



Australian Government
Repatriation Medical Authority

REPATRIATION MEDICAL AUTHORITY

STATEMENT OF REASONS

S 196B(9) *VETERANS' ENTITLEMENTS ACT 1986*

**DECISION NOT TO AMEND THE CURRENT STATEMENT OF PRINCIPLES
CONCERNING MALIGNANT NEOPLASM OF THE LUNG FOLLOWING A REVIEW**

Instrument No. 93 of 2014

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PART I INTRODUCTION

1. The Repatriation Medical Authority (the Authority) pursuant to subsection 196B(9) of the *Veterans' Entitlements Act 1986* (the VEA), has decided not to amend Statement of Principles concerning malignant neoplasm of the lung, Instrument No. 93 of 2014, following an investigation which was notified in the *Commonwealth of Australia Gazette* on 29 October 2019. The investigation related to "insecticides".
2. Having carried out the investigation as notified, the Authority concluded that the sound medical-scientific evidence available to it, including the new sound medical-scientific evidence, is sufficient to justify the inclusion of a factor relating to exposure to the insecticide diazinon in Statement of Principles Instrument No. 92 of 2014. However the sound medical-scientific evidence available to it, including the new sound medical-scientific evidence, is not sufficient to justify inclusion of a factor concerning exposure to diazinon in Statement of Principles Instrument No. 93 of 2014.

PART II BACKGROUND TO THE INVESTIGATION

3. A request dated 30 July 2019, was received from a representative of a veterans' organisation, seeking a review into the association between "exposure to insecticides in Vietnam" and malignant neoplasm of the lung. In support of the request, the applicant provided the following:
 - Mordike J (2013). Insecticide deceit?: the truth about insecticides used at Nui Dat.
 - Denner R (2013). Rampant & uncontrolled use of insecticides in Australian Army bases in South Vietnam. *The Vietnam Veterans Peacekeepers and Peacemakers Journal*; pp 12-13.
 - Tchounwou PB, Patlolla AK, Yedjou CG, et al (2015). Environmental exposure and health effects associated with malathion toxicity. Intech Open Limited. Internet published article. <https://www.intechopen.com/books/toxicity-and-hazard-of-agrochemicals/environmental-exposure-and-health-effects-associated-with-malathion-toxicity>.
4. On 2 October 2019, the Authority, under s 196B(7A) of the VEA, decided to review the contents of the Statements of Principles, Instrument Nos. 92 and 93 of 2014, to find out if there was new information in respect of "insecticides" as a factor in malignant neoplasm of the lung.
5. The investigation notice was signed by the Chairperson of the Authority on 18 October 2019 and was gazetted in accordance with s 196G of the VEA in the *Commonwealth of Australia Gazette* on 29 October 2019. Submissions were invited from persons and organisations wishing to make a submission by 19 November 2019.

PART III SUBMISSIONS RECEIVED BY THE AUTHORITY PURSUANT TO SECTION 196F

6. Following notification of its investigation, the Authority did not receive any information from persons eligible to make submissions pursuant to s 196F of the VEA.

PART IV EVIDENCE/INFORMATION AVAILABLE TO THE REPATRIATION MEDICAL AUTHORITY

7. The following information was available to the Authority:
 - 7.1. The information held by the Authority and obtained during its previous considerations leading to the determination of Statements of Principles concerning malignant neoplasm of the lung, Instrument Nos. 92 and 93 of 2014.
 - 7.2. Literature searches were conducted on 15 October 2019 using the Ovid search engine from 2004 to current, limited to English language and humans. The search terms were: Exp Dieldrin which produced 69 articles, Exp Diazinon which produced 32 articles, Exposure Malathion which produced 41 articles and Exp Organophosphates combined with exp Neoplasms which produced 148 articles. An additional 4 articles were selected for further study. Articles were selected based on relevance, study quality, reliability and journal authority.
 - 7.3. A briefing paper concerning malignant neoplasm of the lung prepared for presentation to the Authority by a Medical Researcher of the Secretariat.

PART V SOUND MEDICAL-SCIENTIFIC EVIDENCE

8. The Statements of Principles are determined on the basis of the available "sound medical-scientific evidence" as defined in s 5AB(2) of the VEA which states:

*"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."*

PART VI REASONS FOR THE DECISION

9. The International Agency for Research on Cancer (2017), in a recent evaluation of the organophosphate insecticide diazinon (Group 2A), concluded that there is limited evidence for an association with leukaemia, non-Hodgkin lymphoma and lung cancer.
10. There is some consistency in the limited number of cohort and nested case-control studies, with two of three studies finding positive associations. Several analyses of the Agricultural Health Study (AHS) (Alavanja et al 2004, Beane Freeman et al 2005, Jones et al 2015) reported that pesticide applicators had a significantly increased risk of lung cancer with lifetime days of exposure to diazinon. A case-control study nested in a cohort of Florida pest control workers (Pesatori et al 1994) reported that ever exposure to diazinon non-significantly increased the risk of lung cancer two-fold. In contrast, no

association was found between ever use of diazinon and lung cancer in the spouses of pesticide applicators in an analysis of AHS (Lerro et al 2015).

11. The strength of the association was moderate; at least around 100 days of exposure to diazinon in a lifetime increased the risk of lung cancer, with relative risks ranging from 1.8 to 3.5 in the AHS study analyses. Evidence for a dose-response was observed in the AHS, reporting a significant positive trend with lifetime days of exposure to diazinon.
12. The correct temporal relationship has been demonstrated by the AHS with exposure to diazinon recorded prior to the development of lung cancer. There is some biological plausibility as diazinon is considered to be genotoxic and produce oxidative stress (IARC 2017).
13. There were some limitations in the available studies which weakened the evidence for the association between diazinon and lung cancer being causal. The AHS and Florida pest control workers cohort adjusted for smoking and other pesticides. However, exposure to particular pesticides is correlated with exposure to other pesticides, and statistical adjustment may not completely account for confounding by other pesticides. The latest analysis of the AHS (Jones et al 2015) stratified the data by smoking status. The risk of lung cancer was still elevated in never smokers, but the dose-response was somewhat attenuated. Chance may also be an alternate explanation, as the AHS performed multiple testing and the association was not statistically significant in the pest control workers nested case-control study. Exposure assessment was based on self-report in the AHS and no biological measurements of diazinon exposure were undertaken.

PART VII SUMMARY AND CONCLUSIONS

14. Overall, results of the available studies indicate that the evidence is too limited to permit a judgement of a probable or convincing causal relationship between malignant neoplasm of the lung and exposure to the insecticide diazinon, but supports a judgement of a possible causal relationship. An association has been observed between exposure to diazinon and malignant neoplasm of the lung, but the evidence is limited in quality and quantity.
15. The VEA requires that the same body of evidence be assessed according to two different standards of proof. For assessment under the reasonable hypothesis standard (s 196B(2)) the VEA requires that the sound medical-scientific evidence must indicate or point to a causal association between a risk factor related to t and the disease in question. On the other hand, for the balance of probabilities standard (s 196B(3)), the sound medical-scientific evidence must show that it is more probable than not that there is a causal association between a risk factor related to t and the disease. In this matter the distinction between those standards of proof is significant.
16. The available sound medical-scientific evidence indicates or points to a causal association between exposure to the insecticide diazinon and malignant neoplasm of the lung, such being sufficient to support a judgement of a possible causal association. The

reasonable hypothesis standard is met and a factor will be included in that Statement of Principles.

17. However, as detailed in the reasons set out above, the sound medical-scientific evidence does not show that it is more probable than not that there is a causal association between exposure to diazinon and malignant neoplasm of the lung. The available evidence is therefore not sufficient to support a judgement of a probable causal association between exposure to diazinon and malignant neoplasm of the lung, and the balance of probabilities standard cannot be met. In these circumstances no factor can be included in that Statement of Principles.

PART VIII DECISION NOT TO AMEND INSTRUMENT NO. 93 OF 2014

18. At its meeting on 11 February 2020 the Authority decided not to amend the balance of probabilities Statement of Principles in respect of malignant neoplasm of the lung for the purposes of subsections 196B(3) and (8) of the VEA as the Authority concluded, for the reasons set out above, that the sound medical-scientific evidence available to it, including the new sound medical-scientific evidence, is not sufficient to justify the inclusion of a factor relating to exposure to the insecticide diazinon in the balance of probabilities Statement of Principles already determined in respect of malignant neoplasm of the lung.



Professor Nicholas Saunders AO
Chairperson
Repatriation Medical Authority

28 February 2020

PART IX BIBLIOGRAPHY

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