

MCS Referral & Resources

*professional outreach, patient support and public advocacy
devoted to the diagnosis, treatment, accommodation and prevention
of Multiple Chemical Sensitivity Disorders*

30 January 2009

Comments on Draft Report entitled:

A Scientific Review of Multiple Chemical Sensitivity: Identifying Key Research Needs

TO: the Australian Department of Health and Ageing, NICNAS and OCS
via email to MCS@nicnas.gov.au

FROM: Albert Donnay, MHS
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COMMENTS

[Cited sections are in italics, with Australian spelling. Comments are in plain text, with US spelling]

Aside from those sections of the draft review that are specifically addressed below, I found no other factual errors in the rest of the text. With the correction of the errors and omissions I've identified, I believe this review would be suitable for publication, although its extremely limited scope (the references include fewer than 20% of all published MCS literature) should be acknowledged in the introduction, along with an explanation of why so much of the literature was not reviewed. I also recommend that the primary authors and editors be identified, along with their professional credentials and affiliations. It is impossible to know from this anonymous draft, for example, if it was written and edited by NICNAS and/or OCS staff and/or by paid consultants, and if those involved were physicians, epidemiologists or toxicologists, as I hope at least some of them were.

Page 6, section 1.1

However, there are no standardised criteria for identifying cases of MCS in clinical settings. The diagnosis of MCS is currently based on self-reported symptoms. No laboratory tests currently exist for diagnosing MCS. This lack of an accepted case definition and objective laboratory markers for MCS has significantly impeded treatment for patients and offers challenges to further research into MCS.

The 1999 Consensus Criteria cited on this same page are widely cited and use in the published literature and do constitute an "accepted" case definition, albeit one dependent on patient self report without any objective biomarkers, but there many other disorders are similarly defined for clinical purposes (such as migraine, for example).

While numerous attempts have been made to define MCS, there is no unequivocal epidemiological evidence or quantitative or qualitative exposure data to distinguish individuals with MCS from others experiencing symptoms such as fatigue, headache, dizziness, lack of concentration or memory loss and labeled with diagnoses such as Chronic Fatigue Syndrome.

Quantitative and qualitative exposure data are not needed to distinguish MCS from other syndromes. MCS is definitively and unequivocally differentiated from CFS and other syndromes that share some symptoms such as "fatigue, headache, dizziness, lack of concentration or memory loss" by their various diagnostic criteria. ONLY the diagnosis of MCS requires that the patient reports experiencing symptoms in multiple organs from exposure to multiple chemicals at or below previously tolerated levels of exposure (according by the 1999 Consensus Criteria and every other

research definition ever published). This is sufficient to distinguish MCS from CFS, fibromyalgia (FM) and other conditions with which it is commonly co-morbid as the diagnostic criteria for these other conditions do not include any type of chemical sensitivity. That these conditions can be readily distinguished is evident from the many published studies that have compared patients with these various diagnoses. None have reported any problem distinguishing people with MCS, CFS, FM from each other using published diagnostic criteria.

Lack of agreement on the underlying cause(s) and pathogenesis of MCS and subsequent lack of agreement on an operational definition of MCS impacts on the clinical management of ...

There is NO “subsequent lack of agreement on an operational definition of MCS.” This is a red herring that should not be cited without some evidence for it. All of the definitions published to date are very similar and they have been sufficiently “operational” to allow researchers to identify and study MCS patients even when comparing them to those with conditions such as CFS and FM that are similar in many other respects but without any chemical sensitivity component.

The need for objective clinical criteria to identify MCS subjects and overcome the shortcomings of self diagnosis is critical. This would allow prevalence data to be collected ...

All the published literature on MCS documents that subjects can be readily identified without any objective clinical criteria. If not, there would not be any studies of MCS patients in the medical literature! And none of the published studies have raised any doubts about the validity of such “self-diagnosis” – or more accurately, about the diagnosis of MCS by physicians and researchers who have had to rely on patients to report their symptoms.

Page 7, section 1.2

Overall, the following primary research needs are evident: ...

** establishing agreed diagnostic criteria that are acceptable to clinical and scientific groups;*

It is not at all evident that there is any research need for any new “agreed diagnostic criteria.” The 1999 Consensus Criteria are widely accepted by both clinical and scientific groups in many countries and most importantly, have not been reported in any forum or literature to be insufficient in any respect by any of the many researchers or clinicians who have used them. Before wasting time and resources trying to establish any other new diagnostic criteria, I urge the Australian government to survey MCS researchers, clinicians and patients to see if they have any problems with the current criteria. Do the 1999 criteria result in unacceptably high rates of either false positive or false negative diagnosis? If not, why bother trying to establish any other definition?

... the following scientific theories of the cause of MCS are recommended for further scientific research and investigation as priorities:

Please consider adding carbon monoxide (CO) poisoning to this list of scientific theories. Why? Because endogenous CO produced heme oxygenase-1, the so-called universal stress enzyme, is known to modulate the nerve action firing potential of all our sensory nerves, and because all the primary symptoms of MCS, as identified in Table 1 of your report on page 10, are all well recognized symptoms of both acute and chronic CO poisoning.

Page 8

Overall, a number of primary clinical research needs are evident:

** Establishing agreed diagnostic criteria that are acceptable to clinical and scientific groups;*

Same comment as above. The existing 1999 Consensus Criteria are already widely used and accepted by both clinicians and research groups, including in 2002 by the New South Wales government in its own epidemiological study of MCS, as your report acknowledges on page 14!

No published studies have reported any problems using these criteria in either clinical practice or research. Why waste time and money developing new diagnostic criteria if no one has identified any sensitivity or specificity problems with the existing criteria? More important and more useful would be to fund research looking for objective biomarkers of abnormality that correlate strongly with the consensus criteria.

Page 9

In some cases, these terms reflect the particular views of individuals or groups regarding the underlying cause and mode of action of MCS. For this reason, the descriptor Idiopathic Environmental Intolerance or IEI is favoured by many, including the World Health Organization (WHO), because it does not make inferences with regards to causative agents. This reflects the lack of an agreed biological basis for MCS symptoms.

The term IEI does make an inference with regard to causative agents: it considers the cause of the intolerances to be “environmental.” But the term is oxymoronic term since if the illness is considered environmental, as distinct, for example, from being considered psychiatric or iatrogenic as some claim it is, then it cannot also be idiopathic, which means of no known cause, and vice versa.

Nor is the term IEI favored by many, which you can easily verify by simply counting the number of research papers indexed by the US National Library of Medicine at www.pubmed.gov which use the term MCS versus those that use IEI. It is MCS, and not IEI, that is still used by the overwhelming majority of researchers in peer reviewed publications.

IEI is also NOT favoured by the WHO. The small invitation-only MCS workshop at which the term IEI originated was sponsored by the International Program on Chemical Safety (IPCS) in Berlin, which is itself jointly sponsored by the WHO, the UN Environment Programme and the International Labor Office. None of these organizations including the IPSC itself has ever endorsed the conclusions or recommendations of the workshop. These were published ANONYMOUSLY, without any references, without any peer-review, and without the consent or even knowledge of most of the workshop’s participants by one of them, Dr. Ronald Gots. He was the medical director at the time of a notoriously anti-MCS chemical industry organization called the Environmental Sensitivities Research Institute or ESRI. Dr. Gots arranged for ESRI to pay for this publication in a supplement to Regulatory Toxicology and Pharmacology (RTP)—the grant is even acknowledged on the title page—that was otherwise devoted in its entirety to the proceedings of a separate ESRI-sponsored conference on MCS chaired by Dr. Gots.

Had the authors of your report read either the original (unpublished) 3-page workshop report or the anonymous version published by Dr. Gots in RTP¹, I am sure they would have noticed the disclaimer attached by footnote to the title which says in its entirety: “These conclusions and recommendations contain the collective views of an international group of experts and do not necessarily represent the decisions or the stated policy of the United Nations Environment Programme, the International Labour Organization, or the World Health Organization.”

Dr. Gots and other anti-MCS advocates then went on (in other publications and legal testimony against MCS plaintiffs) to mis-cite this vanity publication as a statement of the WHO when in fact, as noted above, it was anonymous and at best, only a statement of the workshop participants. Three days after I submitted a complaint about this misrepresentation to the IPCS, the Director General of the World Health Organization issuing a statement to Dr. Gots and the other 16 workshop participants [only 7 of whom, by the way, had ever published anything on MCS] reminding them that the conclusions and recommendations were only those of the participants and NOT to be cited as those of WHO, UNEP or the ILO, none of which have ever issued any position on MCS by any name.

¹ Anonymous 1996. Conclusions and Recommendations of a Workshop on Multiple Chemical Sensitivities. Regulatory Toxicology and Pharmacology 24, S188-S189.

Complete documentation of this scandal is available from me upon request. Unless you can cite some actual WHO source for your statement that IEI is favored by the WHO, I urge you to delete it.

Unfortunately, this lack of agreement on the underlying cause and pathogenesis of MCS, and subsequent lack of agreement on an operational definition of MCS has been a serious hindrance to scientific analysis investigation and clinical recognition of the condition.

As discussed above, there is NO lack of agreement on the operational definition of MCS among MCS researchers. The existing published definitions have obviously facilitated and not seriously hindered the scientific investigation of MCS, as evidenced by the hundreds of MCS studies that have been published using these definitions. And even without any government sponsored definition or code in the International Classification of Diseases, epidemiological studies in the US conducted by state health departments in California and New Mexico have found 2 to 6% of American adults already diagnosed with MCS by a physician or other health care professional, which clearly demonstrates widespread clinical recognition of the condition.

Page 11

In contrast, there is little evidence that other syndromes, such as chronic toxic encephalopathy, CFS, RADS, FM, irritable bowel syndrome or Gulf War syndrome are induced or exacerbated by ambient chemical triggers (Staudenmayer et al. 2003b).

There is actually considerable evidence that high percentages of CFS, FM and Gulf War syndrome cases are exacerbated by ambient chemical triggers. This evidence is contained in studies of both civilians with CFS and/or FM and military veterans with Gulf War Syndrome that showing that high percentages of people with these conditions also meet the criteria for MCS, which by definition means that their symptoms are exacerbated by ambient chemical triggers. One of these studies is that of Buchwald and Garrity 1994, which your review goes on to cite in the same paragraph. But you fail to mention its most relevant findings—namely that 67% of both their CFS and FM cases also met the criteria for MCS! I suggest you also cite the overlap findings of a 1999 study that Dr. Grace Ziem and I conducted of 100 consecutively seen MCS patients in her private practice.² We found that 88% of these MCS cases also met the CDC criteria for CFS, 49% met the ACR criteria for FM, 47% met the criteria for both CFS and FM, and just 10% had MCS alone.

Page 12, Section 2.3

Deployments to war zones has been associated with increased prevalence of MCS and multi-symptom conditions (Gray et al 2002; Thomas et al., 2006; Osterberg et al., 2007).

The actual increased prevalence found in these and other studies should be cited. In trying to check this, I discovered that only Gray et al 2002 is listed in the references at the end of the review. The others obviously should be added. I cannot imagine that their omission was deliberate, which led me to question instead the thoroughness of whoever was assigned to edit this draft review before its release. It also led me to check all the citations in this review to see how many others were omitted from the reference list. I found ten. Rather than continue to identify them page by page, I have instead provided you with a complete list in Appendix A.

Page 13, Section 2.4

Research reports suggest that there is likely to be a psychogenic component in the aetiology of MCS.

This statement should be referenced and quantified in terms of the number of research reports that suggest this compared to the number that suggest a physiological basis. I published such a quantitative comparison in 1999 based on all the peer reviewed English language literature that had

² Donnay A, Ziem G. 1999. Prevalence and overlap of chronic fatigue syndrome and fibromyalgia syndrome among 100 patients with multiple chemical sensitivity. J. Chronic Fatigue Syn;5(3/4):71-80.

been published on MCS up to that time.³ I found the number of papers and first authors that supported an organic basis for MCS outnumbered those that favored a psychiatric basis by more than 2:1. This ratio has remained in 2:1 in the decade since. Since your review already cites my review elsewhere, it should cite it here as well.

QUESTION: are there additional triggers identified in MCS?

The most important trigger not mentioned in your report is carbon monoxide. As noted above, all of the symptoms of MCS listed in Table 1 on page 10 are well recognized symptoms of CO poisoning. Your review should acknowledge this.

Page 13, Section 2.5

Other researchers rejected these case definitions on the grounds that objective measures or physical findings do not exist to permit confirmation of any organic dysfunction and that the disorder is patient defined, ie. the physician relies on the patient's reports of symptoms and exposure when making a diagnosis (Gots et al. 1993; Waddell, 1993; American Academy of Allergy and Immunology, 1999).

It is incorrect and misleading to identify Gots, Waddell and the AAI as "Other researchers." None have ever published any research on MCS, only reviews that are critical of the MCS concept. The Gots 1993 and Waddell 1993 references are both from the un-peer-reviewed proceedings of another MCS conference organized and chaired by Dr. Gots. Also, AAI is mis-identified here but correct in the list of references. It is actually the American Academy of Allergy, Asthma and Immunology.

A World Health Organisation workshop on MCS held in 1996 described the condition as an acquired disorder with multiple recurrent symptoms, associated with diverse environmental factors that are tolerated by the majority of people and that is not explained by any known medical or psychiatric/psychological disorder. The workshop also concluded that use of the term MCS should be discontinued because it makes an unsupported judgement on causation noting the existence of several definitions of what has been caused MCS. The workshop favoured the descriptor "Idiopathic Environmental Intolerances" (IPCS, 1996).

As discussed above, this was NOT a WHO workshop. It was an IPCS workshop, and its anonymously published "conclusions and recommendations" are ONLY those of the workshop participants (not "the workshop"). The citation you give at the top of page 14 to (IPCS 1996) is incorrect, as is the full reference that you give on page 65 listing IPCS as the author and the UNEP, ILO and WHO as the publisher. None of these organizations ever authored or published any report of this meeting. As noted above, the report was only published anonymously in a supplement to RTP that was paid for by ESRI, an anti-MCS organization founded by Dr. Gots, who was one of the workshop participants. No subsequent citation has ever listed the actual authors and most, unfortunately, repeat the same error you make here – misrepresenting this report as a publication of the IPCS and/or the WHO. To correct your error, you should identify this in the text as "A workshop of the International Programme on Chemical Safety" and you should change the citation to (Anonymous, 1996). The full reference should be corrected as well, of course.⁴

Page 14

These Consensus criteria were used in the New South Wales (NSW) Department of Health Adult Health Survey in 2002 where questions on chemical sensitivity were included (NSW Department of Health 2002).

³ Donnay A. 1999. On the recognition of multiple chemical sensitivity in medical literature and government policy. *International J. Toxicology*;18(6):383-92.

⁴ Anonymous 1996. Conclusions and Recommendations of a Workshop on Multiple Chemical Sensitivities. *Regulatory Toxicology and Pharmacology* 24, S188-S189.

This is incorrect. These Consensus Criteria were only cited on page 81 of the NSW survey, but they were not used. As your review correctly notes in Section 4.1.1 on page 33, the NSW survey actually used only two questions about chemical sensitivity, neither of which, unfortunately, correlate with any published definition of MCS.

Page 15 Section 2.6

MCS is not recognised as a classified disease identity in any country in the world.

In Germany, MCS is included in the alphabetical index of the German version of the International Statistical Classification of Diseases and Related Health Problems (ICD-b-SGB-V) first published in November 2000 by the German Institute of Medical Documentation and Information (DIMDI). However, this index is a collection of phrases or diagnoses used by some German clinicians and is not a list of diseases "officially recognised" by Germany (M. Schopen, DIMDI, Personal Communication, 2004).

This information is only partially correct and quite misleading. While it is true that Germany added "Multiple-chemical-sensitivity-syndrom" to the main alphabetical index its version of the International Classification of Diseases (ICD-10-SGBV, version 3.1) in November 2000, it also chose to list MCS under "syndromes" and under "Chemical-Sensitivity-Syndrom, Multiple." Most importantly, your report should note that Germany referenced all these index entries to code "T78.4" in the section on injuries and poisonings. Note that this is not a code for psychiatric disease! T78.4 is a pre-existing code for "Allergie, nicht naher bezeichnet" (=allergy, not otherwise specified or NOS) which is an officially recognized disease category. The German ICD-10 even specifies three subtypes of T78.4 which it would not bother doing if the condition were not recognized. These are: Allergische Reaktion o.n.A. (= Allergic Reaction, NOS), Idiosynrasie o.n.A. (= Idiosyncratic, NOS) and Uberempfindlichkeit o.n.A. (= Hypersensitivity, NOS).

Page 16 Section 2.7

Currently, there are no epidemiological data that link MCS subjects or those who may be susceptible to MCS with particular chemical exposures or lifestyles.

This is incorrect and contradicted by statements made in other sections of this review (see 3.1.6) that acknowledge higher rates of MCS among veterans of the Persian Gulf War compared to non-deployed military from the same era. In fact, every epidemiological study of MCS among military veterans of the Persian Gulf War era (British, Canadian and US) has found statistically significant higher rates of chemical sensitivity and/or "MCS"—however it was defined—among those deployed to the Gulf region compared to undeployed controls. A meta-review of 23 such studies published between 1990 and 2004 found that Gulf War veterans were approximately 3.5 times more likely to report MCS than undeployed controls.⁵ These findings should be reported here, especially since they are already reported in Section 4.1.1 on page 35!. Also extensively documented in these and other published studies, some of which are mentioned on page 35, is the association of MCS and other Gulf War related illnesses with exposure to multiple toxic chemicals on the battlefield, in vehicles, and in living quarters. These studies together make a very strong epidemiological link between MCS subjects and "particular chemical exposures or lifestyles."

Page 18, Section 3

The literature relating to causes of MCS invariably highlights differences in views regarding the primary underlying cause of MCS- ie. psychogenic or toxicodynamic. There is much debate as to whether MCS symptoms are due to psychosomatic response to perceived chemical toxicity or to a physiological/pathological interaction between chemical agents and organ systems. While some physicians believe MCS is purely a psychological disorder, others consider it to be an overt, albeit poorly understood, physiological response to chemical

⁵ Thomas HV, Stimpson NJ, Weightman AL, Dunstan F, Lewis G. 2006. Systematic review of multi-symptom conditions in Gulf War veterans. *Psychol Med*;36(6):735-47.

exposure. It is also possible that both physiological and psychological factors play a part in the pathogenesis of MCS (Bock and Birbaumer 1997; Osterberg et al 2005; Das-Munshi et al., 2007; Haustener et al., 2007).

The wording of this introduction suggests a lack of consensus in the medical literature regarding the psychogenic versus toxicodynamic nature of MCS. In fact, as documented in my previously mentioned review of all MCS literature published up to 1999 (and in my unpublished review of all the MCS literature published since), the number of papers and first authors supporting an organic/physical basis for MCS outnumbers the psychiatric by more than 2:1. Your review should acknowledge this weight of the literature analysis.

You should also note that, as far back as 1994, the US Environmental Protection Agency, Consumer Product Safety Commission, American Medical Association and American Medical Lung Association jointly published a report entitled Indoor Air Pollution, An Introduction for Health Professionals⁶ which, under the heading “What is 'multiple chemical sensitivity' or 'total allergy'?”, states that “The current consensus is that in cases of claimed or suspected MCS, complaints should not be dismissed as psychogenic, and a thorough workup is essential.” Anyone who still claims or even suggests that MCS is only psychogenic is clearly outside this most mainstream consensus. The report is prefaced in on its title page with the following statement: “Information provided in this booklet is based upon current scientific and technical understanding of the issues presented...”

There is no longer ANY serious debate in the medical literature about the primarily toxicodynamic nature of MCS except in reviews such as yours that strive to be “balanced” and in opinion articles written by proponents of the psychiatric view who seek to sow doubt about the overwhelming evidence in favor of a toxicodynamic basis.

Page 18 Section 3.1

Using the mode of action level of proof as the benchmark appropriate to trigger regulatory, clinical or other action on the causative agent(s) of MCS, a review of the available literature...

In the immediately preceding discussion of “mode of action,” your report correctly identifies it as “*useful framework when considering the biological basis for an adverse health outcome*” and correctly notes that “*This concept is used in chemical risk assessment and assists in determining the level of evidence needed in making a regulatory decision in relation to adverse effects observed in animal models or symptoms observed in humans.*”

Understanding the mode of action of a toxin, however, has never been and should never be the only “level of proof” “benchmark” “appropriate” to “trigger” regulatory, clinical or other action on the causative agent(s) of any medical disorder. Is the Australian government really now proposing to make knowing the “mode of action” of any particular toxin the minimum benchmark required to consider taking any action on any hazardous chemical? If so, this review should explain why this standard is being adopted and if it is going to be applied to all outcomes of concern such as cancer, birth defects, and neurodegenerative diseases, or only to MCS (in which case, why only MCS?)

In all other civilized countries that regulate the use of chemicals, knowing the mode of action has never been a required “level of proof” or minimum benchmark needed to trigger regulatory, clinical or other action with respect to causative agents – and it should not be so in Australia, neither for MCS or for any other disease. Lead, arsenic, mercury, asbestos, vinyl chloride, tobacco smoke and almost every other toxin of environmental, occupational and/or public health concern have been the subject of regulatory and clinical action long before their “mode of action” was completely known, and usually based initially on the strength of epidemiological evidence alone. I am sure that many Australian government agencies already regulate thousands of toxic chemicals used in medicine, industry, defense and consumer products whose “mode of action” is not known! Why apply a

⁶ This report is still in print (available from US Government Printing Office, #1994-523-217/81322, and also available free on the US EPA website at <http://www.epa.gov/iaq/pubs/hpguide.html#Intro>)

different standard to chemicals that may cause or worsen MCS? I urge you to heed the Precautionary Principle!

Page 19

Overall, although some researchers acknowledge that allergic or immunotoxicologic reactions could be contributing factors in at least a subset of MCS patients (Selner & Staudenmayer, 1992; Albright & Goldstein 1992; Meggs, 1992; Interagency Workgroup, 1998), ...

The report of the Interagency Workgroup 1998 should not be cited as it never progressed beyond a “predecisional draft” and was never published. It therefore does not officially represent the views of any the US federal agencies that participated in the workgroup.

Page 20

The sensitivity and specificity of chemosensory reactions have been tested in controlled challenge studies in MCS patients. In a double-blind placebo-controlled (DBPC) challenge study by Staudenmayer et al. (1993) using an olfactory masking agent, MCS patients (n=20) were unable to reliably differentiate active agents from the placebo (clean air containing olfactory masker). Sensitivity, specificity and efficiency ratings for each participant did not show a reliable response pattern across the series of challenge tests (Staudenmayer et al. 1993).

Staudenmayer’s study was rightly criticized in letters to the editor for using “clean air containing olfactory masker” as a “placebo” challenge without first testing MCS patients for their sensitivity to this olfactory masker which, of course, is itself a chemical exposure. It is patently absurd to use a chemical odorant as a placebo in a study of reactions to chemical odorants, and your review should acknowledge this.

Page 24, Section 3.1.6

Deployments to war zones are associated with increased prevalence of MCS and multi-symptom conditions (Thomas et al., 2006; Osterberg et al., 2007; also see Section 2.3).

This sentence is almost identical to that in Section 2.3 and gives 2 of the 3 same citations, neither of which, as I noted in my comments above, appears in the list of references. Here again, the actual increased prevalence data should be cited so that readers can judge its significance for themselves.

Page 24, Section 3.1.7

Various investigators claim MCS is a somatoform reaction (i.e. physical symptoms not explained by objective clinical findings), a depressive disorder, post-traumatic stress disorder or a panic disorder (Fiedler & Kipen, 1997; Interagency workgroup, 1998 ...

Since this sentence begins with “Various investigators claim,” the citations that follow should be limited to reports of investigators. The Interagency Workgroup 1998 should not be cited because it did not do any investigations (it is only a review) and, as previously noted, its “Predecisional Draft” report was never finalized or published and so does not represent the official views of any of the US agencies that co-authored it.

Page 27. Section 3.1.9

A recent challenge study on healthy volunteers showed that worrying information that a specific harmless odour cue was associated with a symptomatic episode was more powerful than an actual symptomatic exposure (harmless odour plus CO2 enriched air) in provoking self reported respiratory symptoms (Devriese et al. 2004).

As with the Staudenmayer study discussed above, this study used what it assumed was a harmless (chemical) odor cue without actually first testing it on MCS subjects to determine if it was in fact “harmless.” And by combining this putatively “harmless” chemical odorant with CO2 enriched air,

this study could not determine whether the observed effects from this combined exposure were due to the odorant alone and/or the enriched level of CO₂. Your review should address this issue as it is a common design flaw in MCS challenge studies.

Page 29 Section 3.2

Whether MCS is a disorder with an underlying toxicodynamic cause or a psychogenic cause, or is particularly the result of both is not clear from the analysis of the available scientific literature.

This lead sentence is misleading and unwarranted because, by your own admission, this review did not even attempt to analyze all of the available scientific literature on MCS, which includes hundreds more studies than those cited here. This fundamental limitation of your review should be acknowledged, especially since your ambivalent conclusion stands in such stark contrast to the 1994 consensus of the US EPA, CPSC, AMA and ALA discussed above that said MCS is NOT psychogenic. I recommend that ending of this sentence be changed to “...is not clear from this limited analysis of the scientific literature on MCS that we chose to review, which included less than 20% of all the available literature.” I suggest you also add a sentence explaining how and why you selected to review those MCS studies that you did, and why you decided not to review so many more.

Page 30

A fundamental principle of toxicology is that exposures to individual chemicals elicit predictable dose-related adverse effect(s) in predominantly single but also multiple, related organ systems. The symptoms triggered by low-level exposure in MCS subjects generally do not conform to this toxicological principle.

This is NOT a fundamental principle of toxicology. It is, however, an oft-repeated claim in the anti-MCS publications of Dr. Ronald Gots, which I assume is where you found it. Many of the most widely studied poisons in toxicology, including lead, mercury, and carbon monoxide, are well known for their ability to cause adverse effects in multiple organs that are neither consistently predictable or dose-related. Most toxicologists are also aware of and accept as valid the fundamental dose-response-defying principles of sensitization (to low levels of exogenous exposures) and habituation (to high levels) that underlie the fields of allergy and addiction.

Page 31 Section 3.3

The scientific weight-of evidence currently suggests that while physiological mechanisms may play a part in MCS, there is also a psychological or psychogenic component in its pathogenesis.

This sentence misleadingly suggests that there is more evidence in the MCS literature for a psych basis (“there IS a psychological or psychogenic component...”) than for physiological mechanisms (which you say only “MAY play a part”). But as discussed above, my comprehensive review of peer-reviewed MCS literature published in 1999 documented that the “scientific weight-of evidence” significantly favors physiological mechanisms over psychiatric by a 2:1 ratio. This ratio applies not just to the number of papers with these opposing perspectives but also to the number of first authors writing them and the number of journals publishing them, which shows that the preponderance of evidence in favor of a physical basis for MCS is not due to a few prolific authors publishing in a few sympathetic journals. Your review should acknowledge this 2:1 ratio in the MCS literature and explain by what other measure of “scientific weight-of evidence” you conclude otherwise.

While there are a number of proposed mechanisms warranting further consideration, based on biological plausibility, testability and identified existing research gaps, the following are identified as priority areas for further scientific research and investigation:

Immunological variables

Immunological variables are clearly neither significantly or consistently associated with MCS, and so MCS is clearly not an immunological disease. This has been apparent to most MCS researchers for

over a decade, which is why so little immunological research on MCS has been done in the last decade. As someone who once served as the research coordinator of the Johns Hopkins Multi-Center Study of MCS Immunology, I am confident in recommending that no further immunological research is warranted. I strongly urge you to drop this from your list of research priorities.

Page 33 Section 4

The lack of agreement on an operational definition, or even an appropriate label, has been a hindrance to scientific analysis and an understanding of MCS.

Stop repeating this nonsense! Virtually the same sentence already appears above on page 6 and 9 and below on page 41. This statement is belied by the great extent and variety of MCS research literature published in the last 40 years, less than 20% of which is cited in this review. Clearly neither the lack of agreement on an “operational definition” or an “appropriate label” (whatever you mean by these phrases, which I recommend that you either delete or explain) has proven to be a hindrance to scientific analysis and understanding of MCS.

There are numerous studies (including Australian State health surveys) that have examined the extent to which people report sensitivity to chemical(s). However, it is not clear how many of these individuals would be classified as having MCS.

In each of these numerous studies, including the Australian State health surveys, it actually is quite clear how many of these people would be classified as having MCS because the participants were asked if they had multiple chemical sensitivity—with questions that included all the criteria of whichever definition(s) the study chose to evaluate—and if they had been diagnosed with MCS by a physician. Since MCS is defined and diagnosed by patient self report, such survey questions are a perfectly adequate way to estimate its prevalence.

The lack of a case definition means that MCS is often identified on the basis of self-reporting in the absence of a confirmable medical diagnosis.

MCS does NOT lack a case definition, as this review acknowledges in its discussion of the many case definitions that have been published and used in MCS research! This is obviously false and should be deleted. What you should emphasize is that all MCS case definitions lack objective biomarkers, but the same can be said of the case definitions of many other both physical and psychiatric diagnoses (see for example autism, Alzheimer's, Asperger's, migraines, etc). But the fact that these disorders are ALWAYS (not just “often”) identified ONLY on the basis of self-reporting (and/or behavioural observation) without any diagnostic “test” does not mean that their diagnosis is not “confirmable.”

The diagnosis of MCS, like the diagnosis of any of other “self-reported” medical condition, is “confirmed” when a physician “confirms” that the patient's case fulfills all the criteria of whatever definition they are using. This simple standard applies in research as well as clinical medicine. To be thorough, of course, those doing the “confirming” should also do whatever questioning and/or testing they feel is necessary to be sure that the patient's symptoms are not better explained by some other diagnosable condition or by malingering, feigning, etc. I suggest you also remind Australian physicians that they should always rule out ALL possible physical causes for any psychiatric symptoms (such as lead, mercury, solvent or CO poisoning) before considering ANY purely psychiatric diagnosis.

Page 33, Section 4.1.1

In NSW, a 2002 survey of adult health conducted by the Department of Health, 24.6% of respondents (from a total of 12,491 individuals) answered "yes" to the question "Do certain chemical odours or smells regularly make them (or their children) feel unwell?". Moreover, 2.9% answered "yes" to the question "Have you been medically diagnosed with a chemical sensitivity?" The severity of these health effects and their conformity to the 1999 Consensus Criteria (Section 1.2) are not known. . Interestingly, the survey did not find significant

variations in the proportion of people reporting diagnosed chemical sensitivity based on level of socio-economic disadvantage.

More interesting are the demographic variations found in the NSW study that your review does not report but should, including higher rates among women (28.9% vs 20.1% to the first question and 3.4% vs 2.4% to the second, although only the first was statistically significant), lower rates in the elderly (over 65) and young (age 16-25), and significantly lower rates in two regions (the North Sydney are in response to the first question and the Mid Western area in response to the second), but otherwise no significant difference between urban and rural areas.

Page 34, Section 4.1.2

The diagnosis of MCS was reported to be more common in the United States, Canada and Germany than in the United Kingdom (Reid et al, 2001). The best overseas estimates for prevalence of MCS are from the United States where prevalence appears to be less than 1% (Reid et al. 2001).

The cited study by Reid et al 2001 is a study by British researchers of MCS among UK Gulf War veterans. It is not a study of the prevalence of MCS in the US or any other country and should not be cited as such, especially since its estimate of the prevalence of MCS in the United States is significantly lower than that reported by all US studies of randomly surveyed adults--as evidenced by the actual US studies that your review goes on to discuss on this same page. There is therefore no reason to Reid's estimate that the prevalence "appears to be less than 1%" and so this sentence should be deleted.

Page 35

In summary, worldwide, there are only a small number of studies that have reported the prevalence of medically diagnosed MCS. In these studies, the prevalence of MCS ranges from 0.2 – 4% for populations or selected population subgroups.

This prevalence range is incorrect. It is contradicted by the results of the Kreutzer 1999 study which found 6.3% of 4000 randomly selected adults in California with medically diagnosed MCS – as reported on page 33 of this same section!

Page 35 Section 4.2

At present, it is difficult to determine the prevalence of MCS in the population as the reporting of MCS is based on self diagnosis or on uncertain medical diagnostic criteria.

As documented in the immediately preceding section, it is not all difficult to determine the prevalence of MCS in any population. All researchers have had to do was ask people if they have been diagnosed with MCS by a doctor or medical professional. While the results they obtained were admittedly self-reported (all information in any survey is self-reported!), it is not true that the reporting of MCS is based on self diagnosis. This is false and should be deleted. You also should clarify that even though no surveys have asked physicians who diagnose MCS what criteria they use to do so, and even though it is likely that many different criteria are in use in any particular country since no country has told physicians what criteria to use—it is likely that most physicians who make the diagnosis in any fashion are doing so consistently, according to whatever criteria they chose.

There have been numerous studies overseas to determine the prevalence of MCS, but most have suffered from poor reporting details that have made it difficult to ascertain which, if any, published case definitions were employed to diagnose MCS subjects.

It is misleading and unfair to say that these MCS prevalence studies suffer from poor reporting details, because were not designed to ascertain by what published definition these MCS cases had been diagnosed! They were designed to ascertain MCS prevalence by asking people if they had been diagnosed with MCS by a physician, and this they do very reliably. As reported in the editorial that accompanied Kreutzer's study, "The use of BRFS [the US CDC's Behavioral Risk Factor Survey

design] makes these data highly reliable and generalizable..."⁷ Indeed when Kreutzer's survey questions were inadvertently asked again a year later in another BRFS survey of another 4000 randomly selected adults in California, the results of the second survey were within 1% of the first!⁸

Page 36

The use of strictly validated blinded challenge test is a vital tool in obtaining objective data regarding the presence of any organic dysfunction in those individuals who identify themselves as suffering from MCS.

Blinded challenge tests are useful but certainly not vital tools for obtaining objective data on the presence of organic dysfunction in individuals with MCS. Numerous studies document both organic dysfunction and genetic differences in MCS cases compared with non-MCS controls even when the subjects are not challenged in any way but simply at rest in a clinical setting. You should clarify this sentence to emphasize that, although challenge studies are needed to look for physiological and psychiatric differences in responses to both blinded and non-blinded chemical exposures, they are NOT needed to obtain objective data on the presence of organic dysfunction in MCS cases, as such dysfunction may be detectable with or without any chemical challenge.

Page 36 Section 4.3

Individuals who complain of sensitivity or intolerance to environmental chemicals or other agents are frequently referred to mainstream specialist allergy clinics for care.

Unless you can cite some study of people who complain of chemical sensitivity that actually assessed the frequency of their referral to mainstream allergy clinics, you should delete this claim. I have read almost all the MCS literature ever published and am not familiar with any data to support this. The sentence that follows does not support this claim -- just because 50% of patients at a particular allergy clinic present with vasomotor rhinitis, 1/3 of whom complain of smell intolerance-- does not mean that the majority of chemical sensitivity patients are referred to similar clinics!

Page 37

In the past, there have been specific private facilities in Australia catering for the chemically sensitive.

Is this not also still true in the present? Your review should identify these facilities by name and location, or at least provide an estimate of their number. If known, your review should also report how many cases they see per year, and whether this number has been increasing or decreasing over the last few years.

The patient's symptoms are recorded and a diagnosis is made based on diagnostic criteria presented in the literature (MCS: Cullens criteria; CFS and FM: Anon 2003a, b).

I find it hard to believe that the Nova Scotia clinic is using Cullen's (not "Cullens") criteria for MCS. Based on my personal communications with the medical director, I believe they use the 1999 Consensus Criteria.

Page 38

Pharmaceutical treatments for MCS currently do not exist. Psychotherapy, biofeedback and relaxation and other behavioural therapies are regarded as efficacious (Wolf 1996; Stenn and Binkley 1998; Sparks 2000a,b; Bornschein et al. 2001).

⁷ Kipen HM, Fiedler N. 1999. Invited commentary: sensitivities to chemicals--context and implications. Am J Epidemiol;150(1):13-6.

⁸ Kreutzer R. Discussion. Am J Epidemiol;150(1):17.

You should point out that these studies involve very few subjects (Stenn and Binkly 1998 only one) and that behavioral therapies are not rated as highly efficacious by MCS patients themselves, as in the survey conducted by Gibson et al (2003) which you discuss in the following paragraph.

Page 39

The lack of official recognition of MCS as a distinct clinical entity, together with difficulties in establishing aetiology and inconsistencies in the diagnosis of MCS, are reflected directly within the different views clinical views on the approach to treatment/management of MCS as found in the Australian clinical review.

The word “views” appears twice in this sentence -- “the different views clinical view” – which presumably should be “the different clinical views”

Page 39, Section 4.5

The clinical review has highlighted difficulties with agreed criteria for the diagnosis of MCS, identifying an underlying pathological process and treating or managing MCS.

This is misleading. The clinical review highlighted only differences, not difficulties, with agreed criteria for the diagnosis MCS. None of the clinicians who specialize in this illness have any “difficulty” recognizing it, although they clearly do have trouble treating and managing it, which they acknowledge. This is a critical distinction and your review should acknowledge it.

Overall, a number of primary clinical research needs are evident:

- * *Establishing agreed diagnostic criteria that are acceptable to clinical and scientific groups;*

Diagnostic criteria for MCS already exist that are widely used in both clinical practice and research, with the 1999 Consensus Criteria being the most commonly cited. If you think it is important for the Australian government to recommend that only one definition be used henceforth in clinical practice and/or research, then I suggest you simply survey Australian physicians and researchers who specialize in MCS and ask them to vote on which one they want everyone to use. Then give this definition a specific code in the Australian ICD-10 and instruct all physicians in Australia to start diagnosing it by whatever specific criteria are involved. It would be a waste of time and money, however, to try to come up with yet another definition if the majority of Australian MCS clinicians and researchers are willing to use an existing definition!

- * *Determining the prevalence of MCS, for both self-reported cases and those that are medically diagnosed;*

I agree that this is a priority. All Adult Health Surveys conducted by state and federal government agencies in Australia should be required to include the same questions about MCS every year, and to at least ask all adults if a doctor or other health care professional has given them diagnosis of “multiple chemical sensitivity” a) ever and b) in the last 12 months (in order to determine the incidence as well as prevalence) . Do not repeat the mistake of the NSW survey by asking only about the diagnosis of “a chemical sensitivity”

Page 41, Section 5

The lack of agreement on an operational definition, or even an appropriate label, has been a hindrance to scientific analysis and an understanding of MCS.

Virtually the identical sentence appears on page 10, and the same comments apply.

A survey of clinical diagnosis and management of MCS was conducted by clinical medical consultants in two phases.

Your should identify the name of the clinical medical consultants here. Was this survey all by done one consulting firm? Or by one or more individual freelance consultants? Did they have any

relevant experience is conducting such surveys, or were they just the lowest bidder? And most importantly, did they have any prior experience with or knowledge of MCS, and if not, were they given any advance training in MCS and by whom?

Phase 1 consisted of a literature survey ...

You should describe how this MCS literature survey was conducted and how the reviewed papers were selected. Given that the 623 articles on MCS and/or IEI (dating back to 1991) are available from the US National Library of Medicine via www.pubmed.gov, why does this review reference only 189? Were any others consulted but rejected for some reason(s), or were these 189 the only ones reviewed?

Page 44, Section 5.1.4

The workshop sought to reach agreement about:

- * *Recognising likely presentations that would lead to the diagnosis;*
- * *Defining the range of possible management;*
- * *Determining what research might be undertaken to assist in understanding, MCS including diagnosis and management;*
- * *Determining whether any specific education or training programs would be likely to improve the understanding and management of MCS.*

Your review should clarify whether this list of issues that the workshop tried to reach agreement about was compiled by the sponsoring agencies, the consultants who conducted the workshop, or the participants themselves. And given this review's obsession with the lack of agreement on an MCS case definition, why was this not included in the list? Was no attempt made to reach agreement on a case definition?

Page 45, Section 5.2

1. A lack of authoritative published research specifically related to MCS

While there are many articles and books published about MCS in the world literature, much of which is featured on the websites of interest and advocacy groups including papers presented at meetings, little evidence could be found in peer reviewed journals that supported the diagnosis of MCS.

This statement is simply not credible. As noted above, numerous epidemiological studies—including those cited above in Section 4 and especially Kreutzer's replicated study in the peer-reviewed American Journal of Epidemiology (considered by most to be the premiere epidemiology journal in the world)—document that MCS is being diagnosed by physicians in the US, Canada, Germany, England and even Australia at rates similar to those of adult asthma. The diagnosis is "supported" by hundreds of research studies documenting significant differences in both physical and psychological measures between MCS cases (however defined) and non-MCS controls.

Your review should clarify exactly who in this survey claimed that "little evidence could be found in peer reviewed journals" to support the diagnosis of MCS. Only 15 medical professionals were interviewed. Surely this is not the belief of those who make the diagnosis of MCS in their clinical practice, as your review acknowledges in Section 5.3. So how many of the 15 actually believe this? Or is this statement only the summary opinion of the consultants hired to conduct the survey? Were the participants given any MCS literature to review before opining on this question, or were they asked how many MCS research papers they had ever read? Given how little evidence your literature review appears to have considered – as noted above, the references include fewer than 1/3 of the MCS literature published since 1991—it would be more informative to report here how many peer-reviewed MCS studies each participant had ever read.

On the other side of the debate, some clinicians, respected overseas medical organisations

and at least one local clinical organisation stated strongly that MCS is neither a diagnosis nor a syndrome but a range of sometimes disparate disabilities with some common presenting symptoms. Some described the presentations as a somatoform disorder, with symptoms in the

Page 45, Section 5.3

On the other side of the debate, some clinicians, respected overseas medical organisations and at least one local clinical organisation stated strongly that MCS is neither a diagnosis nor a syndrome but a range of sometimes disparate disabilities with some common presenting symptoms.

Your review should either list those “respected overseas medical organizations” on EACH side of this debate, or it should not list either, but it is grossly biased to suggest as this text does that respected medical organizations are to be found only on this side of the debate. As discussed further below, however, many of the position statements described in Section 6 of your review have either been withdrawn or updated. I urge you to keep this section focused on the opinions of the Australian individuals and organizations who were surveyed by your consultants.

Page 51, Section 6

Several American organisations have issued formal statements about MCS pointing out the shortcomings of the MCS diagnosis, the unreliability and misuse of certain diagnostic procedures and the lack of scientific support for and clinical evidence of the alleged toxic effects from environmental chemicals in these particular patients.

This introduction is grossly biased as it is misleadingly suggests that the formal statements on MCS issued by American professional organizations have all been negative in one or more respects. This is not true (see for example the statement of the AAEM which follows in the very next paragraph) and so I recommend that it either be deleted in its entirety or balanced with a second statement of introduction acknowledging that several other American organizations have issued statements recognizing MCS as a real and non-psychiatric disorder.

Page 50, Section 6.1.1, AAEM

In 1965, Randolph founded the American Academy of Environmental Medicine (AAEM), composed mainly of medical and osteopathic physicians practising the principles of clinical ecology. AAEM has published its philosophy in An Overview of the Philosophy of the Academy of Environmental Medicine (AAEM, 1992). This statement suggests that a wide variety of symptoms arising from many different organs may result from biological system dysfunction triggered by environmental stressors in susceptible people (Interagency Workshop, 1998).

Randolph founded the Society for Clinical Ecology in 1965. It was only much later renamed AAEM. The cited overview also does not “suggest” that ... symptoms ... “may result from...” -- this misleading mischaracterization of the AAEM’s position by the Interagency Workshop (sic) should be deleted and the statement itself should be quoted.

Page 50, Section 6.1.2, AAAAI

The American Academy of Allergy, Asthma and Immunology (AAAAI) is the largest medical speciality organisation in the US representing allergists, asthma specialists, clinical immunologists and other allied health professionals.

This description of the organization is unnecessary and should be deleted, but if it is kept, similarly descriptive introductory sentences should be included for each of the other medical organizations in this section. The AAEM above, for example, should be described as “...the largest medical organization in the U.S. representing physicians and other health professionals who specialize in the diagnosis and treatment of environmentally related diseases. “

Page 50, Section 6.1.3, ACP

The American College of Physicians published a position paper in 1989, which was later adopted by the American College of Occupational and Environmental Medicine (ACOEM) until it drafted its own in 1991. It concluded that there is inadequate support for the beliefs and practices of clinical ecology. The existence of an environmental illness as presented in clinical ecology theory must be questioned because of the lack of a clinical definition. Diagnoses and treatments involve procedures of no proven efficacy (American College of Physicians, 1989)

This section should acknowledge that the ACP withdrew this statement over 10 years ago and no longer has any official position on clinical ecology or MCS. This can be verified by contacting the ACP Archives at archives@acponline.org

Page 51 Section 6.1.5, AMA

In 1992, the AMA stated that until accurate, reproducible, and well-controlled studies are available, it believes that MCS should not be considered a recognised clinical syndrome (American Medical Association Council on Scientific Affairs, 1992). The AMA now has no position statement on MCS.

This is incorrect. As discussed in my comments on Section 3 above, the AMA does have a more recent and still current position on MCS, and you should quote it here: “The current consensus is that in cases of claimed or suspected MCS, complaints should not be dismissed as psychogenic, and a thorough workup is essential.” This statement was co-published with the US Environmental Protection Agency, the Consumer Product Safety Commission, and the American Lung Association in 1994 and is both still in print and still available online at the website of the US EPA.

Page 51, Section 6.1.6, CMA

In 1986, the Californian Medical Association Scientific Board Task Force on Clinical Ecology conducted an extensive literature review and reported that there is no convincing evidence supports the hypotheses on which clinical ecology is based, that clinical ecologists have not identified specific, recognisable diseases caused by low-level environmental triggers and that the methods used to diagnose and treat such undefined conditions have not been proven effective (California Medical Association Scientific Board Task Force on Clinical Ecology, 1986).

This section should acknowledge that the CMA withdrew this policy over 15 years ago and reclassified it as a “historical document only.” This can be verified by contacting the CMA at legalinfo@cmanet.org

Page 51, Section 6.1.7, Other (ACSH and AHF)

Other organisations which have issued statements on MCS include the American Council on Science and Health (Orme and Benedetti, 1994) and the American Health Foundation. A review of the mechanisms of MCS by the Environmental Health and Safety Council of the American Health Foundation concluded that:

- * There was no convincing evidence that any olfactory mechanism underlies induction of a sensitised state or triggering of symptoms.*
- * The hypothesis that MCS involves limbic kindling or time dependent sensitisation cannot explain its mechanism because limbic kindling itself is not understood as a mechanism and time dependent sensitisation describes a pattern not a mechanism (Ross et al, 1999).*

This section should acknowledge that the American Health Foundation that published this no longer exists by this name. It was renamed the Institute for Cancer Protection in the late 1990s. See http://www.sourcewatch.org/index.php?title=American_Health_Foundation

A new American Health Foundation, completely unrelated to the old one, was founded in 2002 (see <http://www.americanhealthfoundation.com/about.htm#founder>) but it has no position on MCS.

Whoever compiled this section was clearly biased against the recognition of MCS since they did not include any of the many other organizations that have issued positive statements on MCS. For balance, your review should quote and cite at least a few of these in this section. There are many to choose from, as documented at <http://www.mcsrr.org/factsheets/MCSrecogn.pdf> , including:

- American Lung Association
- Association of Occupational and Environmental Clinics
- National Academy of Sciences, Institute of Medicine
- National Academy of Sciences, National Research Council
- Ontario Medical Association, Committee on Public Health
- World Institute on Disability

Page 51, Section 6.2 US GOVERNMENT

In America, Federal and State government interest in MCS has a relatively long history dating from 1979. The issue has been discussed and examined through workshops and conferences by State governments, Federal agencies, the National Academy of Sciences and professional organisations (Read, 2002). Despite this interest, scientific research into this condition has been limited.

The words “federal” and “state” should not be capitalized in this paragraph. The last sentence is misleading and should be deleted -- obviously no government research into any medical condition is unlimited! What is most significant about the interest of US federal and state government agencies in MCS is not just that they have discussed the issue through workshops and conferences, but that so many state and federal agencies have been funded so many different MCS research studies in the last 20 years, amounting to millions of dollars per year, and that so many—including 25 federal agencies or authorities—have adopted positions that officially recognize MCS in some fashion, as documented at www.mcsrr.org/factsheets/MCSrecogn.pdf

In contrast, this review mentions the MCS interests of only six agencies in the US federal government no agencies of state government. Even if your review cannot list them all, the fact that so many have adopted positions recognizing MCS should be acknowledged here.

Page 51, Section 6.2.1 Agency for Toxic Substances and Disease Registry

The ATSDR keeps a watching brief on the issues surrounding sensitivity to low levels of chemicals. In the past, given the need for additional scientific research, the ATSDR has funded MCS conferences to further well-designed scientific research into MCS aetiology. The first meeting was sponsored by the National Academy of Sciences in March, 1991 and the second was sponsored by the Association of Occupational and Environmental Clinics in September, 1991.

The last sentence is incorrect and should be changed. ATSDR has sponsored several MCS conferences, but it did not sponsor the March 1991 meeting, which was organized at the request of US EPA by the National Research Council’s Board on Environmental Studies and Toxicology, neither of which is affiliated with ATSDR. The first meeting sponsored by ATSDR was the one held in September 1991, and this was only co-sponsored by the AOEC. This section should acknowledge that ATSDR also funded the MCS prevalence study conducted by the California State Department of Health Services (Kreutzer et al 1999).

Page 52 Section 6.2.1 continued

Throughout these efforts, ATSDR has served as a conduit of information about the issues surrounding MCS (Interagency Workgroup, 1998).

This is not true. The ATSDR has done nothing on MCS since 1998. And as noted repeatedly above, the “Predecisional Report” of the Interagency Workgroup 1998 was never completed or published and should not be cited. As documented at <http://www.mcsrr.org/fedmcsgroup/index.html>, the draft is full of errors, misrepresentations and critical omissions. It is also now eleven years out of date, and so to whatever degree your review relied upon this source, I urge you to seek confirmation of its information from more recently published sources or better yet, from agency spokespeople.

Page 52, Section 6.2.2 Department of Defence

Due to the work environments that employees of the Department of Defence (DOD) face, the DOD has sponsored several projects to investigate chronic multi-symptom illnesses, focusing on the relationship between Gulf War illnesses and other diseases such as CFS, MCS and FM. Such projects have included an investigation of dysregulation of the normal neuroendocrine-mediated stress response as a possible mechanism underlying these illnesses. Another study examined neuropsychological function in a group of treatment-seeking Gulf War veterans and non-deployed Gulf era veterans. In 2003, the DOD Appropriations Bill provided US\$ 5.2 million to further fund this research on chronic multi-symptom illnesses (Department of Defence Appropriations Act, 2003).

Your review should also acknowledge here that Department of Defense has also funded at least five epidemiological studies of Persian Gulf War veterans that included questions on MCS and/or chemical sensitivities. In addition, the US Army has diagnosed active duty personnel with MCS and that its Medical Evaluation Board has certified the diagnosis of “Multiple Chemical Sensitivities Syndrome” in Persian Gulf veterans, as documented in www.mcsrr.org/factsheets/MCSrecogn.pdf

Page 52, Section 6.2.3 Department of Veterans Affairs

The Department of Veterans Affairs has funded three Environmental Hazards Centres for the purpose of conducting research on environmental health and toxicology related to military service. Some of the centres performed research into MCS. Detailed studies of those diagnosed with MCS (according to Cullen's criteria) include psychiatric status, neuropsychological function, symptom reports, occupational and economic outcomes, pulmonary function, neurologic status and evaluation of possible triggers. The results from some of these studies have been published (eg. Black et al. 1999, Gray et al. 2002). Black et al. (1999) noted that of 3695 Persian Gulf-War military personnel, 4.6% met Cullen's criteria for MCS, with most reporting they were on Veteran's affairs disability status or receiving Veteran's affairs disability compensation.

In the last sentence, Veteran’s affairs should be written as Veterans Affairs. Your review should acknowledge that the DVA has also funded over a dozen epidemiological studies of Persian Gulf War veterans that included questions about MCS and/or chemical sensitivity (separate from the funding of its Environmental Hazards Centers), and that it has recognized MCS a medical diagnosis in the case of at least one Persian Gulf veteran, as documented in www.mcsrr.org/factsheets/MCSrecogn.pdf

Page 52, Section 6.2.4 National Centre for Environmental Health, Centre for Disease Control

The Centre for Disease Control, NCEH was established to promote health and quality of life by preventing and controlling disease, injury and disability associated with the interactions between people and their environment outside the workplace.

The Centers for Disease Control is plural, not singular, and NCEH is just one of its many Centers.

The impact of its programs is amplified through close interaction with public health departments in every State and with many public, private, and international organisations. Its major activities include biomonitoring for environmental toxicants, lead poisoning surveillance and prevention, birth defects surveillance and prevention, and exigent public health investigations where environmental exposures may be involved (Interagency Workgroup, 1998).

As repeatedly discussed above, the Interagency Workgroup 1998 should not be cited.

NCEH does not have any programs directly devoted to MCS, however, a number of its activities are relevant to the issues surrounding MCS. Through its division of Environmental Health Laboratory Sciences, NCEH has a leadership role in measuring more than 200 toxicants in human biologic samples. Analyses of samples from large population studies have established the extent of exposure in the U.S. population to volatile organic compounds, pesticides, halogenated aromatic compounds (eg. PCBs), toxic metals (eg. lead and cadmium), and environmental tobacco smoke. This information helps to clarify relationships between exposures to toxicants and human health effects (Interagency Workgroup, 1998).

This review should not include any agency that has no position on MCS and no programs devoted to it. I urge you to delete this entire section and replace it with sections devoted to any of the many other agencies and departments of the US government that do recognize MCS in one fashion or another. Most important is the work of the National Institute on Deafness and Other Communication Disorders (part of the National Institutes of Health) whose Chemical Senses Branch has been funding MCS-related olfactory research since NIDCD's creation in 1988; including \$29,583,000 in fiscal year 1998. NIDCD was not included in the Interagency Workgroup because none of the other members of the workgroup were not aware of its existence.

Page 53. Section 6.2.5 National Institute of Environmental Health Sciences (NIHES), National Institute of Health

The NIHES has provided research support for studies related to MCS and to areas of research associated with MCS outcomes, and has supported a number of workshops and meetings concerning MCS to assist NIEHS in developing new and innovative research ideas to better understand MCS (Interagency Workgroup, 1998).

The correct acronym is NIEHS, not NIHES, and you should note that its parent institute, the NIH, is part of the Department of Health and Human Services. You should mention that NIEHS offers information about MCS on its website, including the 1999 Consensus Criteria. And as noted repeatedly above, you should not cite the Interagency Workgroup 1998.

Page 53, Section 6.2.6, US Environmental Protection Agency (USEPA)

For consistency, you should refer to USEPA simply as EPA (or else add the US prefix to the acronyms of all the other federal agencies discussed in Section 6.2)

The USEPA sponsored a Federal government Interagency Workgroup on MCS that was co-chaired by the ATSDR and the NCEH of the Centers for Disease Control and Prevention. A draft report intended to be a guide to public health policy-making and research planning was released for public consultation in August 1998. The draft report provided a public health evaluation of the extent and nature of MCS and recommended future actions for federal agencies to consider.

EPA was a member of the workgroup but did not sponsor it. It was formed by the Environmental Health Policy Committee of the Department of Health and Human Services and co-chaired by the representatives from ASTDR and CDC's NCEH. For confirmation, see <http://www.health.gov/environment/mcs/xiii.htm>

The workgroup concluded that there is a need for research in the areas of case definition, basic epidemiology and challenge studies are necessary to address the concerns surrounding MCS. These recommendations are consistent with those from several expert workshops held since 1990 (Interagency Workgroup, 1998). The report received some criticism from MCS advocates for procedural problems and not including all available literature (Donnay 1999).

I am glad that you acknowledge some of the criticisms of MCS advocates, but your review should note that the most significant criticisms were that the workgroup:

- a) failed to include or even mention any of the many other federal agencies with positions on MCS including NIDCD, which funds more chemosensory research annually than all other federal agencies combined,
- b) failed to disclose the MCS research funding or findings of ANY of the 8 federal agencies that the workgroup did include, and
- c) failed to disclose that relevant affiliation—and obvious conflict of interest—of the consultant hired to draft the report, Dr. Frank Mitchell, who was at the same time a member of the board of directors of the Environmental Sensitivities Research Institute, the anti-MCS organization founded by Dr. Gots and funded entirely by chemical industry interests.

In January 2002, a US Senate Bill (SB 6302) was passed to allow MCS sufferers compensation under the workers' compensation system. Workers seeking compensation for MCS syndrome must prove that their illness would not have occurred but for workplace conditions. If a worker has been diagnosed with MCS syndrome prior to developing a chemically-related occupational disease in the workplace, the worker does not need to prove that the illness would not have occurred but for the work environment. The worker only has to prove that work-related conditions exacerbated the pre-existing MCS syndrome. The worker can only be compensated for conditions resulting from the workplace exacerbation of the condition, not conditions resulting from the pre-existing illness (Senate Committee on Labour, Commerce & Financial Institutions, 2002).

This entire paragraph should be deleted from Section 6.2.6 because it has nothing to do with EPA. It should be put in a separate section devoted to the US Congress, and if such a section is created, it should include the MCS-related appropriations actually passed by Congress rather than unsuccessful examples like this of legislation that only passed the Senate. See for example the DVA/HUD Appropriations Bill for FY1993 signed by President Bush in 1992 appropriating “\$250,000 from Superfund funds for chemical sensitivity workshops.” These funds were used by the ATSDR to co-sponsor scientific meetings on MCS with various other organizations and fund the MCS prevalence study conducted by the California State Department of Health Services (Kreutzer et al 1999). For FY 1998, Vermont Congressman Bernard Sanders proposed and Congress appropriated \$800,000 to start a new 5-year civilian agency research program into MCS among Gulf War veterans.

Other more relevant MCS related actions of various EPA offices that your report should acknowledge (all documented in www.mcsrr.org/factsheets/MCSrecogn.pdf) include:

EPA’s Office of Pollution, Prevention and Toxics, Health Effects Division, Occupational and Residential Exposure Branch, Special Review and Registration Section,

which in a peer-reviewed 1997 memorandum entitled “Review of Chlorpyrifos Poisoning Data” from EPA’s Jerome Blondell, PhD, MPH, and Virginia Dobozy, VMD, MPH, to Linda Propst, Section Head, Reregistration Branch, discussed data from several sources on acute and chronic health effects, including MCS, associated with exposure to Dursban and other chlorpyrifos-containing pesticides. It recommended many changes (subsequently agreed to by DowElanco, the manufacturer) in the use and marketing of these products, including the phase out of all indoor sprays and foggers, consumer concentrates, and all pet care products except flea collars. Most significantly, the memo documents that of 101 cases of unambiguous chlorpyrifos poisoning reportedly directly to EPA in 1995, 38 had chronic neurobehavioral effects (including 4 who also had peripheral neuropathy), while 59 “reported symptoms consistent with multiple chemical sensitivity”

EPA's Office of Radiation & Indoor Air, Indoor Air Division,

which in its August 1989 Report to Congress on Indoor Air Quality, entitled Assessment and Control of Indoor Air Pollution (EPA/400/1-89/001C), describes MCS as “a subject of considerable intraprofessional disagreement and concern (Cullen, 1987). While no widely accepted test of physiologic function has been shown to correlate with the symptoms, the sheer mass of anecdotal data is cause of concern.” In 1991, EPA/IAD asked the National Research Council to sponsor a scientific workshop on “Multiple Chemical Hypersensitivity Syndrome,” the proceedings of which are published in Multiple Chemical Sensitivities: Addendum to Biologic Markers in Immunotoxicology [National Academy Press, 1992]. And in 1994, EPA/IAD co-authored with the US CSPC, AMA and ALA the consensus statement on MCS discussed in Section 6.1.5 above.

EPA Office of Research & Development,

which in 1987 described “chemical sensitivity” as an “ill-defined condition marked by progressively more debilitating severe reactions to various consumer products such as perfumes, soaps, tobacco smoke, plastics, etc.” in The Total Exposure Assessment Methodology (TEAM) Study, (Summary and Analysis: Volume 1, by Lance Wallace, Project Officer, Environmental Monitoring Systems Division, EPA Office of Research and Development). EPA/ORD then began conducting human subjects chamber research at its Health Effects Research Branch in Chapel Hill in 1992 to identify possible diagnostic markers of MCS. In the 1997 justification for its fiscal year 1998 budget, ORD devotes one paragraph to MCS in the section on Air Toxics, saying that it plans to release “information comparing individuals who identify themselves as belonging to a particular subgroup (multiple chemical sensitivity) against established norms for a variety of health-related endpoints,” and will make “recommendations for follow up to evaluate the potential relationship between the signs/symptoms reported by these individuals and objective/quantitative health endpoints”

Page 54, Section 6.2.7, Social Security Administration and Department of Housing and Urban Development

The US Social Security Administration granted affected individuals protection under the US Social Security Act (Donnay, 1999). In 1992 the Department of Housing and Urban Development stated that MCS is a "handicap" under the Fair Housing Act, and people with MCS can seek protection or "reasonable accommodation" under federal housing discrimination laws (Orme & Benedetti, 1994).

SSA and HUD are not related. SSA is actually part of the Department of Health and Human Services, while HUD is a separate department. Your review should devote a separate section to each, and these paragraphs should correctly state the policies of SSA and HUD with respect to MCS, both of which are mis-stated in the above paragraph. As documented in www.mcsrr.org/factsheets/MCSrecogn.pdf, SSA has officially recognized MCS ‘as a medically determinable impairment’ on an agency wide basis since 1997 and as far back as 1997 said that evaluation of disability claims “should be made on an individual case by case basis to determine if the impairment prevents substantial gainful activity.” HUD affirmed in 1990 that it recognized “MCS as a disability entitling those with chemical sensitivities to reasonable accommodation under Section 504 of the Rehabilitation Act of 1973” and also “under Title VIII of the Fair Housing Amendments Act of 1988.” This was followed in 1992 by a formal guidance memorandum from HUD Deputy General Counsel G.L. Weidenfeller to all regional counsel, detailing HUD's position that MCS and environmental illness “can be handicaps” within the meaning of section 802(h) of the Fair Housing Act and its implementing regulations.

Some American States, including Florida, have passed legislation creating a pesticide notification registry for persons with MCS. Typically, these registries require that pesticide application to adjacent property is notified in advance to those on the registry. Medical certification of chemical sensitivity is usually required before residents can enroll on the register (Interagency Workgroup, 1998).

Medical certification of chemical sensitivity is NOT usually required. Such certification is required only in Florida. It is not required by the pesticide notification registries established in at least 10 other states, as documented in www.mcsrr.org/factsheets/MCSrecogn.pdf.

Some jurisdictions, including the cities of San Francisco, Santa Cruz and the State of Washington, include MCS within their disability access regulations and recommendations. Generally these policies call for well-ventilated, 'chemical-free' rooms that use less toxic building materials, furnishings, floorings and supplies than traditional building methods. These policies require the public to be notified of any areas undergoing renovations or pesticide application prior to commencement, as well as the provision of 'chemically-free' medical treatment facilities.

I am pleased that your review includes examples of MCS recognition by US state and local governments, but they should be discussed in a separate sections (one for state governments and one for local governments). They also should be described correctly, which they are not in above paragraph. For correct descriptions of the MCS policies of San Francisco, Santa Cruz, the State of Washington and other US state and local governments, see www.mcsrr.org/factsheets/MCSrecogn.pdf.

Page 54, Section 6.2.8, MCS in the US Courts

In the USA, legal activity and consequences surrounding MCS has been noted to outpace the science (Gots 1995). Some courts have recognised MCS as a compensable disease whereas others disregard causation and award benefits to the plaintiff considered disabled by a somatisation disorder or psychological impairment. This is despite the equivocal scientific evidence that MCS is an organic disease (Barrett, 2000a).

Both Gots and Barrett have served as defense expert witnesses paid to testify against MCS plaintiffs. If you must quote their opinions regarding MCS, you should acknowledge their bias and preface the first sentence by saying that "In the USA, defense witnesses in MCS litigation have opined that ..." There really is no evidence in Gots' 1995 article (or any since) to support the claim that legal activity surrounding MCS has outpaced the science.

Barrett 2000a should not be cited at all since this reference is not a peer-reviewed article but a page from his personal website. Although your citation gives the correct url address, <http://www.quackwatch.org/01QuackeryRelatedTopics/mcs.html>, the publication year should be changed 2005 to match the last revision date at the bottom of the page.

Regardless of their legal opinions, most MCS legal cases in the US do not depend on the science as they focus on issues of disability and discrimination which, according to most US laws, are supposed to be evaluated independently of diagnosis. Legal arguments over diagnoses and claims of causation are usually only relevant in workers' compensation and toxic tort cases.

Some courts have excluded testimony by MCS proponents on the grounds that MCS lacks scientific corroboration and does not fulfill these criteria (see Barrett, 1998 for a list of MCS court cases).

Since Barrett 1998 lists only those MCS court cases that have been decided against MCS plaintiffs, your review should add a paragraph describing at least some of the many MCS court cases that have been decided in favor of MCS plaintiffs. These include federal toxic tort cases in which plaintiff experts have been allowed to testify about MCS despite being challenged under the Daubert rule and cases involving the rights of MCS patients under the Fair Housing Act, Rehabilitation Act, and Social Security Act. MCS plaintiffs have also won cases in US state courts involving discrimination in housing, employment, and health care services, workers' compensation, and toxic torts. Examples of each are documented in www.mcsrr.org/factsheets/MCSrecogn.pdf.

Page 54, Section 6.3, Canadian Government

The Canadian Government first examined the problem of MCS in 1985 and has since sponsored several workshops to aid the understanding of the complex issues surrounding MCS.

This claim should be referenced or deleted. As documented at www.mcsrr.org/factsheets/MCSrecogn.pdf, the earliest recognition of MCS in Canada was in 1985 but it did not come from the Canadian federal government. It came from the Ontario Ministry of Health, which appointed and commissioned an Ad Hoc Committee on Environmental Hypersensitivity Disorders. The report it issued in 1985 was subsequently reviewed and for the most part endorsed in the Ministry's 1996 "Report of the Advisory Panel on Environmental Hypersensitivity." The Ministry sponsored a networking workshop for MCS clinicians and researchers in 1990 and every year since it has funded a variety of MCS medical research projects. In 1994, it provided \$1.5 million for the creation of a new environmental health clinic at the Womens' College Hospital in Toronto which will focus on diagnosis and treatment of environmental hypersensitivity/MCS.

Your report should at least acknowledge if not detail the other Canadian provincial and federal government agencies that have recognized MCS in some fashion. These include:

Canada Department of Finance
Canada Mortgage and Housing Corporation (a federal "Crown Corporation")
Canadian Human Rights Commission
Department of National Health and Welfare (now Health Canada, a cabinet department)
Nova Scotia Department of Health
Ontario-Carelon Regional District Health Council
Ontario Management Board Secretariat
Ontario Ministry of Housing
Ontario Ministry of the Solicitor General, Office of the Chief Coroner

Page 55 Section 6.3 continued

The municipality of Nova Scotia has established Environmental Health Centres for the treatment and care of people who identify themselves as suffering from chemical sensitivities.

This is incorrect. Nova Scotia is a province, not a municipality, and as documented at www.mcsrr.org/factsheets/MCSrecogn.pdf, its Department of Health established just one Environmental Medicine Clinic (later renamed the Nova Scotia Environmental Health Centre) . I recommend that you include a link to the clinic's website in this section:

<http://www.cdha.nshealth.ca/default.aspx?page=SubPage&category.Categories.1=265¢erContent.Id.0=7664>

Page 55 Section 6.5 German government

[to be consistent with Sections 6.2 and 6.3, Government should be capitalized in this title]

Germany is often reported to be the only country to "officially recognise" MCS, since it is included in the alphabetical index of the German version of the International Statistical Classification of Diseases and Related Health Problems (ICD-10-SGB-V) published in November 2000 by the German Institute of Medical Documentation and Information (DIMDI). While MCS is included in the alphabetical listing of the ICD-10-SGB-V, it is important to note that this index is a collection of phrases or diagnoses used by some German clinicians and is not a list of diseases "officially recognised" by Germany. Not all phrases are used or indeed recognised by clinicians.

This section is devoted to recognition of MCS by the German Government. Whether the phrase MCS is used or recognized by clinicians is irrelevant and so the last sentence in this paragraph should be deleted. (Obviously there are still physicians in all countries who do recognize MCS!)

As is the case for MCS, some phrases have not been allocated a unique disease code, as the phrase does not represent a distinct disease entity. Germany's DIMDI has stated that even though MCS may be incorporated in the ICD-10-SGB-V alphabetical listing, this does not imply that it is a recognised disease (M. Schopen, DIMDI, Personal Communication, 2004).

As discussed above in Section 2.6, this information is incorrect and misleading. The phrase MCS in the German ICD-10 index is in fact linked with a unique disease code, #T78.4. This code should be acknowledged and cited in this section.

Page 56, Section 6.5.2 British Society for Allergy, Environmental and Nutritional Medicine

The statements of the BSAENM differ from those of other medical organisations.

This sentence should be deleted. The statements of the BSAENM on MCS are actually very similar to that of another UK medical organization, the British Society for Ecological Medicine.

Page 56, Section 6.5.3 Institute of Occupational Medicine, Edinburgh

The Institute of Occupational Medicine, Edinburgh conducted a comprehensive review of the MCS literature in 1999 for the UK Health & Safety Executive.

This statement is incorrect. The review included less than half the published literature on MCS and so should not be called “comprehensive.” I urge you to instead describe this as a “limited” or “partial” review of the MCS literature. The authors themselves describe their literature review as “systematic” in their abstract but acknowledge that from among several hundred references identified, only (71) key papers were selected.

The purpose of the review was to determine whether there was convincing evidence that low-level exposure to environmental chemicals could result in a clinical response in some people.

This statement is incorrect. According to the abstract, the review focused on considering two questions: “does MCS exist and what causes MCS.”

This review was presented to the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment which undertakes independent scientific and medical reviews of chemicals and advises the Department of Health's Chief Medical Officer. The Committee agreed that on the basis of current knowledge, there was insufficient evidence to make comments on potential mechanisms of MCS or to recommend further research in this area (Read, 2002).

The last sentence of this paragraph is copied verbatim from Read 2002 and so should be placed within quotation marks. Your review should note that the committee’s recommendations do not agree with the conclusions of Graveling et al., who recommended further research in many areas. They concluded—as should you—that “Current evidence does not prove beyond reasonable doubt, in all cases, the existence of a condition fitting the review criteria for MCS, but available evidence in some people cannot be ignored and warrants further investigation.”

Page 56, Section 6.6 New Zealand government

[to be consistent with Sections 6.2 and 6.3, Government should be capitalized in this title]

I am not familiar with the history of MCS research, claims and policy in New Zealand and have not reviewed these sections of Read 2002 to see his information on New Zealand is accurately presented here. But given how many other errors and misrepresentations I have found in Section 6 of this review, I urge you to verify that all the statements attributed to Read 2002 are in fact accurately reported.

Page 57, Section 6.7 Danish government

[to be consistent with Sections 6.2 and 6.3, Government should be capitalized in this title]

As with New Zealand, I am not familiar with the history of MCS research, claims and policy in Denmark. I also have not reviewed Silberschmidt 2005 and so cannot comment on the accuracy of the information in this section. Obviously, someone should fact check it carefully!

The Danish MCS Organisation has approached the Danish Environmental Protection Agency

regarding the reduction of scents in the environment.

Your review should give the name of this MCS organization and, if known, both the year in which it approached the Danish EPA and the response it received.

Page 57, Section 6.8 INTERNATIONAL PROGRAM ON CHEMICAL SAFETY (WHO/ILO/UNEP)
[to be consistent with Sections 6.2 and 6.3, the I, P, C and S in IPCS should be capitalized]

Invited participants represented a range of disciplines involved in researching, investigating, and treating MCS and other environmental illnesses.

This statement is false and misleading. Of the 17 invited participants, only 7 had ever published anything on MCS or treated MCS patients, and none have ever publicly attached their name to this document. (I was able to check their MCS experience because one of the participants provided me with a list of both participants and observers on IPCS letterhead, as well as the original report.)

The recommendations of the workshop included DBPC challenge studies to distinguish psychogenic from toxicogenic origins and epidemiological research directed at the prevalence of relevant symptoms and correlates such as demographics and time trends and the

The research recommendations (on page 3 of the original report) specify “Challenge studies to distinguish psychogenic from toxicogenic or other responses are deemed essential and urgent.” The recommendations do NOT specify “DBPC” challenge studies and so the DBPC acronym should be deleted.

Page 58, Section 6.8 continued

concurrent presence of other disease states, such as CFS and sick building syndrome (IPCS, 1996).

The recommendations regarding epidemiological research specify “... the concurrent presence or absence of known and unexplained conditions (e.g. Chronic Fatigue Syndrome (CFS), “Gulf War Veterans’ Illnesses”).” They say nothing about sick building syndrome and so this should be deleted.

Finally, and for the last time, you must change this citation and the associated reference from IPCS 1996 to Anon. 1996. The disclaimer printed at the bottom of the first page of the original anonymous and unpublished “Conclusions and Recommendations of a Workshop on “Multiple Chemical Sensitivities (MCS)” –which also appear at the bottom of the first page of the anonymous version that Dr. Gots arranged for RTP to publish with a grant from his ESRI organization—is quite clear: “These conclusions and recommendations contain the collective views of an international group of experts and do not necessarily represent the decisions or the stated policy of the United Nations Environment Programme, the International Labour Organization, or the World Health Organization.” Neither do they represent the IPCS, which have never published any statement on MCS or IEI. The most that can accurately be said of IPCS is that it co-sponsored the workshop.

Page 59-72 References

I have not checked the references for their accuracy, but obviously someone should. I recommend that some notation be added to distinguish those references that were not published in peer-reviewed journals.

Appendix A. Citations in text that are missing from the list of references

Garrity 1994

McCaffrey 2000

Miller 1991

Miller 1998

Miller et al 1997 (refs include only Miller alone in 1997)

Osterberg et al. 2005

Osterberg et al., 2007

Pennebaker 1994

Staudenmayer et al 2000 (refs include only Staudenmayer alone in 2000)

Thomas et al., 2006