



Australian Government
Specialist Medical Review Council

Minutes

Review of SoPs concerning chronic multisymptom illness, and Gulf War syndrome

Date: Wednesday, 16 December 2015 – Start Time 10.00 QLD time

Location: 4th Floor, 259 Queen Street, Brisbane

Participants

Presiding Councillor: Associate Professor David Newman (Presiding)

Councillors: Professor Dino Pisaniello
Dr Bradley Ng
Professor Andrew Grulich
Associate Professor John Waterston

Secretariat: Jan Bowman – Registrar
Anthony Fuster

DISCUSSION

1. Welcomes & Introductions
 - A/Professor Newman welcomed participants and outlined the purpose of the meeting.
 2. Purpose of meeting
 - To provide an overview of the function and role of the review council.
 - To consider the application to this review and the scope of the review.
 3. Role of Council
 - An overview for the legal context for the review was provided and the Council was referred to the Members Handbooks.
 - Members confirmed that they understood the function of the Council and the two statutory tests.
 4. Scope of the Review
 - Council agreed to consider the applications and submissions in detail before drafting the scope of the review at the next meeting.
 5. The Information

The 'available' information is that information that was in fact used by the RMA. It does not include information that may have been available for the use of the RMA at the time but was not accessed by the RMA.
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6. New information
'New information' is information the RMA advises was not available to it when it made the decision under review. This may include relevant information published before or after the date that the RMA determined the SoPs under review, including during the time the SMRC undertakes the review.

Jan advised that there is 'new' information identified by the applicant in submissions to the RMA and to the SMRC.

Actions

The Council discussed the selection of the sound medical-scientific evidence relevant to the contended factor. The following actions were agreed.

- a. Of the 38 page list of papers relied on by the parties to the review, councillors will divide their preliminary reading as follows:
- David, pp1-8
 - John, pp 9-15
 - Andrew, pp16-23
 - Bradley, pp 24-31
 - Dino, pp32-38
- b. Of the list of papers attached the Applicant's submission to the RMA, councillors will divide their preliminary reading as follows:
- Dino and Bradley, papers 1-41
 - John and Andrew, papers 42-81

Comments on papers will be discussed at the next meeting.

Jan will advise of any additional 'new' information.

7. The next meeting

Two hour teleconference. Date to be confirmed.

8. The meeting was closed by A/Professor Newman at 15:00. Duration of meeting – 5 hours.

Minute taker: *Jan Bowman*

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Presiding Councillor: *David Newman*



Australian Government
Specialist Medical Review Council

Minutes

Review of SoPs concerning chronic multisymptom illness, and Gulf War syndrome

Date: Wednesday, 3 February 2016 – Start Time 14.00 EST

Location: by teleconference

Participants

Presiding Councillor: Associate Professor David Newman (Presiding)

Councillors: Professor Dino Pisaniello
Dr Bradley Ng
Professor Andrew Grulich
Dr John Waterston

Secretariat: Jan Bowman – Registrar
Anthony Fuster

Medical/Science Writer: Dr Kate Claydon-Platt

DISCUSSION

1. Welcomes & Introductions

- A/Professor Newman welcomed participants and outlined the purpose of the meeting as:
 - Reconfirming the Council's Tasks
 - Settling the Scope of Review
- The Council confirmed the minute of the previous meeting with one minor amendment.

2. Council's Tasks

The Council considered a background paper clarifying its role in determining what constitutes a disease or injury as set out in the legislation.

3. Scope of Review

The Review Council decided that subject to legal advice the scope would be as follows:

The Council has decided that it will have particular regard to whether there was sound medical-scientific evidence (SMSE) on which the Repatriation Medical Authority could have relied to:

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- a. create Statements of Principles for Gulf War Syndrome (SoPs) (or Illness) that would include factors for:
 - environmental hazards such as, depleted uranium, oil well smoke, chemical and biological weapons medical countermeasures (such as pyridostigmine, and vaccinations for anthrax, plague, pertussis), contaminated food and water, pesticides exposure (including DEET)
 - psychological stressors
- b. amend either or both of the SoPs for Chronic Multisymptom Illness in any or all of the following ways:
 - the possible inclusion of a factor or factors as contended, for exposure to environmental hazards such as, depleted uranium, oil well smoke, chemical and biological weapons medical countermeasures (such as pyridostigmine, and vaccinations for anthrax, plague, and pertussis), contaminated food and water, pesticides exposure (including DEET).

There was some question of whether to include clarification in the scope that the Council would not be limited to the listed factors.

Actions:

- Jan to ask Legal Adviser to review the draft scope before the Council writes to the Applicant.
- Draft letter to Applicant to be circulated to Council before being set.

4. Discussion of papers as agreed at the last meeting.

The Council discussed the selection of the SMSE relevant to the contended factor as agreed at the first meeting.

Action: Jan to circulate a list of selected papers.

5. Managing additional new information
 - Jan reminded Councillors that there is additional new information in the Council's Folder in FILEForce for consideration. "List of Binns papers - available and new" in FILEForce – FF ID 31471.

Action: Deferred for future discussion.

6. The next meeting

Council agreed to have a two hour teleconference in March. A decision on the date and location for the oral hearing will be made at the next meeting.

Action: Anthony to send a Doodle Poll to settle meeting date.

7. The meeting was closed by A/Professor Newman at 16:00. Duration of meeting – 2 hours.

Minute taker: *Jan Bowman*

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Presiding Councillor: *David Newman*



Australian Government
Specialist Medical Review Council

Minutes

Review of SoPs concerning chronic multisymptom illness, and Gulf War syndrome

Date: Wednesday, 20 April 2016 – Start Time 14.00 EST

Location: by teleconference

Participants

Presiding Councillor: Associate Professor David Newman (Presiding)

Councillors: Professor Dino Pisaniello
Dr Bradley Ng
Professor Andrew Grulich
Dr John Waterston

Secretariat: Jan Bowman – Registrar
Anthony Fuster

Medical/Science Writer: Dr Kate Claydon-Platt

DISCUSSION

1. Welcomes & Introductions
 - Review progress on the reading of identified papers
 - Discuss grouping papers by factor
 - Agree on approach to analysis
 - Plan for the Oral Hearing
 2. Council's Tasks
 - The Council Reviewed progress on the reading of identified papers.
 3. Structuring its approach to Council's analysis task
 - The Review Council agreed to group papers by factor and using the RMA grading criteria for overall assessments
- Action:**
- Jan and Kate to structure a consolidated excel reading list with drop-down boxes for papers by factor and grade and make available to councillors.

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4. Structuring and drafting the Reasons

Jan outlined the structure of the Reasons document (as provided) and brought members' attention to those aspects that will require Council input.

5. Oral Hearing

- Council agree that the Oral Hearing should be held in Melbourne in late August or early September.

Action: Jan to advise Applicants and look for suitable dates

6. The next meeting

Council agreed to have a two hour teleconference in July.

Action: Jan to send a Doodle Poll to settle meeting date.

7. The meeting was closed by A/Professor Newman at 16:00. Duration of meeting – 2 hours.

Minute taker: *Jan Bowman*

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Presiding Councillor: *David Newman*



Australian Government
Specialist Medical Review Council

Minutes

Review of SoPs concerning chronic multisymptom illness, and Gulf War syndrome

Date: Wednesday, 17 July 2016 – in conjunction with Oral Hearing

Location: Melbourne

Participants

Presiding Councillor: Associate Professor David Newman (Presiding)

Councillors: Professor Dino Pisaniello
Dr Bradley Ng
Professor Andrew Grulich
Dr John Waterston

Secretariat: Jan Bowman – Registrar
Steven Dare

Medical/Science Writer: Dr Kate Claydon-Platt

DISCUSSION

1. Welcomes & Introductions
 - Review progress on the reading of identified papers
 - Discuss grouping papers by factor

2. Council's Tasks
 - The Council Reviewed progress on the reading of identified papers

Secretariat Actions:

- complete the transfer of councillor comments from the spreadsheet into FILEforce.
- Once all available comments are on FILEforce, councillors will check those papers marked “yes” and “maybe” (these papers can then later be grouped by factor and grade).
- circulate the most up-to-date list of new papers provided by Mr Watts in his two submissions to the SMRC (see attached).
- circulate papers provided by Mr Watts at the Oral Hearing:

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- Craddock TJA, Fritsch P, Rice MA Jr, del Rosario RM, Miller DB, Fletcher MA, et al. (2014) A Role for Homeostatic Drive in the Perpetuation of Complex Chronic Illness: Gulf War Illness and Chronic Fatigue Syndrome. PLoS ONE 9(1): e84839. doi:10.1371/journal.pone.0084839 <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0084839>
- Rayhan RU, Stevens BW, Timbol CR, Adewuyi O, Walitt B, VanMeter JW, et al. (2013) Increased Brain White Matter Axial Diffusivity Associated with Fatigue, Pain and Hyperalgesia in Gulf War Illness. PLoS ONE 8(3): e58493. doi:10.1371/journal.pone.0058493 <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0058493>

The other paper contained correspondence between TGA and Defence about the importation of drugs for 'prospective combat zones'.

3. The next meeting

- Next meeting face-to-face in Brisbane, December.

Minute taker: *Jan Bowman*



Presiding Councillor: *David Newman*



Australian Government
Specialist Medical Review Council

Minutes

Review of SoPs concerning chronic multisymptom illness, and Gulf War syndrome

Date: Wednesday, 27 July 2016 – 11.00am – 13.00pm EST (10.30am SA)

Location: Teleconference

Participants

Presiding Councillor: Associate Professor David Newman (Presiding)

Councillors: Professor Dino Pisaniello
Dr Bradley Ng
Professor Andrew Grulich
Dr John Waterston

Secretariat: Jan Bowman – Registrar
Steven Dare

Medical/Science Writer: Dr Kate Claydon-Platt

DISCUSSION

1. Welcomes & Introductions
 - Review progress on the reading of identified papers
 - Discuss grouping papers by factor

2. Council's Tasks
 - The Council Reviewed progress on the reading of identified papers

Secretariat Actions:

- re-circulate the RMA's Levels of Evidence Paper
- add "Multiple Factors" and "Disease Definition" to the Factors dropdown list at column R
- identify the papers in the meta-analysis by Gwini et al 2016
- Councillors to continue to identify papers for further reading
- Kate will organise papers by factor/grade based on Councillor feedback
- Kate to prepare a summary of the history of approaches to disease definition for CMI/GWS for Council consideration

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3. Preparation for Oral Hearing
 - Jan provided an overview of the Oral Hearing process and plans for 17 August meeting
4. The next meeting

Oral Hearing, 17 August in Melbourne

Minute taker: *Jan Bowman*

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Presiding Councillor: *David Newman*



Australian Government
Specialist Medical Review Council

Minutes

Review of SoPs concerning chronic multisymptom illness, and Gulf War syndrome

Date: Tuesday, 6 December 2016

Location: Brisbane

Participants

Presiding Councillor: Associate Professor David Newman (Presiding)

Councillors: Professor Dino Pisaniello
Dr Bradley Ng
Professor Andrew Grulich
Dr John Waterston

Secretariat: Jan Bowman – Registrar

Medical/Science Writer: Dr Kate Claydon-Platt

DISCUSSION

1. Finalising Council's evaluation of the SMSE by Factor:
 - The Council finalised its consideration of the relevant SMSE by factor
2. For GWS - Preliminary decision on Applicants' contentions re GWS:
 - The Council agreed that the literature (SMSE) does not provide sufficient evidence to support separate SOPs for Gulf War Syndrome/Illness
 - Andrew Grulich will draft reasons for this decision for all members to consider, that will include comment on post war syndromes generally
 - The Reasons will acknowledge Gulf War veterans' experiences, but Council considers that the symptoms are not sufficiently distinct from other post-war syndromes to support separate SoPs.
3. For CMI – Preliminary decisions on Applicants' contended new factors:
 - Andrew Grulich to consider the definition of CMI as used in the SoPs against the SMSE
 - Kate has already documented the various definitions for GWS and CMI which is available as a guide
 - Each councillor to draft sections for all members to consider, on a factors basis as listed and provide to Jan and Kate for circulation by 30 March 2017.

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Factor	Decision	Who
Depleted Uranium		David
Oil well Smoke		Dino
Sarin		Dino
pyridostigmine	SMSE does not support a factor – no biological plausibility	John/Bradley
Vaccinations		John/David
Pesticides		Dino/David
Psychological stressors		Bradley
Contaminated food and water	No SMSE	

Secretariat Actions:

- Provide Andrew Grulich with the legislative definition of a ‘disease or illness’ along with the RMA reasons.
- Circulate the updated list of papers from the meeting – ensuring it matches Image silo
- Kate to update and circulate the EndNote library – by factor
- Kate’s to update and circulate summary paper by factor
- Jan to summarise Applicants’ contentions and note the relied on papers specifically referred to in submissions for Councillors’ reference and for inclusion in the Reasons.

4. The next meeting

Council agreed to hold a face-to-face meeting in June 2017.

Action: Jan to send a Doodle Poll to settle meeting date.



Australian Government

Specialist Medical Review Council

MINUTES: SMRC Review - Council Meeting

For: **CMI and GWS**
Date: Thursday 29 June - 09.00 – 16.30
Venue: Lorne Meeting Room, Parkroyal, Melbourne Airport

ATTENDEES: Associate Professor David Newman (Presiding), Professor Dino Pisaniello, Dr Bradley Ng, Professor Andrew Grulich, Dr John Waterston, and Ben Dube (Legal Advisor) Dr Kate Calydon-Platt (medical writer) and Jan Bowman (SMRC Secretariat).

1. Welcomes and Introductions – **David Newman**

2. Legal Questions– **Ben Dube**

- Council has been asked to review two decisions of the RMA which refer to two different sections of the Veterans' Entitlements Act (VEA), it is therefore appropriate to make two separate decisions.
 - That the RMA was not satisfied that GWS/I is a particular kind of disease within the meaning of the VEA ([see VEA s. 5D](#)), and so did not create a SoPs;
 - That the RMA was satisfied that CMI is a particular kind of disease within the meaning of the VEA, and so created SoPs and formulated factors.
- [Section 196W](#) sets out the powers of the SMRC.
- The test of whether GWS/I is a particular kind of disease within the meaning of the VEA is on the Balance of Probabilities, having regard to the Sound Medical Scientific Evidence (SMSE).
- Council can have regard to diagnostic criteria, but the condition in question does not need to meet diagnostic criteria.
- Council needs to arrive at a majority decision. Presiding Councillor has a deliberative vote.
- Council reminded that its decisions need to be in respect to the material available to the RMA.
- There is potential in respect to CMI, to ask the RMA to include a statement that CMI could be contracted through participation in the Gulf War.

3. Draft reasons for GWS - ALL

Discussion	Action	By Whom	By When
Conclusions of Council	<ul style="list-style-type: none"> Insufficient SMSE 		
Wording for Paragraph 1 (declaration)	<ul style="list-style-type: none"> Draft new wording 	Ben	Completed
Overarching summary	<ul style="list-style-type: none"> Draft summary, with any pertinent observations. E.g., about the extent of reported illnesses/ill health in this cohort of veterans; the availability of data on exposures; reliance on self-report; animal studies; proposed biological mechanisms, the extent and quality of papers etc. Explain any issues re reliance on factor analysis 	Andrew	14 July
New information provided by Applicant: apart from Kuehn, those cited in draft reasons not relevant to the question.	<ul style="list-style-type: none"> Retain Kuehn only, and consider the other papers for inclusion in CMI Reasons Include Steele et al in CMI Reasons in reference to PB 	All	Completed
Council Review	<ul style="list-style-type: none"> All members to read decision with care for content, and provide feedback using 'track-changes'. Legal Adviser to review Secretariat to Finalise 	All Ben Jan	28 July

4. Draft reasons for CMI - ALL

Council's Tentative Conclusions on Factors

Factor	Council's Conclusion
Depleted uranium	Insufficient SMSE
Oil well smoke	To be confirmed
Chemical and biological weapons (in Sarin)	To be confirmed
Medical countermeasures (such as pyridostigmine)	Insufficient SMSE
Vaccinations	Insufficient SMSE
Contaminated food and water	To be confirmed
Pesticides Inc. Deet	To be confirmed
Combined Exposures	To be confirmed

Council reminded that its decisions need to be in respect to the symptoms for CMI as described in the SoPs.

Discussion	Action	By Whom	By When
Sarin	<ul style="list-style-type: none"> Separate new papers from discussion 	Jan/Kate	14 July
	<ul style="list-style-type: none"> Dino to review/finalise draft with focus on CMI symptoms Pay particular attention to the Japanese studies 	Dino John W/Dino	21 July
	<ul style="list-style-type: none"> Insert section into Reasons 	Jan/Kate	11 Aug
Pesticides	<ul style="list-style-type: none"> Separate new papers from discussion 	Jan/Kate	14 July
	<ul style="list-style-type: none"> David/Dino to review/finalise draft with focus on CMI symptoms 	David/Dino	21 July
	<ul style="list-style-type: none"> Insert section into Reasons 	Jan/Kate	11 Aug
Oilwell Smoke	<ul style="list-style-type: none"> Separate new papers from discussion 	Jan/Kate	14 July
	<ul style="list-style-type: none"> Dino to review/finalise draft with focus on CMI symptoms 	Dino	21 July
	<ul style="list-style-type: none"> Insert section into Reasons 	Jan/Kate	11 Aug
Combined Exposures	Identify papers on the effects of combined exposures for: <ul style="list-style-type: none"> Sarin and PB, and Organophosphates and PB. 	Kate/Jan	21 July
“	<ul style="list-style-type: none"> Prepare draft on combined exposures for Sarin & PB, and Organophosphates and PB 	Bradley	11 Aug
All other factors and draft Reasons	<ul style="list-style-type: none"> All subject matter experts to review their sections and ensure all relevant OR's and CI's are included for those papers relied on by the Applicant (refer to Comment Boxes) 	All	11 Aug
Available Papers - subject matter experts to ensure all relevant papers have been identified.	All subject matter experts to review their sections and ensure all relevant available SMSE has been reviewed <ul style="list-style-type: none"> Circulate lists to members Members to check lists and advise Jan 	All Jan All	21 July
New Papers - subject matter experts to ensure all relevant new papers have been identified	All subject matter experts to review their sections and ensure all relevant new papers provided by the Applicant have been reviewed:	All	21 July

Discussion	Action	By Whom	By When
	<ul style="list-style-type: none"> • Check new papers included in the draft reasons • Check lists of new papers – Jan to send 		

5. Finalising reasons

Discussion	Action	By Whom	By When
Overarching summary	<ul style="list-style-type: none"> • Draft summary, with any pertinent observations. E.g., about the extent of reported illnesses/ill health in this cohort of veterans; the availability of data on exposures; reliance on self-report; animal studies; about proposed biological mechanisms, the extent and quality of papers etc. 		11 Aug
Council Review	<ul style="list-style-type: none"> • Circulate final Draft • Legal Adviser to review • All members to read decision with care for content, and provide feedback using ‘track-changes’. 	Jan Ben All	18 Aug 25 Aug 25 Aug

6. Other matters - Jan

- **Reasons for Decision:** The SMRC is required to make a declaration and give reasons for its decisions ([see VEA s. 196W](#)). A statement of reasons is intended to explain to an applicant and other relevant parties to a Review how the decision/s were made. Reasons:
 - explain the basis for the Council’s ultimate conclusion(s) by setting out the evidence it considered and how it applied that evidence to the legislative test it was required to apply.
 - provide transparency
 - allows those affected to understand the matters taken into account by the Council; and
 - enables affected persons/organisation to identify grounds of appeal if they decide to exercise their review rights.
- SMRC Declarations are published in the Government Gazette, and the associated Reasons are provided to all parties to a review, and also published on the SMRC website.

7. Next Meeting – 3.00pm, Friday 1 September, by phone.

Minute taker: *Jan Bowman*

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Presiding Councillor: *David Newman*



MINUTES: SMRC Review - Council Meeting

For: **CMI and GWS**
 Date: Friday 1 Sept - 15.00 – 17.30
 Venue: Teleconference

ATTENDEES: Associate Professor David Newman (Presiding), Professor Dino Pisaniello, Dr Bradley Ng, Professor Andrew Grulich, Dr John Waterston, and Dr Kate Calydon-Platt (medical writer) and Jan Bowman (SMRC Secretariat).

1. Welcomes and Introductions – David Newman

2. Draft reasons for GWS – ALL

- Members confirmed their decision of 29 June that there is insufficient SMSE to support new Statements of Principles for Gulf War Syndrome/Illness
- Andrew will:
 - review the comments provided by members in the current draft
 - draft an overarching summary
 - add comments about the existing SoPs for CMI and the use of interchangeable terminology
 - add comments acknowledging the health experiences of Gulf War veterans
 - add one or two paragraphs on ALS (Motor Neurone Disease) – possibly as a footnote.

Timeframe:

- All changes to be provided to the Secretariat by 30 September (sooner if possible) for circulation to full council.

3. Draft reasons for CMI - ALL

- Members confirmed their tentative decisions on the contended factors:

Factor	Council's Conclusion
Depleted uranium	Insufficient SMSE
Oil well smoke	Insufficient SMSE
Chemical and biological weapons (in Sarin)	To be confirmed once summary completed
Medical countermeasures (such as pyridostigmine)	Insufficient SMSE
Vaccinations	Insufficient SMSE
Contaminated food and water	Insufficient SMSE
Pesticides Inc. Deet	To be confirmed once summary completed
Combined Exposures	Insufficient SMSE

Tasks:

- All member to review and finalise their summaries:
 - paying particular attention to the symptoms described in the papers and the SoPs definition of CMI

- ordering papers with the best quality/most persuasive listed first, giving reasons for the assessment of papers, quality of study, and any flaws etc. (giving particular attention any positive studies cited)
- ensuring all relevant OR's and CI's are included for those papers relied on by the Applicant
- adding final conclusions where this has not been done
- checking that all relevant papers have been cited
- Andrew to prepare general comments on odd ratios and how data is evaluated by epidemiologists.

Timeframe:

- All changes to be provided to the Secretariat by 30 September (sooner if possible) for circulation to full council.

4. Next Meeting – TBA if required

Minute taker: *Jan Bowman*

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Presiding Councillor: *David Newman*

DRAFT



MINUTES: SMRC Review - Council Meeting

For: **CMI and GWS**
 Date: Wednesday 31 Jan - 11.00 – 13.00
 Venue: Teleconference

ATTENDEES: Associate Professor David Newman (Presiding), Professor Dino Pisaniello, Dr Bradley Ng, Professor Andrew Grulich, Dr John Waterston, and Dr Kate Calydon-Platt (medical writer) and Jan Bowman (SMRC Secretariat).

1. **Welcomes and Introductions** – David Newman
2. **Decisions available to the Review Council**

The Council may find that:

- the Sound Medical Scientific Evidence (SMSE) is sufficient to direct the RMA to amend the SoPs to insert a factor(s) – and would go on to draft the relevant factors
- there is no, or there is insufficient SMSE (ie, *the SMSE is not convincing enough*) to direct the RMA to amend the SoPs to insert such a factor(s)
- there is information to support remitting the matter to the RMA for reconsideration in accordance with any directions or recommendations the SMRC may make.

3. **Review Decisions on factors in scope** – ALL

Members reviewed and confirmed their decisions on the contended factors:

Factor	Council’s Conclusion
Depleted uranium	Insufficient SMSE
Oil well smoke	Insufficient SMSE
Chemical and biological weapons (in Sarin)	Insufficient SMSE
Medical countermeasures (such as pyridostigmine)	Insufficient SMSE
Vaccinations	Insufficient SMSE
Contaminated food and water	Insufficient SMSE
Pesticides Inc. Deet	Insufficient SMSE
Combined Exposures	Insufficient SMSE

Members commented that for all contended factors:

- the SMSE generally lacked statistical power, is inconsistent, and too limited in quality or quantity to make firm conclusions.
- problems with the SMSE included:
 - reliance on self-reported and hypothetical exposures in the absence of definitive exposure data
 - limited, or on many cases no, evidence that matches the SoPs definition for CMI, making interpretation and extrapolation difficult.

More details are on the attached table.

Members agreed that:

- there is insufficient SMSE to support new factors for CMI for all exposures in scope, and also agreed
- there was insufficient evidence in the new information provided by the Applicants to recommend a fresh investigation by the RMA.

TASKS

- The Secretariat will:
 - Circulate an updated draft based on comments received to date, with sections reorganised into a more logical order
 - Reduce the section on new information to include commentary only on papers identified by councillors (if any).
- Members will:
 - review the comments provided by members in the current draft
 - review each section, revise, and refine conclusions.

Timeframe:

- *All changes to be provided to the Secretariat before the next tele-conference to be held on Wed 21 February.*

4. Next Meeting – Wed 21 February 2018

Minute taker: *Jan Bowman*

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Presiding Councillor: *David Newman*

SUMMARY

Chronic Multi-symptom Illness

Factor/definition	Conclusion/Grade	Comments from Summaries	CMI Symptoms	Actions:	Key Papers (please list)
<p>Chemical Warfare, inc Sarin</p>	<p>Conclusion: Insufficient SMSE</p> <p>Grade 4</p>	<p>Discussion Points:</p> <ul style="list-style-type: none"> • No evidence of acute exposure, lack of exposure data • The chemical alarms produced a lot of false positives - not a good measure of exposure – made for sensitivity, rather than specificity, and could be set off by containments such as oilwell smoke and dust. • Literature does not detail base-line exposure • Aust GW veterans’ Health Study – none of the alarm logs had positive results • US DoD no confirmation by secondary testing • Problem with Japanese studies that exposure was classified on a measure of severity • Lack of human evidence – lot of reliance on animal studies • No evidence that long-term chronic exposure causes illness in the absence of an acute cholinergic episode • So many variable, complex. <p>Summary and Conclusions</p> <p>The evidence of long-term health effects occurring after acute exposure to sarin gas during the Gulf war is circumstantial and there is no evidence to support the hypothesis that chronic toxicity can occur in the absence of acute exposure symptoms. Much of the evidence is based on self-reported and hypothetical exposures in the absence of any definitive exposure evidence.</p> <p>The evidence is inconsistent and the studies are limited in quality or quantity.</p>	<p>No evidence that matches the SoPs definition of CMI, making interpretation and extrapolation difficult.</p> <p>There is some evidence that exposure causes something, but not enough evidence that, that something can be described as CMI.</p> <p>Illness in Japanese studies does not equate to CMI.</p>	<p>Update section at para 188 on chemical alarms.</p> <p>Review section, revise, and refine conclusions.</p>	<p>References re chemical alarms.</p> <ul style="list-style-type: none"> • Aust, GW veterans’ Health Study • US DoD • Others

Factor/definition	Conclusion/Grade	Comments from Summaries	CMI Symptoms	Actions:	Key Papers (please list)
Pesticides	<p>Conclusion: Insufficient SMSE</p> <p>Grade 4</p>	<p>Discussion Points:</p> <ul style="list-style-type: none"> • Similar to above. • Literature inconsistent, reliance on self-reports, no one really knew what they were exposed to – no objective data. • No or limited exposure data • Often no distinction made between unique chemical agents, ie reference is to pesticides and a generic term • The studies <i>leave open</i> the possibility of pesticides (Ops) making a contribution (Golomb – not the answer, but may make a contribution). <p>The available SMSE does not suggest a clear and unequivocal association between pesticide use and/or exposure and the multifactorial multi-symptom illnesses reported in Gulf War veterans.</p> <p>The evidence is inconsistent and the studies are limited in quality or quantity.</p>	<ul style="list-style-type: none"> • Some biological plausibility, but can't be extrapolated to CMI. 	<p>Review section, revise, and refine conclusions.</p>	<p>Golomb – letter to RMA</p> <p>Spencer paper – best quality, in terms of definition – looks at exposure variables, and clusters of exposure variables - case definition in papers relatively good, but exposure analysis has not been done.</p>

Factor/definition	Conclusion/Grade	Comments from Summaries	CMI Symptoms	Actions:	Key Papers (please list)
Depleted uranium	Conclusion: Insufficient SMSE Grade: 4 or 5b	Discussion Points: Overall, the study samples have been small and there are limitations with measurements or records to quantify the amount of depleted uranium Gulf War veterans were potentially or actually exposed to. There is also relatively little information available from epidemiologic studies concerning veterans' exposure to depleted uranium and its possible link to chronic multisymptom illness. Overall, the weight of SMSE suggests that depleted uranium has not been shown to be a factor in the development of symptoms of chronic multisymptom illness.	No studies related to CMI?	Review section, revise, and refine conclusions.	
Combined Factors	Conclusion: Insufficient SMSE Grade 4	Discussion Points: <ul style="list-style-type: none"> • Problems with the other literature is magnified in the attempt to combine factors. • Spencer – BP & pesticides with relatedly close match to SoPs definition found that there wasn't an interaction. 		Review section, revise, and refine conclusions.	Spencer

Factor/definition	Conclusion/Grade	Comments from Summaries	CMI Symptoms	Actions:	Key Papers (please list)
<p>Contaminated Food and Water</p>	<p>Tests – Reasonable Hypothesis Balance of Probabilities</p> <p>Conclusion: Insufficient SMSE</p> <p>Grade: 4</p>	<p>The quality of the available evidence concerning exposure to contaminated food and water and the development of chronic multisymptom illness is limited. The Council noted that of the SMSE identified, only one paper by Unwin et al(27) used the CDC definition for chronic multisymptom illness to examine the association between exposure to contaminated food. Unwin et al(27) demonstrated a non-significant association of eating local food and chronic multisymptom illness.</p> <p>Overall, there were limitations with the quality of the comprised SMSE. The use of different outcome measures such as increased symptom reporting of Gulf War illness, which was defined differently by different authors, made it difficult to assess the research in relation to the symptoms seen in definition of chronic multisymptom illness as set out in SoPs. In particular the papers were limited in quality by possible exposures to multiple agents, the lack of exposure information including concentrations or cumulative exposures levels, the possibility of confounding (from other exposures), and recall bias from self-reported health symptoms.</p>	<p>Only one paper specific to CMI?</p>	<p>Review section, revise, and refine conclusions.</p>	

Factor/definition	Conclusion/Grade	Comments from Summaries	CMI Symptoms	Actions:	Key Papers (please list)
Smoke from oil well fires	Conclusion: Insufficient SMSE Grade: 4	<p>In its review of the SMSE, the Council identified a number of studies, two studies examined exposure to oil well smoke and chronic multisymptom illness (CDC defined),(27, 28) two other studies compared two definitions of Gulf War illness (CDC and Kansas defined)(37) and Gulf War unexplained illness (CDC and PEHRC defined),(6) and two studies used different definitions of Gulf War illness (Gray defined)(29) and (Lucas defined).(38) One study examined association with burn pit emissions and chronic multisymptom illness (CDC defined).(36) Others examined exposure to smoke from oil well fires and respiratory disease,(22-24, 35, 44) post-war morbidity from exposure to oil well fire smoke,(30, 39) and one study examined the biological uptake of oil-fire associated volatile organic compounds concentrations in whole blood of US military Army personnel and firefighters and medical and para-medical personnel working at the burning oil wells.(43)</p> <p>Insights into smoke-related morbidity and mortality may be gained by examining occupational studies of firefighters. Three studies of firefighters were reviewed.(40-42) Overall, in assessing a potential causal relationship between chronic multisymptom illness and exposure to oil well fire smoke, it is pertinent to note that the neurological symptoms of chronic multisymptom illness have not been associated with firefighting.(40-42).</p>	It is pertinent to note that the neurological symptoms of chronic multi-symptom illness have not been associated with firefighting.(40-42).	Review section, revise, and refine conclusions.	

Factor/definition	Conclusion/Grade	Comments from Summaries	CMI Symptoms	Actions:	Key Papers (please list)
<p>Chemical warfare counter measures (Pyridostigmine bromide) – for chem/biological warfare agents see below.</p>	<p>Tests – Reasonable Hypothesis Balance of Probabilities</p> <p>Conclusion: Insufficient SMSE</p> <p>Grade: 4 or 5a?</p>	<p>The quality of the available evidence concerning exposure to pyridostigmine bromide and the development of chronic multisymptom illness is limited. The Council noted that of the three papers (6, 27, 28) which used the CDC definition for chronic multisymptom illness to examine the association between exposure to pyridostigmine bromide. Unwin et al(27) and Wolfe et al(28) each demonstrated a mild significant association of pyridostigmine bromide and chronic multisymptom illness. While Spencer et al(6) did not demonstrate a significant association. However, there were major limitations with the overall quality of the evidence. All of the studies relied on self-reporting and the Spencer et al(6) study was the only study which combined self-reporting with clinical evaluation.</p> <p>In all studies, exposure assessment of pyridostigmine bromide in military personnel have been based on individuals’ recall of the measures they received or took, frequently under stressful situations, and have seldom been verified by records. This potential for recall bias also contributes to the difficulty in identifying specific causes of the veterans’ health problems. It is unclear whether the actual exposure or the belief in exposure is the most important aetiological factor.</p>	<p>Three papers</p> <p>Lack of plausible biological mechanism</p>	<p>Review section, revise, and refine conclusions.</p>	

Factor/definition	Conclusion/Grade	Comments from Summaries	CMI Symptoms	Actions:	Key Papers (please list)
Vaccinations	<p>Tests – Reasonable Hypothesis Balance of Probabilities</p> <p>Conclusion: Insufficient SMSE</p> <p>Grade 4.</p>	<p>Although the quality of the available SMSE was limited, the Council considered the most informative studies on exposure to vaccinations and the development of chronic ill health in Gulf War veterans were those studies where vaccination books, electronic documentation of vaccinations and medical chart reviews were used to support data analysis.(27, 109, 120, 121, 123) Of these studies, four found no association between vaccinations and the development of chronic ill health in Gulf War veterans,(27, 120, 121, 123) and the only positive study(109) produced conflicting results when the data were re-analysed using a different paradigm.(122)</p> <p>Overall, there seems to be insufficient evidence to incriminate a definite pathophysiological link between exposure to vaccines and the development of chronic multisymptom illness. The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between vaccinations and chronic multisymptom illness.</p>	<p>Only one positive study</p>	<p>Review section, revise, and refine conclusions.</p>	

Bowman, Jan

From: Bowman, Jan
Sent: Thursday, 19 April 2018 10:25 AM
To: 'David Newman'; 'Andrew Grulich'; 'Dino Pisaniello'; 'Brad Ng'; 'John Waterston'
Cc: 'Kate Claydon-Platt'
Subject: RE: Update from Today's SMRC meeting - CMI draft - 18.04.2018

Dear All

I spoke with Ben Dube this morning.

I explained that the Council did not like this wording in the summary and conclusions – “Therefore the evidence does not support a judgement that exposure to oil well smoke has a causal relation to chronic multisymptom illness”

He suggested deleting that sentence, or its alternative, as it is somewhat repetitive, and retaining the overall conclusion. So for oilwell smoke for example it would read:

Summary and Conclusions

1. While a significant association was suggested in some studies between exposure to oil well smoke and the development of symptoms of chronic multisymptom illness, the conclusions in those studies are inconsistent and the studies are limited in quality and quantity. ~~Therefore the evidence does not support an association between exposure to oil well smoke and chronic multisymptom illness.~~

THE COUNCIL'S CONCLUSIONS ON WHETHER THERE SHOULD BE FACTOR(S) FOR OIL WELL SMOKE

In summary, based on the criteria described above at [34-37], the Council considers that the SMSE is insufficient to point to a link between chronic multisymptom illness and exposure to oil well smoke. On that basis, the SMSE does not indicate a reasonable hypothesis connecting chronic multisymptom illness to exposure to oil well smoke. As the Council has concluded that the reasonable hypothesis test is not established, the balance of probabilities test necessarily could not be met.

If Council is happy with that, I will amend the conclusions for all factors.

Regards Jan

Jan Bowman

SMRC Registrar
Ph 07 3223 8420 - ex470420

From: Bowman, Jan
Sent: Wednesday, 18 April 2018 1:22 PM
To: 'David Newman' ; 'Andrew Grulich' ; 'Dino Pisaniello' ; 'Brad Ng' ; 'John Waterston'
Cc: 'Kate Claydon-Platt'
Subject: Update from Today's SMRC meeting - CMI draft - 18.04.2018

Dear All

Below are the next steps as discussed today:

1. All Councillors to review comments starting with **#303 (Haley and Kurt) on page 100**, to the end of the reasons and provide comments to Jan (**cc to all**) **as soon as possible, by email**
 - Andrew will add some general observations about Binns, the IOM papers, and the Monash studies from #44 and then any repetition in factor summaries will be deleted
 - Bradley will review/check Haley & Kurt 1997, re Binns
 - John to check reference to McDiarmid (ref 20) and Cherry (33)
 - Jan to check concluding wording for factors with Ben and to ensure consistent – now changed to “Therefore, the available evidence does not support an association between exposure to <> and chronic multisymptom illness.”
 - All references to for ‘Gulf War illness’ will be in quotes
2. Kate/Jan will incorporate all comments and provide a clean version of the reasons **by the end of April**.
3. Councillors to do a final review of both CMI and GWS reasons before sign off, and to revise any gradings of papers to ensure consistent with its conclusions
4. Aim to have Reasons **published by end May**

Regards Jan

Jan Bowman
SMRC Registrar
Ph 07 3223 8420 - ex470420

From: Bowman, Jan
Sent: Tuesday, 17 April 2018 12:09 PM
To: 'David Newman' <s 47F(1)>; Andrew Grulich <s 47F(1)>; 'Dino Pisaniello' <s 47F(1)>; 'John Waterston' <s 47F(1)>; 'Brad Ng' <s 47F(1)>
Cc: 'Kate Claydon-Platt' <s 47F(1)>
Subject: SMRC - CMI draft for discussion 18 April
Importance: High

Dear All

Attached is the draft reasons dated 17 April 2018 for reference tomorrow.

Kate has incorporated feedback received to date, or placed in a comments box.

The Council will work through the document as proposed by David in my email of yesterday.

Regards Jan

Jan Bowman
SMRC Registrar
Ph 07 3223 8420 - ex470420