to extent the follow-up of the TRACY cohort in the future in the following statement (page 18):

“Extended follow-up and pooled analyses of these cohorts, including TRACY, are needed to produce more statistically precise estimates”

The significant excess observed was for pleural mesothelioma. Ascertainment of mesothelioma prior to ICD-10 (1999) has been problematic. If this classification issue applies to this cohort, it should be addressed in the discussion.

Thank you for this relevant comment. We checked further about this issue and subsequently added the following statement to the Discussion section (page 13):

“We acknowledge that the diagnosis and ascertainment of mesothelioma on death certificates has been problematic until at least the early 1990’s (Liddel and Miller 1991). This limitation applied both to the TRACY cohort and to the comparison group, the French general population (Arveux 2002). The ascertainment of mesothelioma improved with the introduction of ICD10 (Pinhero 2004), which was used since year 2000 for French death certificates.”

Minor points:

Results – some additional detail on reasons for exclusion of >8,000 workers would be informative (how many were, contractors, etc.)

We added a sentence in the first paragraph of Results describing the population of excluded workers (page 10):

“Workers excluded were permanent status workers who cumulated less than 6 months of employment (N=641), trainees (N=2561), short-term workers (N=2036) and others special contracts (military service, scientific advisor, N=129). Excluded workers cumulated an average duration of work of 0.50 years. Contractors were not mentioned in the employee personnel files and therefore could not be considered.”

Discussion – Some of the SMRs with non-significant excesses are quite low. For pancreatic cancer, the SMR is 1.05, with CI 0.79-1.38. This finding may not warrant a paragraph in the discussion; if the intent is to compare with other cohorts, then presentation of the magnitude of the findings from the other cohorts would be helpful (likewise for some of the other outcomes).

We confirm that our purpose was to compare the excesses we observed (whether they were statistically significant or not) with findings from comparable cohorts. In order to allow interested readers to do so without extending the main text, we reported the findings from other cohorts in Appendix table 6.

Reviewer: 3

Michaela Kreuzer
Federal Office for Radiation Protection in Germany

Please leave your comments for the authors below

This is a very well written, clearly structured and interesting paper. It provides for the first time information on characteristics of the new TRACY cohort of uranium workers and on comparisons of the mortality in the cohort with that of the general population. An improved health risk assessment in relation to internal emitters, and particularly uranium exposure, is a key issue in radiation protection. The cohort is very large and is highly valuable in this field.

Specific comments:
P3, line 15: Typing error: Instead of “investigation or uranium-related” please correct into “of”

Thank you for noticing this typing error. We corrected accordingly.

P6, line 17-23: If there is an overlap of the TRACY cohort with one of the two addressed French cohorts, the number of cohort members with overlap might be mentioned.

We have added this sentence after the mentioned lines (page 6):

“The overlaps between TRACY and the French cohorts of uranium miners and nuclear workers are of 158 and 5057 subjects, respectively”.

P 6, line 37: It is mentioned that complete individual work histories were reconstructed. It would be interesting to know what kind of information this includes. E.g. Annual information on the type of job (how many different jobs), workplace (how many different work places), etc.

We agree that this point needed to be described more precisely. We therefore modified the previous sentence (page 6-7) as follows:

“Transfers from one company to another were taken into account to avoid duplicate counts and accurately reconstruct time spent in the different companies included in the TRACY cohort where workers were employed. The detailed characterization of workplaces and job titles is a long-term task for this large cohort and is still underway.”

P7, line 18: It is stated that there was a file-matching with the National Vital Status Registry. Is there any experience about the quality of linkage, meaning how sure it is that the correct person was identified and not a false one (e.g. same name and birth date). The procedure might be explained.

We added explanations about the procedure, which was designed to guarantee a perfect quality of linkage (page 7):

“Workers’ vital status, and the date of death for workers who died, were obtained from the National Vital Status Registry (Répertoire National d’Identication des Personnes Physiques) by file-matching on name, surnames, gender, date and place of birth. To avoid erroneous linkages, only workers with one possible match with the registry were considered as identified.”

How many people of the group of lost to follow-up moved to another country?

This information is not available from the sources we had access to. However, we identified that among the 141 workers lost to follow-up, 41 were born abroad and 27 of them were born in ex-French departments of Algeria, Morocco and Tunisia where the civil registration was of lower quality than in metropolitan France. This might therefore contribute to explain a substantial proportion (29%) of people lost to follow-up.

P7, 21-24: Here file-matching with the French national mortality registry is mentioned. How valid is this information? What type of information was transferred? Only the code of the underlying cause of death based on the certificate of death or also other information (contributing causes of deaths) or even written text of the causes of deaths.

As for the vital status, we have detailed the procedure (page 7-8):

"Causes of death (underlying and associated causes) coded according to the International Classification of Diseases (ICD, version 8 for period 1968–1978, version 9 for 1979–1999 and version 10 for period 2000–2008, see Appendix Table 2) and corresponding labels were obtained by file-matching on gender, date and place of birth, and date and place of death with the French national mortality registry (CépiDC-Inserm). In case of multiple matches, no causes could be obtained for these workers."

P10, line 50: The expression "with more than 20 years of employment" is a little bit misleading. I assume you mean "with more than 20 years since end of employment".

Thank you for noticing this mistake. We corrected the sentence as follows (page 12):

"No deficit in cancer mortality is observed in workers 20 years or more after the end of employment"

P14, line 26: It would be useful to mention the other sources of occupational radiation exposure.

We have detailed the other sources (page 16):

"… while taking into account other sources of radiation (external exposure to X and gamma rays, and internal contamination with radionuclides such as for instance uranium decay products, plutonium and tritium)

Table 2: The table is a little bit confusing. Sometimes the main ICD 10 groups are used and sometimes specific subgroups, which is difficult to identify for the reader. It might be useful to mark the main ICD 10 groups and to indent the subgroups (like e.g. diseases of the blood and blood-forming organs).

Table 2, Appendix Table 3 and 4, have been modified taking into account your suggestion

The sum of the number of non-cancer diseases (1012), cancer (912) and external causes (186) is 2110, whereas the total number is 2130.

Thank you for making this point. The difference of 20 cases you noticed can almost entirely be explained by 19 unknown causes of deaths.
However, your comment also helped us identify and correct a mistake: one case of Ischemic heart diseases was missed. We corrected this mistake and subsequently double-checked all our results. SMRs and confidence intervals remain unchanged after 2-digit rounding, but we corrected the number of ischemic heart diseases and circulatory diseases in all tables where this was needed.

We also added the sentence in the Material and Methods section (page 8):

"The "All causes" group included workers with non-identified causes of death".

It would be interesting to see the SMR for the leukemia subgroup non-CLL.

We added a new line for this category on Table 2 and Appendix Table 3. We also modified Appendix Table 2 accordingly.

Table 3: It might be helpful to include the numbers of deaths in each of the categories. I wonder whether the broad group of non-cancer diseases is useful, because it mixes e.g. circulatory diseases and respiratory diseases, which have different etiology and probably latency periods.

We added the numbers of deaths in each of the categories and replaced the category "non-cancer diseases" with separate categories of "circulatory diseases" and "respiratory diseases". We modified the Results section according to these groups of diseases (page 11):

"SMRs for cancer diseases tended to increase with time since hire, with time since end of employment and with attained age (Table 3). Twenty years after the end of employment, the risk of cancer mortality is not significantly different from that in the general population, whereas it remains significantly lower for circulatory and respiratory diseases. No clear trend was observed according to the duration of employment for mortality from all causes and from circulatory diseases. However there was evidence of a decreasing trend along with duration of employment for mortality from cancer and respiratory diseases. For all broad groupings of causes of death, the lowest SMRs were observed in workers with the longest duration of employment (Table 3)."

Appendix Figure 1: In the last two boxes, there is a typing error in the numbers. Instead of 17.712, the correct number is 12.712 and instead of 17649 the correct number is 12649.

Thank you for noticing these mistakes. We corrected them on Appendix Figure 1.

VERSION 2 – REVIEW

REVIEWER	Sharon Silver CDC/National Institute for Occupational Safety and Health, U.S.
REVIEW RETURNED	15-Dec-2015

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.

REVIEWER	Michaela Kreuzer Federal Office for Radiation Protection, Germany
REVIEW RETURNED	22-Dec-2015

GENERAL COMMENTS	Many thanks for the detailed revision of the manuscript. All reviewer comments have been considered adaequately.