



Australian Government

Repatriation Medical Authority

REPATRIATION MEDICAL AUTHORITY

STATEMENT OF REASONS

SUBSECTION 196B(9), *VETERANS' ENTITLEMENTS ACT 1986*

**DECISION NOT TO AMEND THE STATEMENTS OF PRINCIPLES CONCERNING
MALIGNANT NEOPLASM OF THE PROSTATE**

Instrument Nos. 53 and 54 of 2014

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PART I INTRODUCTION

1. On 24 March 2021, the Repatriation Medical Authority (the Authority) received a request from the applicant, seeking a review, by way of an investigation, of the contents of the Statements of Principles (SOPs) concerning malignant neoplasm of the prostate (Instrument Nos. 85 and 86 of 2016). The applicant requested that the Authority review these SOPs and include a factor in relation to asbestos exposure.
2. The request for review was made under s 196E of the *Veterans' Entitlements Act 1986* (the VEA) by a person eligible to make a claim for a pension under Part II or IV of the VEA.
3. At its meeting on 5 May 2021, after an initial review of the available sound medical-scientific evidence (SMSE), the Authority decided to conduct a focussed review in relation to asbestos exposure as a factor for malignant neoplasm of the prostate. A notice of investigation advertising this focussed review was published in the Government Notices Gazette on 1 June 2021.
4. Having completed the review, the Authority decided at its meeting on 4 August 2021 not to amend the SOPs concerning malignant neoplasm of the prostate to include a factor in relation to asbestos exposure. This Statement of Reasons provides the Authority's reasons for deciding not to amend the SOPs to include such a factor.

PART II BACKGROUND TO THE REQUEST

5. Although not specifically stated, a fair reading of the applicant's request indicates that he wished the Authority to consider adding one or both of the following factors to the SOPs concerning malignant neoplasm of the prostate (Instrument Nos. 53 and 54 of 2014):
 - exposure to asbestos generally; or
 - consuming water contaminated with asbestos.
6. This request was supported by the ground that the applicant had located information identifying a positive link between asbestos exposure and malignant neoplasm of the prostate. The applicant also relied on his own personal experience of possible exposure to asbestos while serving as a member of the United Nations Peacekeeping Force in Cyprus in the 1960s.
7. In support of this ground, the applicant provided the following information:
 - Information on 'prostate cancer' which the applicant stated was downloaded from the mesothelioma resource online. This article has no cited author or date, although it did make reference to two other unidentified articles:
 - an autopsy study of 14 cases of pulmonary disease due to asbestos exposure of whom 43% had asbestos bodies in their prostate tissue; and
 - a Danish study published in 1993 reporting an association between asbestos and prostate cancer cases.
 - Information on 'Asbestos exposure and prostate cancer' which the applicant stated was downloaded from the asbestos.com. This article mentioned three studies, two of which were the studies mentioned above. The additional study was a Finnish 2003 prospective study of 23,285 men and 930 women who were exposed to asbestos and followed for eight years. This is likely the study by Koskinen et al (2003), referred to

below. The study reported a higher incidence of prostate cancer than the background Finnish population.

- 'Arsenic mine tailings and health' internet article from BetterHealth channel 2018 by the Department of Health and Human Services for the Victorian state government. This article does not mention prostate cancer, although the applicant queried whether there might be a link between exposure to copper tailings and prostate cancer. However, because the applicant specifically requested that the Authority consider asbestos exposure, the Authority did not consider further the topic of copper tailings.

PART III EVIDENCE PREVIOUSLY CONSIDERED BY THE AUTHORITY

8. At the time that the SOPs concerning malignant neoplasm of the prostate (Nos. 53 and 54 of 2014) were determined, the Authority had before it information including:
 - briefing papers prepared in December 2013 by a Repatriation Medical Authority medical researcher; and
 - an extensive number of articles published in the peer-reviewed literature.
9. In addition to the full review which it finalised in 2014, the Authority considered a discussion paper at its October 2016 meeting on the topic of asbestos exposure and prostate cancer. Under paragraph 196CA(1)(b) of the VEA, the Authority decided not to conduct a focussed review, as the request did not identify sufficient relevant information to justify a review. In making this decision, the Authority had regard to four retrospective cohort studies concerning an association between asbestos exposure and prostate cancer.

PART IV NEW INFORMATION CONSIDERED BY THE AUTHORITY

10. The information provided by the applicant, identified above, was considered. A discussion paper that considered the information supplied by the applicant and other available relevant SMSE was prepared by a Repatriation Medical Authority medical researcher for the Authority's meeting held on 5 May 2021.
11. A briefing paper providing a more detailed analysis of the current SMSE was prepared by a medical researcher for the Authority's meeting held on 4 August 2021, as part of the focussed review into 'asbestos exposure' as a factor in malignant neoplasm of the prostate.
12. The Authority also received a submission to the investigation from a veteran dated 8 June 2021. The veteran had a 20 year career in the Royal Australian Navy from the 1960s to the 1980s, and his submission indicates that the ships and other defence establishments on which he served had large amounts of asbestos-containing material. The veteran was diagnosed with prostate cancer in 2012 and although not specifically stated, it is implied that he considers there to be a link between his asbestos exposure during service and the onset of the prostate cancer. However, there was no SMSE or other supporting information provided with this submission.
13. The Authority greatly appreciates the time and effort which both the applicant and submitter have taken in preparing their submissions. It is important to note that in forming any view during an investigation, the Authority may rely only on SMSE: subsection 196C(3), VEA. Consequently, the Authority was unable to take into account every aspect of the submissions provided.

Asbestos exposure generally

14. Two recent meta-analyses found small but significant overall associations between asbestos exposure and risk of prostate cancer. Dutheil et al (2020)¹ found a relative risk of 1.10 (95% CI 1.05 -1.15, based on 30 studies), while Peng et al (2019)² found a summary risk of 1.22 (95% CI 1.13 - 1.32, based on 17 studies). There was a lack of consistency in the results of studies: only 8 out of 33 studies in the Dutheil et al (2020) meta-analysis found significant positive associations, with all other studies having null or non-significant findings and wide confidence intervals. Stratified results by type of risk demonstrated a small increased risk of prostate cancer incidence (SIR 1.16, 95% CI 1.04-1.27), but no evidence of increased prostate cancer mortality (SMR 1.09, 95% CI 0.98-1.19).
15. Both meta-analyses had significant methodological issues which limit the interpretation of these findings. The article by Peng et al (2019) was retracted by the journal due to concerns about the quality and thoroughness of the literature review, including concerns regarding double-counted observations, the inclusion of some cohorts of oil refinery workers, and the potential for bias in the combination of prostate cancer incidence and mortality.
16. Boffeta et al (2021)³ made similar observations about the analysis by Dutheil et al (2020): studies of incidence and mortality were combined, the most recent updates of findings from four cohort studies were not included, two large studies with null or negative findings were not included, and a study of oil refinery workers with exposure to other potential carcinogens was included.
17. Some cohort studies (many of which were included in the above meta-analyses) have found small but significant associations for groups exposed or possibly exposed to asbestos and prostate cancer:
 - Boice et al (2020)⁴ for prostate cancer mortality in military personnel involved in nuclear testing: SMR 1.13, 95% CI 1.08–1.18.
 - Sorahan (2019)⁵ in electrical workers who may have been exposed to asbestos in previous occupations, SIR 1.06, 95% CI 1.02–1.09.
 - Korda et al (2017)⁶ for prostate cancer incidence in men exposed to asbestos insulation in the Australian Capital Territory, SIR 1.29, 95% CI 1.07-1.54.
 - Reid et al (2013)⁷ for prostate cancer incidence in men exposed to asbestos as children in Wittenoom, for one method of analysis but not the other (SIR1 1.04, 95% CI 0.54 – 1.82, SIR2 2.48, 95% CI 1.28 -4.33).

¹ Dutheil F, Zaragoza-Civale L, Pereira B, et al (2020) Prostate Cancer and Asbestos: A Systematic Review and Meta-Analysis. *Perm J*, 24:19.086.

² Peng R, Fang F, Chen Z, et al (2019). Does exposure to asbestos cause prostate cancer? A systematic literature review and meta-analysis. *Medicine (Baltimore)*, 98(3):e14108.

³ Boffetta P, Franco N, Gullino A, et al (2021). Re: Dutheil et al. Prostate Cancer and Asbestos: A Systematic Review and Meta-Analysis. *Perm J*, Jan 25.

⁴ Boice JD, Cohen SS, Mumma MT, et al (2020). Mortality among U.S. military participants at eight aboveground nuclear weapons test series. *Int J Radiat Biol*, 1-22.

⁵ Sorahan TM (2019). Cancer incidence in UK electricity generation and transmission workers, 1973-2015. *Occup Med (Lond)*, 69(5):342-351.

⁶ Korda RJ, Clements MS, Armstrong BK, et al (2017). Risk of cancer associated with residential exposure to asbestos insulation: a whole-population cohort study. *Lancet Public Health*, 2(11):e522-e528.

⁷ Reid A, Franklin P, Olsen N, Sleith J, Samuel L, Aboagye-Sarfo P, de Klerk N, Musk AW. (2013) All-cause mortality and cancer incidence among adults exposed to blue asbestos during childhood. *Am J Ind Med*. Feb;56(2):133-45.

- Koskinen et al (2003)⁸ for prostate cancer incidence in Finnish construction workers: SIR 1.21, 95% CI 1.09-1.34.
18. These studies were limited by lack of information about exposure to other possible carcinogens, lack of certainty about actual exposure levels, lack of internal consistency with known asbestos-associated cancers (Sorahan et al 2019), possible greater ascertainment of prostate cancer in groups which volunteered for screening (Koskinen et al 2003, Reid et al 2003) and internally inconsistent findings (Reid et al 2003).
 19. Asbestos fibres have been noted in the prostate (Korda et al 2017), but the presence of fibres is not necessarily linked to the development of a disease. The key mechanisms of carcinogenesis in the lung include oxidative stress, chronic inflammation, and genetic and epigenetic alterations as well as cellular toxicity and fibrosis (Dutheil et al 2020). However, it is unknown whether such mechanisms would be relevant to carcinogenesis in the prostate.
 20. Overall, it is difficult to determine whether or not there is a causal association between asbestos exposure and malignant neoplasm of the prostate because of inconsistency in the data, small effects, and lack of information about dose, dose-response effects and screening rates in exposed and unexposed groups.

Asbestos in drinking water

21. A cohort study of cancer risk for people living in a US town with asbestos-contaminated drinking water (Howe et al 1989)⁹ found a borderline significant increase in risk of prostate cancer (SIR 1.7, 95% CI 1.0 - 2.6). In an update of this cohort, Browne et al (2005)¹⁰ found no increased risk of gastrointestinal, respiratory and total cancers, but rates for prostate cancer were not reported.
22. In a Norwegian study of lighthouse keepers who drank water contaminated with asbestos (Andersen et al 1993)¹¹, no statistically significant excess risk was found for any type of cancer in the group with a latency period of 20 years or more, except for stomach cancer. Prostate cancer was not separately reported.
23. Conforti et al (1981)¹² found a significant increase in risk of prostate cancer in areas of Oakland, San Francisco, where natural contamination of water was high. However, exact risk estimates were not provided, individual exposure levels were not quantified, and there was no control in this study for alcohol, smoking, obesity or other cancer risk factors. There were some gender differences in risk for a number of other cancers which suggested that alternative risk factors might account for the findings.
24. Overall, the evidence concerning the association between asbestos in drinking water and prostate cancer is very limited in quality and quantity, and is too limited to determine whether or not a causal relationship exists.

⁸ Koskinen K, Pullala E, Reijula K, Karjalainen A (2003) Incidence of cancer among the participants of the Finnish asbestos screening campaign. *Scand J Work Environ Health* Vol 29(1) pp 64-70.

⁹ Howe HL, Wolfgang PE, Burnett WS, et al (1989). Cancer incidence following exposure to drinking water with asbestos leachate. *Public Health Rep*, 104(3):251-6.

¹⁰ Browne ML, Varadarajulu D, Lewis-Michl EL, et al (2005). Cancer incidence and asbestos in drinking water, Town of Woodstock, New York, 1980-1998. *Environ Res*, 98(2):224-32.

¹¹ Andersen A, Glatte E, Johansen BV (1993). Incidence of cancer among lighthouse keepers exposed to asbestos in drinking water. *Am J Epidemiol*, 138(9):682-7.

¹² Conforti PM, Kanarek MS, Jackson LA, et al (1981). Asbestos in drinking water and cancer in the San Francisco Bay Area: 1969-1974 incidence. *J Chronic Dis*, 34(5):211-24.

PART VI FINDINGS OF FACT

25. In light of the material discussed above, the Authority made the following finding of fact:
- The body of available SMSE does not support the existence of a causal association between exposure to asbestos and the clinical onset or clinical worsening of malignant neoplasm of the prostate. Consequently, the Authority is not satisfied that there is at least a reasonable hypothesis that being exposed to asbestos, either generally or in drinking water, is a factor which causes, or contributes to, the clinical onset or clinical worsening of malignant neoplasm of the prostate.

PART VII REASONS FOR THE DECISION

26. The Authority was cognisant of the provisions of the VEA, and had particular regard to subsection 5AB(2) SMSE, s 5D injury/disease, and Part XIA.

SMSE is defined as follows:

*"Information about a particular kind of injury, disease or death is taken to be **sound medical-scientific evidence** if:*

- (a) *the information:*
- (i) *is consistent with material relating to medical science that has been published in a medical or scientific publication and has been, in the opinion of the Repatriation Medical Authority, subjected to a peer review process; or*
 - (ii) *in accordance with generally accepted medical practice, would serve as the basis for the diagnosis and management of a medical condition; and*
- (b) *in the case of information about how that kind of injury, disease or death may be caused - meets the applicable criteria for assessing causation currently applied in the field of epidemiology."*

27. The Authority noted sub-sections 196B(7), 196B(8) and 196B(9) and section 196E, which relevantly provide:

196B(7)

If the Authority:

- (a) *is asked under section 196E to review:*
- (i) *some or all of the contents of a Statement of Principles;*
- [...]
- (b) *thinks that there are grounds for such a review;[...]*
the Authority must, subject to subsection 196C(4) and section 196CA in a case where paragraph (a) applies, carry out an investigation to find out if there is new information available about:
- (d) *how the injury may be suffered, the disease may be contracted or the death may occur; or*
 - (e) *the extent to which the disease, injury or death may be war-caused or defence-caused.*

196B(8)

If, after carrying out the investigation, the Authority is of the view that there is a new body of sound medical-scientific evidence available that, together with the sound medical-scientific evidence previously considered by the Authority, justifies the making of a Statement of Principles, or an amendment of the Statement of Principles already determined, in respect of that kind of injury, disease or death, the Authority must:

- (a) [...]; or*
 - (b) make a determination amending the Statement of Principles determined under subsection (2) or (3) in respect of that kind of injury, disease or death; or*
 - (c) [...];*
- as the case requires.*

196B(9)

If, after carrying out the investigation, the Authority is of the view:

- (a) that there is no new sound medical-scientific evidence about that kind of injury, disease or death; or*
- (b) that the new sound medical-scientific evidence available is not sufficient to justify the making of a Statement of Principles, or an amendment of the Statement of Principles already determined in respect of that kind of injury, disease or death;*

the Authority must make a declaration in writing:

- (c) stating that it does not propose to make a Statement of Principles, or amend the Statement of Principles already determined (as the case may be); and*
- (d) giving the reasons for its decision.*

196E

- (1) Any of the following:*
 - (b) a person eligible to make a claim for a pension under Part II or IV;*
 - (ba) a person eligible to make a claim for compensation under section 319 of the MRCA;*
 - (c) an organisation representing veterans*
- may ask the Repatriation Medical Authority:*
- (f) to review the contents of a Statement of Principles in force under this Part.*

Basis for commencing review of an existing SOP

28. It is the applicant's request which prompted the Authority to commence an investigation into this particular factor under s 196B(7)(a) of the VEA.¹³

Basis for amending an existing SOP

29. In forming any view during an investigation, the Authority may rely only on SMSE. Subsection 196B(8) provides that where there is a new body of sound medical-scientific evidence available that, together with the sound medical-scientific evidence previously considered by the Authority, justifies the amendment of a SOP the Authority is required to do so. On the other hand where there is no new SMSE or the new SMSE is insufficient to justify an amendment subsection 196B(9) provides that the Authority *must* make a declaration stating that it does not propose to amend the SOP and give reasons for that decision.

¹³ It not otherwise being an application within either subsection 196C(4) or section 196CA of the VEA.

Reasons for deciding not to amend an existing SOP

30. Together with its own expert knowledge, the Authority took into consideration:
- the information provided by the applicant, to the extent that it relied on SMSE;
 - the information held by the Authority and obtained during its previous investigations leading up to the determination of the SOPs concerning malignant neoplasm of the prostate (Instrument Nos. 53 and 54 of 2014);
 - the discussion paper prepared by a medical researcher for the October 2016 meeting;
 - the discussion paper prepared by a medical researcher for the May 2021 meeting; and
 - the briefing paper prepared by a medical researcher for the August 2021 meeting.
31. As noted above, the applicant relied on the following ground for seeking a review of the contents of the SOPs concerning malignant neoplasm of the prostate:
- there is information available which supports a positive link between asbestos exposure and malignant neoplasm of the prostate.

Is there new sound medical-scientific evidence?

32. Since its previous consideration of the SMSE in relation to asbestos exposure in 2016, new SMSE has been published. This new SMSE has been discussed above.

Is the available sound medical-scientific evidence sufficient to justify amendment?

33. The Authority is of the view that the currently available SMSE, including the new SMSE, was not sufficient to justify the amendment which the applicant sought. The available studies are inconsistent in their findings and have significant methodological limitations. Such limitations include a lack of information about levels of asbestos exposure and an inability to examine dose-response effects. There is also a lack of information about stage of prostate cancer or screening rates, which is needed to determine whether or not higher rates were partly due to earlier detection from screening. There is no clear mechanism by which asbestos fibres might cause prostate cancer.
34. There are significant other methodological limitations with many of the studies which show a positive association between asbestos exposure and prostate cancer, including double-counted observations, failure to include some studies in the meta-analysis by Dutheil et al (2020), the inclusion of some cohorts of oil refinery workers (who may have been exposed to multiple other carcinogens), and the potential for bias in the combination of prostate cancer incidence and mortality.
35. Consequently, the evidence is too equivocal to say with any certainty whether exposure to asbestos, either generally or in drinking water, plays a causal role in the clinical onset or worsening of malignant neoplasm of the prostate.

PART VIII CONCLUSIONS

36. Overall, for the reasons set out above, the available SMSE is not sufficient to justify the amendment of the SOPs concerning malignant neoplasm of the prostate by including factors for asbestos exposure.

PART IX DECISION

37. The Authority decided at its meeting on 4 August 2021 not to amend the SOPs concerning malignant neoplasm of the prostate (Instrument Nos. 53 and 54 of 2014) as it considered that the SMSE was not sufficient to justify the amendment sought in the application.

Professor Terence Campbell AM
Chairperson
Repatriation Medical Authority

20 August 2021