Specialist Medical Review Council

Reasons for Decisions

Section 196W
Veterans' Entitlements Act 1986

Re: Statement of Principles No. 153 of 1996 as amended by Instrument No. 7 of 1998 In Respect of Malignant Neoplasm of the Small Intestine
Matter No. 2002/2
Requests for Review Declaration No. 8

SUMMATION

1. In relation to the Repatriation Medical Authority (the RMA) Statement of Principles No. 153 of 1996 as amended by Instrument No. 7 of 1998, both made under subsection 196B(2) of the *Veterans' Entitlements Act 1986* (the VEA) in respect of malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine, the Specialist Medical Review Council (the Council) declares under section 196W(5) of the VEA that it is of the view that the sound medical-scientific evidence available to the RMA at the time it determined, amended or last amended the Statement of Principles was insufficient to justify:

(a) an amendment of the Statement of Principles by including as a factor or factors exposure to:

(i) barium meal x-rays;

(ii) peptic ulceration;

(iii) helicobacter pylori infection;

(iv) cimetidine and abdominal irritation from numerous medications; and

(v) exposure to nitrosamines; and

(b) any other amendment of that Statement of Principles.

2. The Council recommends that the RMA carry out an investigation to find out if there is new information available about how malignant neoplasm of the small intestine may be contracted, or death from malignant neoplasm of the small intestine occur, and the extent to which malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine may be war caused or defence caused.

3. In particular, the Council recommends the RMA find out if there is sound medical-scientific evidence that indicates that exposure to nitrosamines is a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. An investigation should take into account the sound medical-scientific evidence previously considered by the RMA (including those articles mentioned in paragraph 89 below), and any new body of sound medical-scientific evidence disclosed by the investigation.

4. In making this recommendation, the Council notes that the RMA's Reasons for its decision not to amend the Statement of Principles to include as a factor or factors those for which the applicant contended in her submission to the RMA (and subsequently the Council) do not discuss why it (the RMA) rejected exposure to nitrosamines as a possible link or element in such an hypothesis.

5. On the information available to it, the Council was unable to say that the sound medical-scientific evidence available to the RMA at the relevant times pointed to the possibility that exposure to nitrosamines could be a link or element in a reasonable hypothesis connecting malignant neoplasm of the small intestine to operational service.

6. There was some sound medical-scientific evidence (identified in paragraph 89 below) which the Council considered touched on the issue, and left open the possibility of an association, but, as conceded by the learned authors of those relevant articles, the evidence was at best suggestive. The methodologies of the articles were problematic. The Council was unable to identify from them any information which pointed to the particular type of exposure, required level of ingestion, required duration, and other threshold indicators that may apply.

7. Whilst the matter was not entirely free from doubt, the Council concluded that the sound medical-scientific evidence before it did no more than leave open the possibility of an association. Acknowledging that the burden of proof is 'unusually light', the Council nevertheless concluded that the relevant level of satisfaction (of a reasonable hypothesis) had not been reached.

8. Nevertheless, the Council is of the view that the matter warrants investigation by the RMA in light of this sound medical-scientific evidence, and any new body of sound medical-scientific evidence that may be disclosed by the investigation.

THE SPECIALIST MEDICAL REVIEW COUNCIL

9. The Council is a body corporate established under section 196V of the VEA, and consists of such number of members as the Minister for Veterans' Affairs determines from time to time to be necessary for the proper exercise of the functions of the Council as set out in the VEA. The Minister must appoint one of the Councillors to be the Convener. In the absence of the Convener, the Convener must appoint one of the

Councillors selected for the purposes of the review as Presiding Councillor at all meetings of the Council for the purposes of that review.

10. When a review is undertaken of a Statement of Principles made by the RMA, the Council is constituted by 3 to 5 Councillors appointed by the Minister and selected by the Convener. When appointing Councillors, the Minister is required to have regard to the branches of medical science expertise which would be necessary for deciding matters referred to the Council for review.

11. Professor Alex Cohen AO, MD, FRACP was appointed by the Convener as the Presiding Councillor of the Council for this review. The other members of the Council were:

(i) Dr Tony Ryan a Consultant in Public Health and Adjunct Professor and Honorary Senior Fellow of the Department of Public Health at the University of Western Australia;

(ii) Dr David Joske the Head of the Department of Haematology and Director of Bone Marrow Transplantation at Sir Charles Gairdner Hospital and a Consultant Haematologist from the Western Australia Centre for Pathology and Medical Research "Pathcentre" and Clinical Senior Lecturer of the Department of Medicine at the University of Western Australia; and

(iii) Professor Barry Marshall the Burnett Fellow and Professor of Microbiology at the University of Western Australia and Professor of Research in Internal Medicine of the Independent Research Faculty of the University of Virginia.

THE LEGISLATION

12. The legislative scheme for the making of Statements of Principles is set out in Parts X1A and X1B of the VEA.

13. The functions and powers of the Council must be seen in light of the function and purpose of Statements of Principles in the scheme of the VEA. The significance of Statements of Principles to claims under the VEA for pensions in relation to eligible service is apparent from sections 120A and 120B of the VEA. Section 120 is also of importance.

14. Fundamental to Statements of Principles is the concept of 'sound medical-scientific evidence' which has been defined in section 5AB(2) of the VEA. 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.

15. The functions of the Council are set out in section 196W of the VEA. In this case, the Council was asked (under section 196Y of the VEA) by a person eligible to make a claim for a pension, to review the contents of Statement of Principles No. 153 of 1996 as amended by Instrument No. 7 of 1998 in respect of malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine, being a Statement of Principles determined by the RMA under section 196B(2) of the VEA ('the reasonable hypothesis standard').

16. In conducting its review, the Council must review all (and only) the information that was available to the RMA at the time it determined, amended, or last amended the Statement of Principles.

17. Under section 196W of the VEA, the Council can only reach the view that a Statement of Principles should be amended on the basis of sound medical-scientific evidence.

BACKGROUND

18. On 9 December 1996, the RMA under subsection 196B(2) of the VEA determined Statement of Principles No. 153 of 1996 in respect of malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine.

19. On 12 December 1996 and 13 December 1996, in accordance with section 196D of the VEA and sections 46A and 48 of the *Acts Interpretation Act 1901* the Statement of Principles was tabled in both the House of Representatives and in the Senate.

20. On 18 December 1996 the making of that instrument was notified in the Gazette (No. 50, p. 3811).

21. On 22 January 1998 Statement of Principles No. 153 of 1996 was amended by the RMA under subsection 196B(8) of the VEA by Instrument No. 7 of 1998. While the

RMA examined the new sound medical-scientific evidence available to it and the sound medical-scientific evidence it had previously considered, Instrument No. 7 of 1998 only expanded the definition of 'malignant neoplasm of the small intestine'. It made no changes to the factors in the Statement of Principles.

22. On 2 March 1998, in accordance with section 196D of the VEA and sections 46A and 48 of the *Acts Interpretation Act 1901* the Statement of Principles was tabled in both the House of Representatives and in the Senate.

23. On 28 January 1998 the making of that instrument was notified in the Gazette (No. 4, p. 369).

24. The RMA received a request to carry out an investigation dated 25 March 1998 pursuant to section 196E of the VEA. The investigation was sought on the basis that there may be an association between exposure in operational service to any or all of helicobactor pylori infection, cimetidine, abdominal irritation from numerous medications, X-rays, barium meals, and nitrosamines in the diet and jejunal adenocarcinoma (malignant neoplasm of the small intestine).

25. On 13 May 1998 the RMA in accordance with section 196G of the VEA notified its intention to carry out a further investigation into malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. The purpose of the investigation was to ascertain whether there was a new body of sound medical-scientific evidence available about how malignant neoplasm of the small intestine may be contracted, or death from malignant neoplasm of the small intestine may occur, or the extent to which malignant neoplasm of the small intestine or death from malignant neoplasm of the small intestine may be due to eligible service.

26. On 14 January 1999, the RMA under subsection 196B(9) of the VEA declared that it did not propose to amend Statement of Principles No. 153 of 1996 as amended by Instrument No. 7 of 1998 in respect of malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine, for the reason that the new body of sound medical-scientific evidence available to it was not sufficient to justify an amendment to the Statements of Principles already determined in respect of malignant neoplasm of the small intestine.

27. On 27 January 1999 the making of that declaration was notified in the Gazette (No. 4, p. 272).

28. An application dated 26 February 1999 for review of Statement of Principles No. 153 of 1996 as amended by Instrument No. 7 of 1998 was received by the Council. Specifically the application was concerned with the decision of the RMA of 14 January 1999 not to add factors to Statement of Principles No. 153 of 1996 as amended by Instrument No. 7 of 1998 in respect of malignant neoplasm of the small intestine and

death from malignant neoplasm of the small intestine in relation to exposure to barium meal x-rays, chronic irritation of the gastrointestinal tract, helicobactor pylori, cimetidine and nitrosamines.

29. The Council held a meeting for the purposes of this review, and heard oral submissions on Friday 12 July 2002.

30. The applicant submitted a number of written submissions and made an oral submission to the Council, complementing the written submissions, at the Council's meeting on 12 July 2002.

31. The Repatriation Commission submitted a written submission. Dr Keith Horsley, representing the Repatriation Commission, made an oral submission to the Council, complementing the written submission, at the Council's meeting on 12 July 2002.

SUBMISSIONS

Applicant's submission

32. The applicant filed a number of written submissions supporting her application to the Council. The Council also took into account the applicant's applications to the RMA of 25 March 1998, 28 June 1998 and 1 September 1998 with attachments, and previous submissions dated 2 November 1996 with attachments and 18 November 1996.

33. The application to the Council comprised 15 attachments. The material in 7 of these had been available to (ie before) the RMA. There was also considerable material relating to the particular circumstances of the applicant's late husband's illness and death. The applicant relied upon various articles and other materials from the information available to the RMA which she contended supported her submissions. The materials upon which the applicant relied which were before the RMA are set out in Annexure B. The materials upon which the applicant relied which were not before the RMA, are set out in Annexure C**.**

34. The applicant's late husband died of jejunal adenocarcinoma. The applicant submitted that a number of factors contributed to the causation of this cancer, and accordingly should be included in the Statement of Principles in respect of malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. The factors which the applicant contended should be included in the Statement of Principles were exposure to:

(i) barium meal x-rays;

(ii) peptic ulceration;

(iii) helicobacter pylori infection;

(iv) cimetidine and abdominal irritation from numerous medications; and

(v) nitrosamines in the service diet.

35. The applicant in her written application contended that it had been:

> proven absolutely that barium x-rays and in fact all x-rays can be inducive of cancer 5, 10, 15, 20, 50 years later.

36. She also contended that:

> it is a well-known medical fact that irritation anywhere along the intestinal canal from mouth to rectum may set up chronic inflammation inducing of cancer.

37. The applicant submitted that all her husband's gastrointestinal problems could be traced back to the service ration diet. She provided anecdotal evidence that her husband said he returned from service with, as he called it 'pains in the guts', and that he would not eat tinned food thereafter. The applicant contended that nitrosamines are carcinogens, and once they are in the body, they multiply and destroy healthy cells.

38. In her written submissions, the applicant conceded that the particular type of cancer from which her husband had died was rare. She conceded there was no information to prove her thesis. On the other hand, she contended there was no proof that the factors for which she argued were not causative of this particular type of cancer.

39. She sought to draw an analogy with Crohn's disease and Coeliac disease, stating that both conditions were acknowledged by the RMA to be diseases of unknown aetiology, but were nevertheless accepted as factors within Statements of Principles. Her submission was essentially that malignant neoplasm of the small intestine was a condition the aetiology of which is similarly obscure, and which may well be caused by one or more of the factors which she contended should be included in the Statement of Principles.

Repatriation Commission's submission

40. The Repatriation Commission's written submission was prepared by Dr Bev Grehan. The oral submission complementing the written submission was made on behalf of the Repatriation Commission by Dr Keith Horsley, due to Dr Grehan's unavailability to attend the Council's hearing.

41. The Repatriation Commission noted that the issue before the Council concerned a very rare tumour, about which it said there was 'a tremendous paucity of evidence'. The Commission pointed out that in determining the Statements of Principles in respect of malignant neoplasm of the small intestine, the RMA had considered and dismissed the possibility of an association with radiation, duodenal ulcer, helicobacter pylori and cimetidine. A summary of the Commission's submissions addressing each factor contended for by the applicant is set out below.

Ionising Radiation from Barium Meal X-Rays

42. The Commission conceded in its oral submission (apparently based upon comments in the text by Mettler and Upton *Medical Effects of Ionising Radiation* (SMRC folder 4, article 36)) that the theory that exposure to ionising radiation led to, or was otherwise associated with, the development of malignant neoplasm of the small intestine, was not entirely without merit.

43. The Commission conceded in its oral submission that there were 'some vague hints of epidemiological support' for the theory. It cited in its written submission as an example of these, Mettler and Upton's reporting of a Danish thorotrast patient series, having a standardised incident ratio of 7.4 (including unity), with a confidence interval encompassing unity of 0.9. Nevertheless, the Commission reiterated its submission that the sound medical-scientific evidence available to the RMA at the relevant times was insufficient to raise a reasonable hypothesis.

44. The Commission assessed the summary of the studies set out in the information that was available to the RMA. In its submission this disclosed that:

> [m]ost radiation epidemiologic studies do not mention small intestine, but those that do have not shown evidence of a consistent radiation-related carcinogenic effect.

45. The Commission also relied upon reports of Committees inquiring into the health effects of ionising radiation, and the effects of atomic radiation (also as reported in Mettler and Upton). It was submitted that in neither case was there evidence of the carcinogenic effect of radiation on the small intestine. Reliance was placed upon studies which demonstrated there had been no excess for malignant neoplasm of the small intestine observed in Japanese atomic bomb survivors, patients treated with radiation for ankylosing spondylitis or other irradiated populations.

46. The Commission concluded its written submission on this point by submitting that:

> no quantifiable risk of radiation carcinogenesis in the small intestine has been demonstrated … the development of malignant neoplasm of the small intestine has not been shown to be causally related to exposure to ionising radiation. In particular, there is

> no medical-scientific evidence to associate exposure to ionising radiation from barium meals and abdominal x-rays with the development of malignant neoplasm of the small intestine.

Peptic ulceration

47. The Commission submitted there were three relevant studies, in which only a non-significant number of these documented chronic duodenal or gastric ulcer, and in none of which was reported a statistical correlation approaching validity.

48. With respect to the 1994 study by Chen *et al* (SMRC folder 3, article 44) the Commission submitted that:

(a) there were no controls;

(b) the location of the cancer site in relation to the peptic ulcer site was unspecified, and particularly, it was unclear whether the peptic ulcer disease involved the duodenum or the stomach; and

(c) there was no information as to latency.

49. The earliest study referred to by the Commission was a 1966 case series review of cancer of the duodenum (Fawcett, SMRC folder 4, article 38). The Commission submitted that it related to a duodenal cancer developing in a patient with two duodenal ulcers, with the adenocarcinoma rising in the more distal ulcer in the first part of the duodenum. The extensive fibrosis of the ulcer base and fibrinoid necrosis in the ulcer floors were characteristic of chronic peptic ulcer.

50. The third study referred to by the Commission was a 1972 case series of 32 duodenal malignancies (Cortese and Cornell, SMRC folder 4, article 16), in which duodenal ulcer was associated with malignancy in 2 of the 32 patients studied. The Commission submitted that no further information was provided, and that it was not apparent whether the malignancy developed in the ulcer or not.

51. The Commission submitted that very little evidence was available to the RMA, and that what little was available did not point to the requisite association between peptic ulceration and malignant neoplasm of the small intestine. It was submitted that:

> there [was] no evidence in the worldwide literature of an association between past history of duodenal ulcer and adenocarcinoma of the jejunum.

Helicobacter pylori/cimetidine

52. The Commission submitted there was no evidence in the literature suggesting an association between either helicobacter pylori or cimetidine and the development of malignant neoplasm of the small intestine.

Nitrosamines

53. The Commission did not separately address the Council on nitrosamines as a possible aetiological factor in the development of malignant neoplasm of the small intestine.

54. In conclusion, the Commission submitted that the sound medical-scientific evidence available to the RMA at the relevant times for any of the factors contended for by the applicant was insufficient to justify any amendment of the Statement of Principles. When applied to this rare tumour, the Commission submitted the sound medical-scientific evidence available to the RMA at the relevant times was insufficient for conclusions to be drawn as to what are the possible epidemiological factors associated with the development of the tumour.

55. The Commission agreed with the applicant that malignant neoplasm of the small intestine is a rare disease. By comparison, the risk factors contended for by the applicant commonly occur. In the Commission's submission, there was a lack of epidemiological evidence indicating an association between any of the contended factors and malignant neoplasm of the small intestine.

REASONS FOR THE COUNCIL'S DECISION

Pool of information and scope of the review

56. Having reviewed all the information available to (before) the RMA at the time it determined, amended or last amended the Statement of Principles, the Council was of the view that there was no article which was so methodologically flawed that for that or any other reason, it should be excluded from the pool of information. Accordingly, the Council had regard to all the information that was available to the RMA at the time it determined, amended or last amended the Statement of Principles. The Council accepted that all the information in the pool met the definition in section 5AB(2), and was thus sound medical-scientific evidence for the purposes of the VEA.

57. The applicant had submitted to the RMA, and in turn to the Council, a videotape of a programme produced by the BBC, which argued in support of the theory that ionising radiation from diagnostic and therapeutic x-ray and suchlike predisposed to cancer. The Council viewed the videotape in its entirety, but did not consider that the videotape comprised sound medical-scientific evidence as defined in section 5AB(2) of the VEA.

58. The Council did not consider that the video would, in accordance with generally accepted medical practice, serve as the basis for the diagnosis and management of medical conditions (including malignant neoplasm of the small intestine), nor that it met

the applicable criteria for assessing causation currently applied in the field of epidemiology, i.e., it would not be regarded by epidemiologists as appropriate to be taken into account in deciding issues of causation.

59. Even if the Council had considered that the videotape did comprise sound medical-scientific evidence, the Council's conclusions as set out below would have been the same, as the Council accepted the underlying thesis of the programme - ie that any radiation could predispose to cancer.

60. After reviewing all the information, the Council decided to confine its attention to the factors contended for by the applicant. The Council's task was therefore to ascertain whether the sound medical-scientific evidence available to the RMA at the relevant times pointed to whether exposure to:

(i) ionising radiation from barium meal x-rays;

(ii) peptic ulcer;

(iii) helicobacter pylori;

(iv) cimetidine; or

(v) nitrosamines

(if found to exist in a particular case) could provide a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine.

61. Specifically, the Council's task was to determine whether the sound medical-scientific evidence in the pool of information pointed to, as opposed to (merely) leaving open, the relevant possibility (ie whether exposure to any of the various factors contended for (as set out in paragraph 60 above) could constitute a link or element in a reasonable hypothesis connecting malignant neoplasm of the small intestine to operational service). The Council must find that the hypothesis contended for was reasonable, and not one which was too tenuous or remote. It was with that test firmly at the forefront of its collective mind that the Council considered the pool of information and the submissions made by the applicant and Repatriation Commission referable to each of the factors contended for by the applicant. The Council's analysis is set out below under each of the nominated factors.

The Council's Analysis of 'the Information'

Ionising Radiation from Barium Meal X-rays

62. The primary material relied upon by the applicant in support of her contention that exposure to ionising radiation from barium meal x-rays was causative of malignant

neoplasm of the small intestine, was the BBC video referred to above. As mentioned above, the Council did not consider the video constituted sound medical-scientific evidence. Nevertheless, the fundamental premise advanced in the video (that any radiation could predispose to cancer) was accepted by the Council.

63. The Council noted, however, that all individuals have exposure to radiation every day. Studies into the purported link between radiation and cancer focus upon those people who have had exposure to atomic radiation or radiotherapy. These are respectively thousands and hundreds of times more than average dosages in x-rays generally, barium meal x-rays in particular, or other every-day exposure.

64. Notwithstanding there were references in the pool of information which touched on the issue, the Council considered that the evidence did not point to exposure to radiation or barium meal x-rays as being a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine. It noted that in cases studying atomic bomb survivors, the population figures for colon cancer were only 10%, in a situation where exposure to radiation was totally excessive. Further, radiation levels in Denver Colorado were twice as high as those to which people were exposed in New York City, and yet the cancer rate is less in Denver.

65. After reviewing the pool of information and taking into account the submissions made by the applicant and the Repatriation Commission, the Council agreed with the broad contention that any radiation in a sufficiently high dosage could predispose to cancer in the human body. The Council concluded that barium meal examination was not a case where the radiation exposure was in a sufficiently high dosage to constitute a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine.

66. The Council reached this conclusion, notwithstanding the comment in the text by Mettler and Upton (referred to above) that the small intestine is extremely sensitive to ionising radiation.

67. The Council was very conscious that the Mettler and Upton text is a secondary source, in which the authors review articles. The primary sources (ie the articles) were not before the RMA at the relevant times, and so not in the pool of information. The Council noted Mettler and Upton's statement that most radiation epidemiologic studies do not mention small intestine, and that those that do have not shown evidence of a consistent radiation-related carcinogenic effect (see the Repatriation Commission's submission and paragraph 44 above). While the Council considered that this seemed to imply that there may be some studies concerning small intestine which did show a radiation-related carcinogenic effect, in the absence of the primary sources, the Council was unable to form any view as to whether such studies pointed to (as opposed to merely leaving open) the relevant association.

68. The Council concluded that for low levels of radiation what evidence there was in the pool of information which touched on the issue did not point to the relevant association ie that it could be a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. In the Council's view, it merely left open the possibility, and did not reach the level of satisfaction of a reasonable hypothesis.

Peptic ulceration

69. The Council considered it very important to remain cognisant of the fact that the jejunum is quite separate and distinct from the duodenum in distance, and that the proximal gastrointestinal tract has within its lumen, three different types of epithelium. It is inappropriate to generalise across the different sectors of the gastrointestinal tract.

70. It was noted that the literature contains very few references to the development of neoplasm in a duodenal ulcer. The 1966 study by Fawcett referred to by the Repatriation Commission is one such study. Strict criteria have been developed in order to ascertain whether the malignancy is truly situated in an area of the ulcer. In order to establish whether the tumour originates from (was caused by) the ulcer, previous duodenal ulceration must have been documented. Further, the cancer should be 'present only at the edge of the ulcer and absent from its base' (see Fawcett at page 47).

71. None of the factors relevant to the development of neoplasm in a duodenal ulcer, in the Council's view, apply to the jejunum. The Council was of the view that the issue of stomach difficulties and the development of small bowel tumour were separate. The Council refuted the suggestion that the gastrointestinal tract was a unified continuum, such that disturbances in the gastroduodenal area could impact causally upon other portions of the gastrointestinal tract.

72. Of the studies referred to by the Repatriation Commission referable to this factor for which the applicant contended, only one study (Chen *et al*) dealt specifically with small intestinal cancer (the other studies relating to cancer of the duodenum). The Council considered the study was unsatisfactory (although not so methodologically flawed that it should be excluded from consideration) given the non-specificity of the groupings and the other deficiencies identified by the Repatriation Commission as noted in paragraph 48 above. This aside, the study found no correlation of statistical significance.

73. There was material in the pool of information which touched on the possibility of an association between peptic ulceration and malignant neoplasm of the small intestine. However, the Council's view was that that material did not point to the relevant association ie that peptic ulceration could be a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. The primary study was unsatisfactory,

and the evidence did not reach the required level of satisfaction of a reasonable hypothesis.

Helicobactor Pylori

74. Helicobacter pylori occur in the stomach, and consequent ulceration occurs in the duodenum. The jejunum is at least 10 cm below this affected area, and as mentioned above, is a separate element of the gastrointestinal tract.

75. Further, helicobacter pylori only affect the types of epithelium present in the stomach and upper parts of the duodenum. The bacteria does not cause difficulty in the small intestine or further down unless for some reason some type of stomach tissue is present. The bacteria do not occur in the jejunal mucosa.

76. Malignant neoplasm of the small intestine is very rare, yet a very significant proportion of the population is infected by helicobacter pylori. Further, there is an established lack of contiguity between the gastric mucosa (which is susceptible to infection with helicobacter pylori), and the jejunal mucosa (which is not susceptible).

77. The Council identified one article in the pool of information which touched on the issue of an association between helicobacter pylori infection and gastric carcinoma (stomach cancer) (see Gasbarrini *et al*, SMRC folder 4 article 12). That article, however, did not posit any potential association between exposure to helicobacter pylori infection and malignant neoplasm of the small intestine. As mentioned above, helicobacter pylori do not occur in the jejunal mucosa.

78. Accordingly, the Council's view was that the material did not point to the relevant association ie that helicobacter pylori could be a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine.

Cimetidine

79. The applicant contended that medications had upset her late husband, and so argued there was a connection between such medication, particularly cimetidine, and the development of malignant neoplasm of the small intestine. The applicant referred to some studies located in her literature search, in which she said cimetidine was given to healthy patients and caused bacterial overgrowth in the jejunal fluid. She reasoned that cimetidine would have an even more deleterious effect upon persons with a pre-existing chronic gastric irritation.

80. The Council is aware that some concern was expressed about cimetidine in the 1980s. There was a theoretical concern that carcinogens may develop in a person with low acid, and there was a concern that cimetidine could cause nitrosocimetidine. The Council noted, however, that cimetidine was a drug extensively used particularly in the

period from 1979 to 1983, and continually used to date. Literally millions of people took it, and no increased incidence of cancers has been identified. Reports on the posited association have progressively declined.

81. In her written submission to the Council seeking review of the RMA's decision not to include in the relevant Statement of Principles cimetidine as a possible link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine the applicant submitted that, 'US research [had] shown that cimetidine contains potentially dangerous carcinogens'.

82. The Council considered there were two primary references in the pool of information which touched on the issue. The first was an extract of an article by Shindo K, *et al* in the *Journal of Investigative Medicine* 44(8): 462-9, 1996 October (SMRC folder 3, article 17, Citation 22), in which the authors claimed that:

> [h]ealthy volunteers who received cimetidine showed an increased deconjugation of bile acid caused by overgrowth of bacteria in the jejunum, which can deconjugate bile acids.

No further conclusions were drawn by the authors.

83. The Council noted the (contrary) findings set out in an extract of an article by Johnson *et al* in the journal, *Comment in Epidemiology* 7(4): 434 – 6, 1996 July (SMRC folder 3, article 17, Citation 26). This article recorded the findings of an in-depth study as:

> [t]he data provided substantial evidence that long-term H2 antagonist use is not associated with gastric cancer.

84. The Council did not consider it was able to form a view as to which article should be accorded more weight. Both references were only extracts. The full articles were not included in the information before the RMA (and so not in the pool of information considered by the Council).

85. Without the complete articles, the Council was unable to assess whether there were any methodological or other deficiencies with the way in which the studies had been conducted. Significantly too, given the absence of the complete articles from the information which was before the RMA at the relevant times (and so from the pool of information) the Council was unable to draw any conclusion as to whether there was any data in the Shindo article which pointed to (as opposed to merely leaving open) the possibility of an association. Moreover, the extract of the Johnson article was consistent with the Council's view that bacterial overgrowth in the small intestine was not linked with acid treatments.

86. Accordingly, while there was some material in the pool of information which touched on the issue, the Council was of the view that in its abstracted state, it did no

more than leave open the possibility of an association. The unsatisfactory and incomplete state of the sound medical-scientific evidence in the pool did not reach the required level of satisfaction of a reasonable hypothesis.

Nitrosamines

87. The Council noted that the applicant in her submission to the RMA dated 25 March 1998, had nominated nitrosamines as the primary factor which she contended should be included in the Statement of Principles. She submitted that nitrosamines in service rations have been accepted as cancer-related agents in some individual cases before the Administrative Appeals Tribunal.

88. Notwithstanding exposure to nitrosamines was contended for by the applicant in her submission to the RMA as a potential factor to be included in the Statement of Principles, the RMA's Reasons for its decision do not discuss why it rejected exposure to nitrosamines as a possible link or element in a reasonable hypothesis connecting malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine to operational service.

89. The Council when reviewing the pool of information noted several references which touched on the issue, containing material both in favour of, and against, the possibility of an association. Set out below are relevant extracts identified by the Council in its analysis of the articles which touched on the possibility of an association. Notwithstanding the extracts are set out as the 'cases' for and against the possibility, the Council considered the matter holistically, in determining whether the sound medical-scientific evidence pointed to, as opposed to merely left open, the possibility.

The ' case' in favour of the possibility:

- Neugut A I and Santos J in their 1993 article 'The Association between Cancers of the Small and Large Bowel' in *Cancer Epidemiology, Biomarkers and Prevention,* 2: 551 – 553, 1993 December (SMRC folder 4, article 14) discerned a statistically valid relationship between cancers of the small and large bowel, concluding with the statement at page 553:

  > [t]his study found an association between colorectal cancer and adenocarcinoma of the small bowel, confirming other parallels between the two malignancies and suggesting that future aetiological research into adenocarcinoma of the small bowel should focus on risk factors associated with colorectal cancer.

- Neugut *et al* in 'The Epidemiology of Cancer of the Small Bowel' *Cancer Epidemiology, Biomarkers and Prevention* 7(3): 243 – 251, 1998 March (SMRC folder 4, article 13) observed that:

> the risk factors for small bowel cancer include dietary factors similar to those implicated in large bowel cancer, cigarette smoking, alcohol intake, and other medical conditions…

They cited with approval the findings of Chow *et al* (see below) that diet is a cause of cancer in the small intestine, and that there is a statistically significant relationship between the intake of red meat and salt cured/smoked foods and cancer of the small intestine.

- Chow, W H *et al* in their 1993 article 'Risk Factors for Small Intestine Cancer' *Cancer Causes and Control* 4:163 (SMRC folder, 3 article 43) suggested that there were potential dietary risk factors for small intestine cancers, which included frequent consumption of red meat and salt cured/smoked foods.

  They noted salt cured/smoked foods have also been related to stomach cancer, and red meat to colon cancer. They concluded that dietary risk factors associated with small intestine cancer are similar to those seen with colon cancer (meat intake) and stomach cancer (salt-cured and smoked foods), suggesting overlapping etiologic mechanisms (at page 167).

- Wu, AH, Yu, MC and Mack, TM in 'Smoking, Alcohol Use, Dietary Factors and Risk of Small Intestine Adenocarcinoma' in *International Journal of Cancer* 70: 512 – 517, 1997 (SMRC folder 4, article 15) found a 4.5 fold increase in adenocarcinoma of the small intestine in male subjects having a combined intake of fried bacon and ham, barbecued and/or smoked meat and smoked fish.

- Stephen S Hecht in *Approaches to Cancer Prevention Based on an Understanding of N-Nitrosamines Carcinogenesis* (SMRC folder 4, article 10) described the generalised capacity of nitrosamines to act as cancer producing agents, in particular through dietary exposure.

  It is stated that nitrosamines frequently induce tumours at specific sites independent of the route of administration, and that some nitrosamines are extremely powerful carcinogens, inducing tumours at very low doses.

  It is also suggested that nitrosamines exposure can occur, not only in the diet, but in certain occupational settings (the rubber, metal and leather industries), and through the use of tobacco products, pharmaceutical products and agricultural chemicals. It is suggested that exposure to volatile and tobacco-specific nitrosamines is at least 10 times greater through inhalation of cigarette smoke than by dietary exposure or by contact with other products.

The 'case' against the possibility:

- Neugut & Santos in their article 'The Association Between Cancers of the Small and Large Bowel' supra at pages 552 and 553 conclude:

> While the data available in this study were not able to explore familial relationships, future studies could and should explore whether these two malignancies [cancer of the large and small intestine] occur in the same families…
>
> Given the large number of relative risks calculated in this study, **this may represent a chance association** … future etiological research into adenocarcinoma of the small bowel should focus on risk factors associated with colorectal cancer … **These associations require further research and confirmation** (emphases added).

- Neuget *et al* in: 'The Epidemiology of Cancer of the Small Bowel' supra noted as follows:

> Wu *at al* also found **suggestions** of an association with fried, smoked, or barbecued meat and fish, but none was statistically significant … (at page 247).
>
> The associations of medical history and biological factors with small bowel cancer **suggest** that this condition may have a familial basis, but no studies of familial small bowel cancer … have been published (at page 249).
>
> Analysis of small bowel cancer overall may be **suggestive**, but we must ultimately undertake subtype-specific studies of both the descriptive and the analytic epidemiology of small bowel cancer (at page 249).
>
> Well-designed case-control studies with adequate power, obtaining data directly from living cases and controls, would be most helpful … (at page 247 emphases added).

- Chow *et al* in their article, 'Risk Factors for Small Intestine Cancer', supra frankly acknowledge the shortcomings of their study (and the consequent doubt cast upon the veracity of the suggested association).

They concede that death from cancer of the small intestine may have been unreported on death certificates, and that the broad categories of food groups and frequency of intake used, may have limited their ability to examine putative associations.

Further, they concede that next of kin informants may have limited knowledge about the deceased subject's exposure history, and that their ability to detect an association with alcohol and smoking may have been limited because those exposures are generally overrepresented in dead controls.

They note:

> [t]he lack of a linear dose-response with frequency of red meat and salt-cured/smoked foods intake **raises uncertainty about an etiologic relationship** (emphasis added, at page 167);

and conclude:

> [t]he dietary risk factors associated with small intestine cancer are similar to those seen with colon cancer (meat intake) and stomach cancer (salt-cured and smoked foods), **suggesting** overlapping etiologic mechanisms. **Future studies are needed** using different study designs, and more direct and detailed exposure information (at page 167, emphases added).

- Wu *et al* in their article 'Smoking, Alcohol Use, Dietary Factors and Risk of Small Intestine Adenocarcinoma' supra, were stringently critical of the methodologies (and so the suggested association) identified by Chow *et al*. They were particularly critical of the controls used by Chow, who were hospital patients, or deceased subjects whose cause of death was deemed unrelated to tobacco or alcohol (which as noted above, were conceded by Chow to be problematic).

  They note:

  > [t]here is **some suggestion** of an increased risk of small intestinal adenocarcinoma in relation to frequent intake of foods rich in heterocyche amines (based on intake of fried bacon/ham, barbecued or smoked meat and smoked fish) at page 516;

  and conclude:

  > [a]lthough cigarette smoking and high intake of foods rich in heterocyche amines were implicated as risk factors in men, they were not associated with risk in women. However, the number of cases is limited, and larger studies are needed to confirm and investigate these **potential risk factors** further. In particular, better assessment of sugar intake from beverages and foods will be needed to characterise the **suggested association (**at page 517, emphases added).

90. The Council's task in assessing the conflicting material (the 'cases' for and against the possibility) was a difficult one. Whilst there are comments in the articles extracted above which could potentially point to the possibility of an association, the Council noted that the authors of the articles themselves stated that their findings were only **suggestive** of association, and in some cases were probably the result of chance.

91. The authors themselves (apart from Hecht) acknowledged the limited number of studies, and identified a number of scientifically significant deficiencies with the studies that had been done. They all recognised the need for further research. Whilst Hecht did not place a caveat upon his research, the Council noted that his findings were in the nature of assertions, and were not supported by evidence. Further, the Council noted that the article made no specific mention of cancer of the small intestine (dealing rather with cancers of the oesophagus, oral cavity, stomach, aerodigestive tract and naso-pharynx).

92. The Council had particular concerns with the acknowledged deficiencies in the studies, and the premise that the large and small intestine should be treated synonymously when considering the impact of exposure to nitrosamines. The Council agreed with the view expressed by the authors (of the papers which touch on the possibility of an association) that further aetiological research is essential.

93. While the matter is not entirely free from doubt, the Council concluded that the 'case' for the possibility did not reach the requisite level of satisfaction, i.e. that of a reasonable hypothesis. The Council concluded that the articles did not point to, but merely left open the possibility of an association. As is clear from paragraph 89 above, the learned authors of the various potentially positive studies themselves characterised their findings as being **suggestive** of an association (i.e. (merely) leaving open the possibility). In the Council's view this did not reach the required level of satisfaction, ie that there is sound medical-scientific evidence pointing to exposure to nitrosamines as a link or element in a reasonable hypothesis connecting malignant neoplasm of the small intestine to operational service.

94. The Council was strongly of the view that the matter warrants investigation by the RMA i.e. to find out if there is sound medical-evidence indicating that exposure to nitrosamines is a link or element in a reasonable hypothesis connecting malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine with operational service.

95. Accordingly, the Council recommends that the RMA conduct an investigation to find out if there is new information available about how malignant neoplasm of the small intestine may be contracted, or death from malignant neoplasm of the small intestine occur, and the extent to which malignant neoplasm of the small intestine or death from malignant neoplasm of the small intestine may be war caused or defence caused.

96. In particular, the investigation should find out if there is sound medical-scientific evidence that indicates that exposure to nitrosamines is a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. An investigation would need to take into account the information which was available to the RMA at the time it determined, amended, or last amended the Statement of Principles (including the references discussed in paragraph 89 above), together with any new body of sound medical-scientific evidence disclosed by the investigation.

COUNCIL'S CONCLUSIONS

97. For the reasons set out above in its analysis of the various submissions, the Council concluded as follows, with respect to each factor for the inclusion of which the applicant contended.

Ionising Radiation from Barium Meal X-rays

98. The Council accepted the fundamental premise that any radiation could predispose to cancer. However, the Council considered that the sound medical-scientific evidence available to the RMA at the relevant times was insufficient to justify an amendment of the Statement of Principles to include exposure to ionising radiation from barium meal x-rays as a factor. The Council considered it was not a reasonable hypothesis that the low dosage of radiation in diagnostic and therapeutic barium meal x-rays may cause cancer of the jejunum, in circumstances where studies of grossly irradiated populations did not indicate a possible link.

Peptic ulcer

99. The Council considered it necessary to repeatedly separate the small intestine from the rest of the gastrointestinal tract in general, and the duodenum from the jejunum in particular, in considering whether peptic ulcer could provide a possible link or element in a reasonable hypothesis connecting operational service with malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. The small intestine is a separate part of the gastrointestinal tract, and subject to different considerations in assessing associations in the development of malignant neoplasm. In the Council's view the sound medical-scientific evidence available to the RMA at the relevant times was insufficient to point to this as a reasonable hypothesis.

Helicobacter pylori

100. The Council's clear view was that helicobacter pylori infection affects only the gastric tissue of the stomach, and does not occur in jejunal mucosa. Accordingly, the Council considered the sound medical-scientific evidence available to the RMA at the

relevant times was insufficient to justify an amendment of the Statement of Principles by including as a factor exposure to helicobacter pylori as a possible link or element in a reasonable hypothesis connecting malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine with operational service.

Cimetidine

101. The Council considered the sound medical-scientific evidence available to the RMA at the relevant times was insufficient to justify an amendment of the Statement of Principles by including exposure to the drug cimetidine (alone or in common with other medications) as a link or element in a reasonable hypothesis connecting operational service with malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. The Council noted the possibility was too tenuous and too remote; millions of people had taken the drug since 1979, without any correlative increase in cancers being observed.

Nitrosamines

102. The Council considered the sound medical-scientific evidence available to the RMA at the relevant times was insufficient to justify an amendment of the Statement of Principles by including as a factor exposure to nitrosamines as a link or element in a reasonable hypothesis connecting operational service with malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine.

103. Nevertheless, (and bearing in mind that the RMA's Reasons for Decision do not articulate why it rejected exposure to nitrosamines as a factor), the Council strongly recommends that the RMA should undertake an investigation of this issue, i.e., to find out if there is sound medical-scientific evidence which indicates that exposure to nitrosamines is a link or element in a reasonable hypothesis connecting malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine with operational service.

104. The issue warrants investigation by the RMA, taking into account not only the sound medical-scientific evidence available to it at the time it determined, amended, or last amended the Statement of Principles, but any new body of sound medical-scientific evidence disclosed by the investigation.

Other submission

105. The Council noted the applicant's 'argument from analogy' that Crohn's disease and Coeliac disease are diseases of unknown aetiology, and yet appear as factors in Statements of Principles. By extension, she submitted that the factors for which she contended should be included in the Statement of Principles in respect of malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine

even though the aetiology of that disease was unknown. However, the Council must itself be satisfied that the sound medical-scientific evidence available to the RMA at the relevant times was sufficient to justify an amendment of the Statement of Principles in respect of malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine.

106. The Council must be satisfied there was (sufficient) sound medical-scientific evidence which pointed to the factor or factors contended for (if found to exist in a particular case) providing a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine. For the reasons discussed above the Council was not so satisfied, although it considers the sound medical-scientific evidence touching on exposure to nitrosamines as a possible link or element warrants investigation by the RMA.

DECISION AND RECOMMENDATION

107. For the reasons discussed above, the Council was unanimous in its decision that at the time the RMA determined, amended or last amended Statement of Principles No. 153 of 1996 as amended by Instrument No. 7 of 1998, the sound medical-scientific evidence available to the RMA at the relevant times was insufficient to justify:

(a) an amendment of that Statement of Principles by including as a factor or factors exposure to:

  (i) barium meal x-rays;

  (ii) peptic ulceration;

  (iii) helicobacter pylori infection;

  (iv) cimetidine and abdominal irritation from numerous medications; and

  (v) exposure to nitrosamines; and

(b) any other amendment of that Statement of Principles.

108. However, the Council recommends that the RMA carry out an investigation to find out if there is new information available about:

(a) how malignant neoplasm of the small intestine may be contracted, or death from malignant neoplasm of the small intestine occur; and

(b) the extent to which malignant neoplasm of the small intestine or death from malignant neoplasm of the small intestine may be war caused or defence caused

and in particular, to find out if there is sound medical-scientific evidence that indicates that exposure to nitrosamines is a link or element in a reasonable hypothesis connecting operational service to malignant neoplasm of the small intestine and death from malignant neoplasm of the small intestine.

109. Given its conclusions as set out in paragraphs 107 and 108 above, the Council made the Declaration dated and sealed the day of 2003 notified in the Gazette pursuant to section 196X of the VEA (No. page).

EVIDENCE BEFORE THE COUNCIL

110. Information considered by the Council (being information which was available to the RMA and sent to the Council by the RMA in accordance with section 106K of the VEA) was as is listed in Appendix A.

111. As mentioned above, the materials upon which the applicant relied (which were available to the RMA and sent to the Council by the RMA in accordance with section 106K of the VEA) were as is listed in Appendix B.

112. The materials upon which the applicant relied (which were not available to the RMA) were as is listed in Appendix C.

Appendix A

SMRC Folder No	Title No.	Title
1	1	Sindelar WF (unknown). Cancer of the Small Intestine. Chapter 20 of unknown publication, pp 616-643.
3	1	Viamonte M and Viamonte M (1992). Primary squamous-cell carcinoma of the small bowel: report of a case. Dis Colon Rectum, Vol 35, pp 806-809.
3	2	Gilson TP and Sollenberger (1992). Adenocarcinoma of an ileostomy in a patient with familial adenomatous polyposis: report of a case. Dis Colon Rectum, Vol 35, pp 261-265.
3	3	Chiaramonte C and Glick SN (1994). Nodular lymphoid hyperplasia of the small bowel complicated by jejunal lymphoma in a patient with common variable immune deficiency syndrome. AJR, Vol 163, pp 1118-1119.
3	4	Vandelli A, Cariani G and Fontana G (1991). Adenocarcinoma of the duodenal stump. Gastrointestinal Endoscopy, 37(3), p 406.
3	5	Siraganian PA, Miller RW and Swender PT (1987). Cystic fibrosis and ileal carcinoma. Lancet, Vol 2 (8568), p 1158.
3	6	Falk GL, Young CJ and Parer J (1991). Adenocarcinoma arising in a duodenal duplication cyst: a case report. Aust NZ J Surg, Vol 61, pp 551-553.
3	7	Sheridan R, Garland D, Pilar J and Pollard W (1989). AIDS-related small bowel lymphoma presenting with perforation. Military Medicine, Vol 154, pp 381-382.
3	8	Hanid MA, Suleiman M, Haleem A, Al Karawi M and Al Khader A (1989). Gastrointestinal Kaposi's sarcoma in renal transplant patients. Quarterly J Medicine, New Series 73, No. 272, pp 1143-1149.
3	9	Carter D, Choi H, Otterson M and Telford GL (1988). Primary adenocarcinoma of the ileostomy after colectomy for ulcerative colitis. Digestive Diseases and Sciences, 33 (4), pp 509-512.

3	10	Nanus DM, Kelsen D and Clark DGC (1987). Radiation-induced angiosarcoma. Cancer, 60 (4), pp 777-779.
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3	12	Al-Mondhiry H (1986). Primary lymphomas of the small intestine: East-West contrast. Am J Hematology, Vol 22, pp 89-105.
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3	14	Williamson RC, Welch CE and Malt RA (1983). Adenocarcinoma and lymphoma of the small intestine: distribution and etiologic associations. Ann Surg, 197 (2), pp 172-178.
3	15	Bia MJ and Flye W (1984). Lymphoma and cycosporin [letter](1984). Lancet, Vol 1 (8391), p 1408.
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3	17	Medline Search on 14.10.98; 1995 to December 1998 Week 1 of 20 pages.
3	18	Medline Search on 14.10.98; 1995 to December 1998 Week 1 of 48 pages.
3	19	Medline Search of 5 pages.
3	20	Medline Search of 24 pages.
3	21	Woodward T and Levin B (1995) Cancers of the stomach and duodenum. Gastroenterologist, Vol 3, No 1, pp 14-19.
3	22	Witteman BJM, Janssens AR, Griffioen G and Lamers CBHW (1993) Villous tumours of the duodenum. An analysis of the literature with emphasis on malignant transformation. Netherlands J of Medicine, Vol 42, pp 5-11.
3	23	Weedon DD, Shorter RG, Ilstrup DM, Huizenga KA and

Taylor WF (1973) Crohn's disease and cancer. N Engl J Med, Vol 289, pp 1099-1103.

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3 39 Goedde TA, Rodriguez-Bigas MA, Herrera L, and Petrelli NJ (1992) Gastroduodenal polyps in familial adenomatous polyposis. Surgical Oncology, Vol 1, pp 357-361.

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4	18	Su C-C, Jin Y-T, Chien C-H, Yu C-Y, & Lin P-W. Postirradiation angiosarcoma of the terminal ileum. Chin Med J, Vol. 48, pp. 147-152.
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4 38 Fawcett, AN (1966). Ulcer Cancer of the Duodenum. British Journal of Surgery 53 (1), pp 46-49.

Appendix B

SMRC Folder No	Title No.	Title
1	1	Sindelar WF (unknown). Cancer of the Small Intestine. Chapter 20 of unknown publication, pp 616-643.
1	-	Applicant's letter of 15th December 1997 to the RMA
1	-	Applicant's letter of 2nd November 1996 to the RMA.
1	-	Applicant's letter of 18th November 1996 to the RMA.
1 and 5 and 5	- and 5 and 44	Dr Stephen Fairley's (MB BS FRACP), letter of 16th March 1994.
1 and 5	- and 46	Dr Deran J.R. Hood's, DVA Medical opinion of 22nd September 1993.
1 and 5	- and 45	Surgeon Ross Finemore's, 28th November 1996 Medical opinion.
1	-	'Modern Home Medical Adviser' Revised and Re-edited 1942. Two extracts.
1	-	Suzanne Chazin's, November 1993 "The Doctor Who Wouldn't Accept No" Reader's Digest article.
1	-	Unknown Author, 'What is Cancer'. Undated handout.
1 and 5	- and 43	Dr Morris Towers's, 17th December 1995 article "Kitchen sink killers' are cancer suspects". Review - Sunday Mail.
1 and 5	- and 41	Diana Thorp's, 27th February 1993 "New cancer vaccine to save millions" article. The Weekend Australian.
1	-	12th Edition Harrison's 'Principles of Internal Medicine' pages 1245-1247.

2	-	Applicant's 1st September 1998 letter to the RMA.
2 and 5	- and 17	Part of an undated report from Professor John McCaffrey, Chairman QCF Medical and Scientific Advisory Committee.
2 and 5	- and 39	Page headed "GUT FOUNDATION, Prince of Wales Hospital" on H.Pylori Bacteria.
2 and 5 and 5	- and 22 and 49	Applicant's letter of 28th June 1998 to the RMA and attached 2 page submission of the same date to the RMA.
2	-	Applicant's 25th March 1998 application to the RMA and attached 2 page letter of the same date to the RMA.
3	17	Citation 22; Shindo K. et al; Alteration of bile acid metabolism by cimetidine in healthy humans. Medline Search on 14.10.98; 1995 to December 1998 Week 1 of 20 pages.
3	17	Citation 24; Goenka MK.et al; Candida overgrowth after treatment of duodenal ulcer. A comparison of cimetidine, famotidine, and omprazole. Medline Search on 14.10.98; 1995 to December 1998 Week 1 of 20 pages.
3	18	Citation 7; Neugut AI et al; The epidemiology of cancer of the small bowel. Medline Search on 14.10.98; 1995 to December 1998 Week 1 of 48 pages.
3	21	Woodward T and Levin B (1995) Cancers of the stomach and duodenum. Gastroenterologist Vol 3, No 1, pp 14-19.
3	26	Ross RK, Hartnett NM, Bernstein L and Henderson BE (1991) Epidemiology of adenocarcinomas of the small intestine: is bile a small bowel carcinogen? Br J Cancer Vol 63, pp 143-145.
3	29	Mitchell KJ, Williams ES and Leffall LD (1995) Primary malignant small bowel tumours: an atypical abdominal emergency. J Natl Med Assoc. Vol 87, pp 276-279.

3	31	Mayer RJ (1994) Tumours of the Large and Small Intestine. Harrison's Principles of Internal Medicine 13th Edition. Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS and Kasper DL (Eds) McGraw-Hill New York Chapter 257, pp 1429-1431.
3	33	Lashner B (1992) Risk factors for small bowel cancer in Crohn's disease. Dig Dis Sci Vol 37, pp 1179-1184.
3	43	Chow W-H, Linet MS, McLaughlin JK, Hsing AW, Co Chien HT and Blot WJ (1993) Risk factors for small intestine cancer. Cancer Causes and Control Vol 4, pp. 163-169.
3	44	Chen CC, Neugut AL and Rotterdam H (1994) Risk factors for adenocarcinomas and malignant carcinoids of the small intestine: preliminary findings Cancer epidemiology, biomarkers and prevention. Vol3, pp 205-207.
4	10	Hecht SS. (1997). Approaches to cancer prevention based on an understanding of N-nitrosamine carcinogenesis (44168). Proceedings of the Society for Experimental Biology & Medicine, Vol 216 (2), pp 181-91.
4	13	Neugut AI, Jacobson JS, Suh S, Mukherjee R & Arber N. (1998). The epidemiology of cancer of the small bowel. Cancer Epidemiology, Biomarkers & Prevention, Vol. 7, pp. 243-251.
4	23	Kortbeek J, Kelly JK and Preshaw RM (1992). Carcinoid tumors and inflammatory bowel disease. J Surgical Oncology, Vol 49, pp 122-126.
4	36	Mettler FA & Upton AC. (1995). Medical effects of ionizing radiation (2nd Ed.), WB Saunders Company, Philadelphia. pp. 176-177, 200-201, 246-247, 402, 405.
4	37	"The X-Ray Files" Video [1996 BBC Panorama Programme as replayed by Four Corners].
4	38	Fawcett, AN (1966). Ulcer Cancer of the Duodenum. British Journal of Surgery 53 (1), pp 46-49.

Appendix C

SMRC Folder No	Title No.	Title
5	2	Applicant's letter of 26th June 2002 to the SMRC with attached Summary of applicant's husbands' condition and treatment from 1943 Service to Death in 1995.
5	3	Applicant's submission of 25th June 2002 to the SMRC re: Malignant Neoplasm of the Small Intestine. Addition to submission of 4th April 2002.
5	4	Applicant's note to the SMRC with Greenslopes Military Hospital report 12.5.51 to 16.2.51.
5	5	Applicant's note to the SMRC of 1ST June 2002 with attachments: • Dr Fairley report of 1st June 1993 and Mater Hospital 01/06/1993 Endoscopy report. • Small Bowel Series report of 01/06/1993 • Dr Henry Lau Histology report of 01/06/1993 • Dr Fairley report of 4th June 1993. • Dr Bansi 3rd June 1993 CT Scan – upper abdomen report, with Dr Murphy 04/06/1993 Chest report.
5	6	Surgeon Dr Campbell letter to Dr Fairley, 10th June 1993 reports (2). And Townsville Pathology Laboratory Histology reports – Macroscopic and Microscopic of 8th June 1993.
5	7	Mater Hospital Townsville medical investigation reports of 5 pages (Townsville Pathology Laboratory Report of 10th June 93, Histology report of 16th June 93, Histology Report 10th June 93, Dr AH Murphy report of 25th August 93 and Surgeon AD Campbell report of 1st January 94) concerning applicant's husband.
5	8	Applicant's letter of 13th June 2002 to the SMRC in reference to the further RMA Information, specifically RMA ID 7036 article by Fawcett.
5	9	Applicant's 4th April 2002 Submission to the SMRC (sets out applicant's factors) referenced to the RMA Information and attachment of Surgeon Dr AD Cambell reports (2) to Dr S Fairley both dated 10th June 1993.

5	10	Applicant's 4th April 2002 note to the SMRC with Medical Examination report by Dr John Trace dated 16th September 1992.
5	11	Applicant's 4th April 2002 note to the SMRC with Vetaffairs (March 2002 Edition) advertisement on "Repat Commission studies service diet".
5	12	Applicant's 4th April 2002 note to the SMRC, and Applicant's 9th September 1999 check list for AAT hearing, submissions to the AAT dated 1st November 99.
5 and 43	13 and 43	Applicant's note on a 21st March 99 Sunday Mail newspaper clipping headed "Australia alone on vet cancer" by J. Collins Atomic Ex-Servicemen's Association, Toowoomba.
5	14	Applicant's letter of 16th July 2001 to SMRC.
5	15	Applicant's letter of 16th July 2001 to the SMRC.
5	16	Applicant's 16th July 2001 submission to the SMRC.
5	17	Applicant's 16th July note to the SMRC, with Dr John Trace's letter of 29th June 1997 letter to Gilshenan and Luton.
5	18	Undated transcribed Extract from the Anti-Cancer Society, and 1st June 1993 Small Bowel Series medical report, claimed to be by Dr Kewal Banst (Locum), followed by comments by the Applicant.
5 and 5	19 and 42	Applicant's comments on the 1994 50 yr reunion (14ACS Squadron) information on Service Diet, on a photocopy of a Newspaper clipping headed "BEEF KILLS DIGGERS Landmark ruling on cancer death" by Guy Ker.
5	20	Undated copy of page 229 of "The British Medical Association Complete family Health Encyclopaedia on Cancerphobia – Causes";
5	21	Applicant's Undated note.
5	23	Applicant's letter of 26th February 1999 to the Registrar of the Specialist Medical Review Council.
5	24	Applicant's 26th February 1999 submission headed

		"REASONS FOR REVIEW OF STATEMENT OF PRINCIPLES SOP Code 152 Decision 14.01.99 (November 1996)".
5	25	Applicant's 6th July 01 note to the SMRC on a copy of a page of the RMA's 14/01/99 decision.
5 and 5	26 and 38	26th February 1999 Statement by the Applicant headed "Seeking A Review of an RMA decision regarding SOP Code 152 – Malignant Neoplasm of the Small Intestine".
5	27	Applicant's undated notes and list of 'irritants' with comments to the SMRC.
5	28	Applicant's 20th March 2001 Letter to the SMRC.
5	29	Applicant's 3rd November 2000 Letter to The Registrar SMRC.
5	30	Applicant's 14th July 2000 Letter to "The Minister for Veteran Affairs (Mr Scott)".
5	31	Office of the Minister for Veterans' Affairs Adviser - 6th September 2000 reply.
5	32	Applicant's 26th September 2000 Letter to "The Minister for Veteran Affairs" (Mr Scott).
5	33	Office of the Minister for Veterans' Affairs Adviser - 12th October 2000 reply.
5	34	Copy of Application For Review to the SMRC dated 26th February 1999.
5	35	Applicant's letter to the SMRC of 16th March 2000.
5	36	Applicant's undated note on a photocopy of a Vetaffairs Feb/Mar 1999 article headed "Statement of Principles explained at RMA workshop".
5	37	Applicant's letter of 26th February 1999 to the Registrar of the SMRC.
5	40	Dr Morris Towers's 7th May 1995 article "Should we treat ulcer bug?" from the 'The Sunday Mail'.

5	47	Page 452 Headed "Diagnostic Radiology of Cancer" from an Unknown text referred to by Dr Deran Hood's in the medical opinion of 22nd September 93 (ref: Folder 1, and folder 5, article 46).
5	48	Applicant's note with Dr Trace's (predominantly) 5th February 1992 to 19th May 1993 Medical Treatment record for Applicant's husband.