

**A SCIENTIFIC REVIEW OF MULTIPLE  
CHEMICAL SENSITIVITY: IDENTIFYING  
KEY RESEARCH NEEDS  
Working Draft Report**

**SUBMISSION**

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**On behalf of**

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Thank you for the opportunity to comment on your Working Draft. We are sorry that there is so much in it that requires comment. To reduce repetition comments on the Preface and Overview are under the relevant subject headings. There are also notes on references in the attached Word copy using MS Word's review layout.

## **2 UNDERSTANDING MULTIPLE CHEMICAL SENSITIVITY**

### **2.1 WHAT IS MULTIPLE CHEMICAL SENSITIVITY?**

Rather than providing a straightforward description, the first three sentences of the Working Draft sum up its failure to come to grips with the scientific literature and concepts relating to MCS.

- The Working Draft starts on page 6 with:

*Multiple Chemical Sensitivity (MCS) is one of the terms used to describe a complex array of symptoms where the underlying aetiology [sic]/cause(s) remains uncertain and ill defined.*

*There are reports linking MCS to a wide range of environmental agents (including chemicals) and other factors. A common theme reported by individuals is the experience of heightened responsiveness to very low levels of chemicals.*

“One of the terms” suggests that MCS is also known by a number of equivalent and equally valid terms but this is not the case (see below). “Heightened responsiveness to very low levels of chemicals” is not merely “a common theme”; it is the defining characteristic of MCS. “A wide range of environmental agents (including chemicals) and other factors” downgrades the part played by chemicals. “Cause(s) remains uncertain and ill defined” denies the evidence that exposure to pesticides and other toxic chemicals initiate many cases of MCS. The common theme of the Working Draft appears to be minimising the role of chemicals in Multiple Chemical Sensitivity.

It is worth contrasting the Working Draft introduction with that of the section, ‘Sensitivity to Chemicals and Multiple Chemical Sensitivity in Gulf War Veterans’ from the recent report by the Research Advisory Committee on Gulf War Veterans’ Illness (2008:278):

The condition referred to as multiple chemical sensitivity (MCS), like CFS and FM, is characterized by diverse types of symptoms in the absence of other explanatory conditions. The unique hallmark of MCS is that these symptoms are exacerbated by exposure to common chemicals (e.g. household cleaners, motor vehicle exhaust, perfumes, paint, pesticides, tobacco smoke) at levels that do not cause symptoms in healthy individuals. ... About half of MCS patients

report that their condition first developed after identifiable exposures to chemicals of various types, such as remodeling their home, occupational exposure to solvents, or exposure to agricultural pesticides.<sup>212,1044</sup> [Caress et al (2002), Miller and Pihoda (1999)].

- The Working Draft says on Page 9,

*Multiple chemical sensitivity (MCS) is the term most commonly used to describe a disorder which is characterised by a broad array of physical, psychological and emotional symptoms, the cause of which is attributed to exposure to extremely low levels of a wide variety of environmental chemicals*

What characterises MCS is not the symptoms, but that symptoms occur with exposure to low levels of chemicals (see eg Saito et al. 2005).

- The Working Draft says on Page 9,

*controversial discipline of ‘clinical ecology’*

“Controversial” should be deleted as it is prejudicial, uninformative and unsupported by evidence in the Working Draft. Also ‘clinical ecology’ has been known as ‘Environmental Medicine’ since 1981.

- The Working Draft says on Page 9,

*Although MCS is the most common term used to describe this disorder, there are many other terms that are used to describe the range of symptoms that contribute to the disorder described as MCS. Some of these terms are as follows:*

- *Idiopathic Environmental Intolerance (IEI)*
- *Environmental illness*
- *Chemical acquired immune deficiency syndrome (Chemical AIDS)*
- *20th Century disease*
- *Cerebral Allergy*
- *Chemical sensitivity or intolerance*
- *Environmental hypersensitivity*
- *Toxic encephalopathy*
- *Toxicant-induced loss of tolerance (TILT) (p. 9)*

This list is remarkably similar to one in *Multiple Chemical Sensitivities* by the Environmental Risk Management Authority New Zealand (Read 2002). If it is to be included in the report then the source should be referenced. The report should also distinguish between terms currently in scientific use, terms used historically and terms invented by the media. OCS/NICNAS should have tried Googling each term before including it.

These terms don't all describe MCS. It is particularly important to understand that some of them, eg chemical sensitivity and toxicant-induced loss of tolerance (TILT), refer to disorders involving sensitivity to chemicals, and MCS is one or a subgroup of those disorders. Rea (1992:8) described chemical sensitivity as

an adverse reaction(s) to ambient levels of toxic chemical(s) contained in air, food, and water. The nature of these adverse reactions depends on the tissue(s) or organ(s) involved, the chemical and pharmacologic nature of the substance(s) involved (i.e., duration of time, concentration, and virulence of exposure), the individual susceptibility of the exposed person (i.e., nutritional state, genetic makeup, and toxic load at the time of exposure), and the length of time and amount and variety of other body stressors (i.e. total load), and synergism at the time of reaction(s).

Ashford and Miller (1998:173) said,

We are not persuaded that multiple symptoms involving several organ systems are the only manifestation of toxicant-induced loss of tolerance. Single organ systems may be involved. Further, subsets of conditions with other labels, such as intrinsic asthma, migraines, depression, or chronic fatigue syndrome, may well be due to a toxicant-induced loss of tolerance.

Although the Working Draft's brief is only to examine MCS, understanding MCS involves understanding that it is part of this bigger picture. The Working Draft asks whether MCS is related to other disorders or syndromes. MCS is related to other disorders involving chemical sensitivity – it is the general mechanism that is important, not the symptoms. There is evidence linking an extensive range of diseases to chemical sensitivity in Ashford and Miller (1998:345-358) and Rea (1996).

In the U.S. Material Safety Data Sheets for organophosphate pesticides commonly say,

Repeated exposure to cholinesterase inhibitors may, without warning, cause increased susceptibility to doses of any other cholinesterase inhibitor.

and

**MEDICAL CONDITIONS GENERALLY AGGRAVATED BY EXPOSURE:**  
Any disease, medication, or prior exposure which reduces normal cholinesterase activity may increase the susceptibility to the toxic effect of the active ingredient. (eg U.S. Department of Health & Human Services 2008)

This is a form of chemical sensitivity (Lieberman 2003).

In Australia the government and medical profession have shown very little interest in chemical sensitivity, but the significant size of the problem can be seen in the growing number of products aimed at people who are sensitive to fragrance or other chemicals.

Unilever Australia and Unilever New Zealand (2009) state on their website, “Omo Sensitive and Omo Sensitive Front Loader with no added perfumes or dye are the best option for people with sensitivities.” These products were not developed solely for people with MCS.

- The Working Draft says on Page 9, pages 13-14 and page 57,

*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. (p. 9)*

*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). (p. 13-14)*

*Invited participants represented a range of disciplines involved in researching, investigating, and treating MCS and other environmental illnesses. (p. 57)*

However, Ashford and Miller (1998:279-284) say of this workshop, ‘The four “NGO representatives” were full-time employees of BASF, Bayer, Monsanto, and Coca Cola, the first three of which claimed affiliation with an industry-funded science institute (the European Centre for Environment and Toxicology).’ Ronald Gots, director of the Environmental Sensitivities Research Institute, whose members included DowElanco, Monsanto, Procter and Gamble, and the Cosmetic Toiletries and Fragrances Association, was a participant and ‘was also invited to give the “U.S. perspective” on MCS’. Various outside “observers”, some of whom were involved in a lawsuit about “wood preservative syndrome”, were involved in drafting and possibly voting on the recommendations. After certain participants wrongly claimed that IEI was now WHO’s official name for MCS and IPCS received a letter of protest from 80 prominent U.S. scientists and physicians, ‘IPCS clarified the status of the IEI name by issuing a notice stating that WHO had “neither adopted nor endorsed a policy or scientific opinion on MCS.”’ The report now contains disclaimers, including ‘that the document does not necessarily represent the decisions or stated policy of UNEP, ILO, or WHO, that it does not constitute a formal publication; and that it should not be reviewed, abstracted or quoted without the written permission of the Director of the IPCS.’

The Working Draft’s comments on this workshop are misleading and inappropriate. The statement that WHO favours the term “Idiopathic Environmental Intolerances” is incorrect.

It is also wrong to say that “Idiopathic Environmental Intolerance or IEI ... does not make inferences with regards to causative agents”. Idiopathic means “of unknown cause” so it denies the possibility that MCS can be initiated by chemical exposure. And there is a growing body of evidence pointing to the cause(s) of MCS (Pall 2007) making the term IEI obsolete and inaccurate.

- The Working Draft says on Page 9,

*This is an important concept as the search for single causative mechanisms and single treatment regimes will not be fruitful if there are a number of conditions existing under the general label of MCS*

This observation should inform the whole of this report, but it doesn't.

- The Working Draft says on Page 9,

*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*

It has been used as an excuse not to recognise MCS, assist people with MCS or fund research into MCS. It needn't be a barrier to research. In the U.S. the National Institute of Health's 2005-2008 funding for research into MCS was zero, but their funding for research into Chronic Fatigue Syndrome was \$22 million (U.S. Department for Health & Human Services 2008a), despite the CDC stating that “The cause or causes of CFS remain unknown ...” (Centers for Disease Control and Prevention 2007).

The lack of agreement is part of the politics of MCS. This report should acknowledge that certain industries have a financial interest in promoting the view that MCS is psychological and preventing research that would prove otherwise, and that certain doctors and researchers have assisted them. McCampbell (2001) is very instructive in this matter.

## **2.2 WHAT ARE THE SYMPTOMS OF MCS?**

- The Working Draft says on Page 10,

*A recent review by Lacour et al (2005) noted also the preponderance of nonspecific CNS symptoms, such as headaches, fatigue and cognitive deficits in self-reported MCS subjects.*

It is important to note that although these are very common symptoms, many individuals with MCS have other symptoms when exposed to chemicals which are more disabling, eg asthma, migraine headaches, seizures or Crohn's disease.

## 2.3 IS MCS RELATED TO OTHER SYNDROMES OR DISORDERS?

- The Working Draft says on Page 11,

*Other syndromes and disorders have been reported to either cause MCS or predispose patients to MCS*

For more comprehensive and evidence-based lists of medical conditions linked to chemical sensitivity see Ashford and Miller (1998) and Rea (1996),

- The Working Draft says on Page 11,

**Table 2. Syndromes that may be associated with MCS**

<b>Syndrome</b>	<b>Possible Triggers</b>
<i>Sick building syndrome (SBS)</i>	<i>Poor building ventilation and volatile organic compounds</i>
<i>Dental amalgam-induced mercury toxicity</i>	<i>Mercury exposure</i>

As far as we can ascertain in our literature searches, the term ‘Dental Amalgam-Induced Mercury Toxicity Syndrome’ has only been used by Staudenmayer and this Working Draft. We find it hard to justify using the term in this context.

- The Working Draft says on 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)*

This statement is not at all accurate and should be deleted. Staudenmayer et al. may not have been able to find evidence but it is out there, for example see the Research Advisory Committee on Gulf War Veterans’ Illnesses (2008) or see the case studies of RADS in Brooks et al. (1985). It’s not appropriate to depend on just one heavily biased article which ignores much relevant research. See Pall (2007:218-225) for analysis of Staudenmayer et al (2003b).

## 2.4 WHAT TRIGGERS THE SYMPTOMS OF MCS?

- The Working Draft says on Page 13,

*Reported chemical triggering agents for MCS are diverse and often chemically unrelated. Research reports suggest that there is likely to be a psychogenic component in the aetiology of MCS.*

There are a number of problems with this paragraph:

- it is a non sequitur;
  - the first sentence is ambiguous. Presumably you mean “chemical triggering agents for symptoms in people with MCS” rather than “chemicals that initiate MCS”;
  - the second sentence is inaccurate and misleading because research reports that could be said to “suggest that there is likely to be a psychogenic component in the aetiology of MCS” are in the minority. They were in the minority in 1999 (MCS R&R 2000) and since then research into physiological mechanisms has leapt ahead while research into “a psychogenic component” has stagnated, and still doesn’t offer adequate explanations of proposed psychogenic mechanisms;
  - there are no references.
- The Working Draft says on Page 13,

*QUESTION: are there additional triggers identified in MCS?*

Yes, see Rea (1994) *Chemical Sensitivity Volume 2: Sources of Total Body Load*.

## **2.5 CAN MCS BE CLINICALLY DEFINED?**

- The Working Draft says on Page 13,

*Ashford and Miller (1991) argued that Cullen’s criteria are too narrow to be used in clinical settings. They proposed a definition based on one used by the journal Clinical Ecology, with an additional statement that can be used for diagnostic purposes. Their definition stated that: “MCS is a chronic multisystem disorder, usually polysymptomatic, caused by adverse reactions to environmental incitants, modified by individual susceptibility and specific adaptation”.*

That isn’t Ashford and Miller’s definition of MCS. It is the one from the journal Clinical Ecology, but in the journal it is a definition for ecologic illness. Ashford and Miller’s definition (1989) (quoted in both editions of their book, *Chemical Exposures: Low Levels and High Stakes*) is this operational one:

The patient with multiple chemical sensitivities can be discovered by removal from the suspected offending agents and by rechallenge, after an appropriate interval, under strictly controlled environmental conditions. Causality is inferred by the clearing of symptoms with removal from the offending environment and recurrence of symptoms with specific challenge.

- The Working Draft says on Page 13,

*For diagnosis, Ashford and Miller (1991) additionally proposed that a patient could be shown to have MCS under carefully controlled double-blinded conditions when, upon removal of the offending agents, their symptoms*

*cleared and returned when rechallenged by the specific agents.*

This is also inaccurate. Ashford and Miller (1998) said, “Challenges conducted for research purposes should be performed in double-blind, placebo controlled manner. They did not say that double-blind testing was necessary for diagnosis.

- The Working Draft says on Page 13,

*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*

This is illogical because the case definitions referred to don’t exclude the possibility of using objective measures, eg before and after a challenge test in an ECU. Many people with MCS have symptoms that are easily measured, such as asthma or a drop in blood pressure.

- The Working Draft says on Page 14,

*Bartha et al. (1999) also noted that a diagnosis of MCS can be excluded if another single multi-organ disorder can be attributable to the entire spectrum of signs and symptoms resulting from a chemical exposure.*

What Bartha et al. (1999) said was, “MCS should be excluded only if a single other multi-organ disorder can account for both the entire spectrum of signs and symptoms and their association with chemical exposures, such as mastocytosis or porphyria, but not CFS or FM, which are not so associated.” Your paraphrasing doesn’t mean quite the same thing. It’s not just the spectrum of signs and symptoms that matters – it’s that they are reactions to chemical exposures.

## **2.6 DOES MCS HAVE A DISEASE CLASSIFICATION?**

- The Working Draft says on Page 15,

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

It is recognised in Germany, as you state in the paragraph immediately following the above statement.

- The Working Draft says on Page 15,

*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)*

We have grave difficulties with this statement, 1) isn't listing a disease in an ICD code a high level of official recognition? 2) If the substance of this *pers com* is accurate and valid then we would expect to find published evidence of it. *Pers com* is inadequate on such an important point as this. Find and reference the published source or delete this part and reconcile this paragraph with the preceding one sentence paragraph.

- The Working Draft says on Pages 15 & 16,

*While the experts involved in considering this proposal in 2003 agreed that there is a set of symptoms that represents an important clinical problem, the proposal for a unique code in ICD-10-AM for MCS was rejected on the following basis (J Rust, NCCH, Personal Communication, 2004):*

- *There is no clinical or laboratory evidence of an underlying pathological process in patients who have acquired this descriptive label, despite many attempts to identify one over the past 20 years;*
- *There is a wide spectrum of intolerance/irritation from smells and fumes in the general population and it is not possible to draw any clear dividing line to delineate patients who might fall into the category of the proposed classification;*
- *There are no internationally accepted diagnostic criteria, nor validated diagnostic tests;*
- *There are a number of syndromes (i.e. symptom complexes) that appear to overlap with the clinical features proposed for the category of MCS such as CFS and FM. The relationship between these entities and MCS syndrome is unclear at present and this creates difficulty with diagnostic categorisation.*

For such a strong and important statement (and following dot points) there should be supporting material presented. *Pers com* is thoroughly inadequate, particularly since you have cited authors in this document whose papers contradict the first dot point (see Pall 2007, In Press). Also, it is easy to draw a clear dividing line between people who are annoyed by smells and fumes, and those who experience symptoms when exposed to them, whether or not they can smell them. As the distinguishing feature of MCS is that symptoms occur with exposure to low levels of chemicals most lay people can tell the difference between MCS and CFS or fibromyalgia, and understand that some people have more than one condition. There is no valid reason why the NCCH should have difficulty with this. The overlap in symptoms between CFS and FM apparently doesn't create difficulty with diagnostic categorisation.

## **2.7 DO INDIVIDUALS WITH MCS SHARE COMMON CHEMICAL EXPOSURES?**

- The Working Draft says on Pages 16,

*Currently, there are no epidemiological data that link MCS subjects or those who may be susceptible to MCS with particular chemical exposures or lifestyles. In the published literature, MCS subjects generally are described as female, between the ages of 30-50 years, and with an above-average socioeconomic status (Black et al. 1990; Asford [sic] & Miller, 1991; Cullen et al. 1992; Sparks et al. 1994; Lax and Henneberger, 1995; Miller & Mitzel, 1995; Fielder & Kipen, 1997; Levy, 1997). (p. 16)*

It is very odd that the Working Draft cites Miller & Mitzel (1995) as evidence that MCS subjects “generally are described as female, between the ages of 30-50 years, and with an above-average socioeconomic status”, but fails to mention that their study found that:

Pesticide-exposed and remodeling-exposed multiple chemical sensitivity groups reported similar patterns of symptoms and identified similar inhalants and ingestants as triggers for their symptoms; these results suggested a common mechanism (biological and/or psychological) for their conditions. The pesticide-exposed group, however, reported significantly greater symptom severity than did the remodeling-exposed group, especially for neuromuscular, affective, airway, gastrointestinal, and cardiac symptoms.

For information about epidemiological studies, read the section entitled ‘Epidemiological Studies’ in Ashford and Miller (1998: 211-218).

Further, in the case of Gulf War veterans, this group is not characterized as “as female, between the ages of 30-50 years, and with an above-average socioeconomic status” and this exception has important implications which should be discussed here. Also, in their prevalence study of MCS in Atlanta, Georgia, Caress and Steinemann (2003) found that 32.4% of people with MCS developed it before the age of twenty and 35.2% developed it between 21 and 35.

- The Working Draft says on Pages 17,

*Overall, available data are currently inadequate to identify individuals who are at risk of developing MCS on the basis of the type or extent of their chemical exposures. (p. 17)*

Ashford and Miller (1998:235) wrote, “there is accumulating evidence that exposures to organophosphate pesticides, volatile organic chemicals in sick buildings, and various solvents may initiate MCS, based upon observations by independent scientists looking at different groups of individuals. Near-simultaneous onset of MCS in a group of individuals following an identifiable exposure event strongly suggests causation.” They listed over a dozen studies – there have been more in the ten years since they wrote the second edition of

their book. Exposure to organochlorine pesticides has also been linked to MCS (eg Rea et al. 2001).

There is adequate data to identify individuals at risk of developing MCS on the basis of their chemical exposures. What is unknown is how high the risk is. Some individuals are likely to be at higher risk for genetic or other reasons.

- The Working Draft says on Pages 17,

*The new Australian National Occupational Disease System developed in 2007 is noted.*

Why and how specifically is this relevant?

- The Working Draft says on Pages 17,

*The Australian Safety and Compensation Council (ASCC) has developed the Australian Hazard Assessment database (AHEAD) which contains data arising from surveys of workers self reported exposures and measures of actual exposure. The data base will also cover chemical exposures. It is anticipated that the top line findings from the initial survey data are expected to be published by ASCC in mid 2008.*

The purpose of this paragraph isn't made at all clear. Is MCS somehow a part of this 'initial' survey and exposure data base? What about other sources of exposure, eg pesticides in the home or local area? Have any findings been published yet?

### **3 WHAT CAUSES MULTIPLE CHEMICAL SENSITIVITY**

- The Working Draft says on Pages 18,

*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 exposure. It is also possible that both physiological and psychological factors play a part in the pathogenesis of MCS*

Actually there isn't much debate any more. The psychogenic camp prefer to ignore the

scientific evidence the physiological camp are coming up with (eg see Pall's comments on Staudenmayer's work (Pall 2007))

What physicians *believe* is irrelevant. This report should be critically analysing scientific evidence. This passage should be deleted because it is unnecessary and misleading in this context. There appears to be a double standard in this report: physiological theories are criticized for lack of evidence but no evidence is required to support psychological theories. Yet despite the lack of critical assessment of the psychological theories in this Working Draft they are presented here as equally valid views in the debate, that is bad science. In Pall (2007) there is a worthwhile and thoughtful critique of the psychological view that you should become familiar with, you should also make yourselves familiar with the work of Goudsmit and Howes (2008) where they review a number of challenge studies cited in the Working Draft, which we discuss later in this submission. And for a good example of a psychological paper that unwittingly contradicts itself with its own evidence look at Binkley et al (2001) which we have discussed later in this report (and which the Working Draft cited inappropriately).

- The Working Draft says on Pages 18,

*the underlying biological basis for MCS and its range of variable symptoms remains unresolved. Indeed, a review by Winder (2002) identified no less than 24 possible causative mechanisms.*

There may be more than one causative mechanism for MCS and looking for a single causative mechanism may obscure that.

### **3.1 OVERVIEW OF POSSIBLE MCS MODE (S) OF ACTION**

First, a general comment on this section: The 'Hypothesis' sections were a confusing muddle and generally did not clearly deal with the hypothesis. It would be best to separate out the hypothesis part, the theory part, the evidence part and the discussion part. At least get everything into their correct paragraphs and in order. Some of the material in the 'Hypothesis' section should be in the research challenge section. You could even drop the Hypothesis heading as it constricts what you appear to be trying to achieve.

We found the 'Research Challenge' sections to be unclear as to what the authors are trying to say, what they thought were important areas to study and why. There was much material in these sections that was not relevant to the section. Many of the 'Hypotheses' in the Working Draft did not have a 'Research Challenge' section and should have had one. The 'Research Challenge' sections need clarifying and tightening up. We would like a more explicit explanation in the Working Draft for OCS/NICNAS's choices of theories to recommend for further research as priorities.

- The Working Draft says on Pages 18,

*a review of the available literature was undertaken*

Only some of the available scientific literature was reviewed in the Working Draft. A similar review of similar length by Pall (In Press) has twice as many references as the Working Draft. We have included some key references later in this submission that we urge should be seriously considered for inclusion in the Working Draft.

- The Working Draft says on Pages 18,

*a review of the available literature was undertaken to identify which scientific reports of the cause(s) of MCS are most discussed as reflecting biologically plausible and scientifically testable hypotheses.*

You didn't apply this standard the psychological hypotheses, they too should have been critically assessed in the Working Draft for their plausibility and whether they were scientifically testable. This is the double standard that pervades the Working Draft. For recent critical discussion on the testability of psychological hypotheses of MCS see Pall (2007) and read Goudsmit and Howes (2008).

- The Working Draft says on Pages 18,

*NOTE: Given difficulties in characterising MCS, this discussion of hypotheses is not exhaustive and may be regarded by some as incomplete. Additionally, there may be views that the weight of evidence for particular hypotheses is stronger than summarised here.*

The discussion is incomplete and does not do the subject justice.

### **3.1.1 Immunological dysregulation**

- The Working Draft says on Pages 19,

*However, details of pathogenetic mechanisms supporting immune dysregulation as a cause of MCS have not been provided.*

We suggest deleting this. It is unsupported and doesn't make sense here.

- The Working Draft says on Pages 19,

*Further work is needed to examine whether immunological dysregulation is associated with MCS. Such work should include validated immune measurements with appropriate quality controls, well-defined clinical groups and specific chemical challenges (Mitchell et al. 2000).*

This 'Research Challenge' section is rather scant. More specific information and more than one reference should be included.

### **3.1.2 Respiratory disorder/neurogenic inflammation**

- The Working Draft says on Pages 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).*

Isn't this paragraph contradicted by the previous paragraph in the Working Draft? Also, it has been claimed that Staudenmayer is a very controversial author, you would be well advised to must check his claims against every one of his original sources. We suggest you delete any unverified or uncritical use of his work.

- The Working Draft says on Pages 20,

*Research challenge: The available data suggest that there may be some effects on nasal or upper airways in at least some MCS patients. However, altered nasal mucosa and other respiratory changes such as increased nasal resistance alone cannot account for the multiple organ system pathology reported in MCS. Further, the involvement of a neurogenic switching mechanism to explain multiple organ pathology (Meggs & Cleveland 1993; Meggs 1995; 1999) has not yet been demonstrated in MCS sufferers (Graveling et al., 1999).*

Also need to explore non-odourous chemical vapours more extensively, there is plenty of evidence of non-odourous chemicals being involved in MCS. So, from your review what do you surmise are the important directions or goals for research here.

### **3.1.3 Limbic kindling/neural sensitisation**

- The Working Draft says on Pages 22,  
*Research Challenge*

A weak and confused section. You need to more explicitly state what you think the research challenges are and propose future directions, goals and priorities for research. Delete or move paragraphs that don't belong here.

*It has also been proposed that sensitisation of the limbic system can be induced or augmented by psychosocial stress or “life trauma” events. Once sensitised, the limbic system reacts to a greater number of triggering events that include chemicals, noise and electromagnetic radiation (Arnetz, 1999). Support for the Arnetz model of limbic sensitisation in MCS may be drawn from an animal study by Friedman et al. (1996) demonstrating that in mice, stress significantly increased blood brain barrier permeability to peripherally administered Evan’s blue–albumin, plasmid DNA and the acetylcholinesterase inhibitor pyridostigmine. These findings suggest that peripherally acting chemicals administered under stress can reach the brain and affect centrally controlled functions (Friedman et al. 1996). Indeed, some researchers have reported that one of the strongest predictors of MCS is psychiatric morbidity prior to the onset of MCS symptoms (Simon et al. 1990; Reid et al. 2001)*

Doesn’t belong in the ‘Research Challenge’ section.

### **3.1.4 Elevated nitric oxide, peroxynitrite and NMDA receptor activity**

- The Working Draft says on Pages 23,

General comment on this ‘*Research Challenge*’ section. This particular section is merely arguing against the theory. What are the research challenges you perceive?

- The Working Draft says on Pages 23,

*there is no de novo scientific evidence to support it.*

We thoroughly disagree, have another look at Pall (2007) and Pall (In Press).

- The Working Draft says on Page 23,

This theory suggests that hypersensitivity arises through a limbic kindling/neural sensitization process involving short-term stressors such as viral or bacterial infections, chemical exposure or psychological stress that stimulate NMDA receptors producing elevated levels of nitric oxide and peroxynitrite. This is followed by cycles of interconnected reactions such as a) nitric oxide acting as a retrograde messenger and stimulating neurotransmitter (glutamate) release, leading to increased NMDA receptor activity

This is inaccurate. Read Pall (2007).

- The Working Draft says on Page 23,

this theory implicates hydrophobic organic solvents and organophosphate- or carbamate-based pesticides as the triggering agents (stressors), but the triggers of MCS symptoms are diverse and often include hydrophilic solvents such as alcohol (ie. perfumes) or other pesticides, such as malathion.

You have confused chemical exposures that initiate MCS (stressors in Pall's theory) with chemical exposures that trigger symptoms in people who have MCS.

- The Working Draft says on Page 23,

*malathion*

Probably everyone who has submitted has told you this (and we would hope that you knew this anyway), but malathion *is* an organophosphate.

### **3.1.5 Toxicant-induced loss of tolerance (TILT)**

- The Working Draft says on Page 24,

*Research challenge: According to Miller et al, studies generally have failed to unmask patients before challenge*

This isn't a research challenge. You need to explain what you think the research challenges are. A full reference is required.

### **3.1.6 Behavioural conditioning**

- The Working Draft says on Page 24,

*Van den Bergh et al (1999) demonstrated that subjects can acquire and then lose somatic symptoms and altered respiratory behaviours in response to harmless, but odorous chemical substances*

What criteria were used for determining "harmlessness"?

- The Working Draft says on Pages 24,

*The conditioned responses were modest...*

Does 'modest' mean statistically insignificant? If not statistically significant then delete this material.

The Working Draft says on Pages 24,

Research challenge: *Behavioural conditioning, however, does not explain directly the diverse range of symptoms reported by MCS sufferers. Additionally, in many cases, there appears to be no substantial initial exposure event that would constitute the unconditional stimulus (Sparks, 2000b).*

Delete 'directly' as unnecessary and unsupported. Also, what research priorities and direction do you suggest.

### **3.1.7 Psychiatric disorders**

Saito et al. (2005) concluded that "MCS patients do not have either somatic or psychological symptoms under chemical-free conditions, and symptoms may be provoked only when exposed to chemicals."

In our long experience at AESSRA we have found that although all cases of MCS might appear bizarre to people who are unfamiliar with it, and each case is different, and sometimes people with MCS are floundering and very confused, there are patterns. Occasionally we have been approached by, or been told about, someone who says they have MCS but whose description of their sensitivities and symptoms doesn't sound, to us, like MCS, or sounds as if there is something else wrong as well. It concerns us that some doctors may base their opinion of MCS on an encounter with someone like this, because they aren't representative of the vast majority of people with MCS.

We have also known people who believed they had very severe MCS and were very distressed about it and fearful about the future, when their MCS was actually relatively mild and manageable. If they had had access to tests for chemical sensitivities earlier this problem would have been prevented. People with many medical conditions can have related psychological problems. It doesn't mean that their underlying medical condition isn't physiological.

It should be noted that the current climate of disbelief and hostility towards people with MCS causes psychological distress and may exacerbate any comorbid psychiatric conditions. Also, people with MCS don't have the same access to mental health services as other Australians because of the chemical exposures and inappropriate food in inpatient facilities.

Pamela Reed Gibson, a professor of psychology at James Madison University, Virginia, said,

To truly make the case that people with MCS are psychiatrically disturbed, all of the following conditions would have to be satisfied:

1. Any physical causes for the psychiatric symptoms would have to be ruled out.
2. The psychiatric symptoms would have to have caused the MCS.

3. The group with MCS would have to have more psychiatric symptoms than people *with other chronic physical illnesses*.  
There are no studies that have demonstrated these conditions. (Gibson 2000:157)

In 2009 there are still no studies that have demonstrated these conditions.

The Working Draft devotes an excessive amount of space to psychogenic theories that are seriously flawed and misleading. For example;

- the Working Draft says on page 25,

*Further support for the association between panic disorder and MCS comes from genotypic analysis of MCS subjects, which show the presence of panic disorder-associated cholecystinin B receptor alleles in 41% of MCS subjects compared to controls (9%) (Binkley et al., 2001).*

This is an overly simplistic analysis of Binkley et al (2001) and misses a fundamental implication of their findings. They use their finding to support the view that there is a psychogenic mechanism for MCS. Pall (2007:208-209) agrees with their inference that “The association of specific CCK-B receptor alleles in patients with both IEI and panic disorder suggests they may share an underlying neurogenetic basis.” but Pall goes on to point out an important consequence of that observation which escaped both Binkley’s group and the authors of your report. He points out that

The irony is that their study helps refute the term they prefer, idiopathic environmental intolerance, because idiopathic means of unknown causation, and their study provides support for the view that part of the cause can be excessive CCK-B activity.

and further points out that

Because the CCK-B receptor can, in turn, stimulate NMDA activity, it provides support for the NO/ONOO- cycle and neural sensitization mechanisms for MCS.

Binkley et al (2001), by reporting a significant genetic role in the aetiology of MCS has provided important evidence supporting a biological rather than a psychological causation. The paper should be more correctly placed in support of the genetic evidence for MCS &/or NO/ONOO- cycle and neural sensitization mechanisms for MCS. It is not correct to use it to support the Psychiatric disorder view of MCS, and thus should be removed from that section and reassessed.

If somatoform disorders are going to be discussed then the problems psychiatrists are having defining and classifying somatoform disorders should be discussed. In the literature the very use and legitimacy of the term and classification “somatoform” is under serious discussion and challenge. For example, Mayou et al. (2005) said, “The somatoform

disorder term, concept, and category have failed psychiatrists, nonpsychiatric physicians, and patients.” They explain that DSM-III introduced Somatoform Disorders as a “speculative diagnostic category” and argue for the abolition of the Somatoform Disorder category from DSM-V.

Maes (2009) concluded that

'Functional' symptoms, as occurring in CFS and somatization, have a genuine organic cause, that is activation of peripheral and central IO&NS [inflammatory and oxidative and nitrosative stress] pathways and gut-derived inflammation. The development of new drugs, aimed at treating those disorders, should target these IO&NS pathways.

Bear in mind that in the past the following diseases have been falsely claimed to be psychological: multiple sclerosis, Parkinson's disease, lupus, migraine, rheumatoid arthritis, asthma, ulcerative colitis and gastric ulcers (Pall 2007:202-206).

- The Working Draft on Page 25,

These statistical ranges were used; 42-100%; 71-100%; 36-100%.

These wide ranges need to be explained in terms of what they mean statistically, what do they represent, are they significant and are they statistically valid. What is the statistical significance of all the other statistical data cited on this page?

- The Working Draft says on Pages 25,

*Research challenge:*

As with the other Research Challenges, how do you suggest resolving the challenge.

### **3.1.8 MCS as a 'belief system'**

The absurdity of the theory that MCS is a belief system is shown by cases of MCS in babies and young children (Rea 1996:1935-2006) and animal models for MCS. Overstreet and Djuric (2001) said, “The Flinders Sensitive Line (FSL) rats were established by selective breeding for increased responses to an organophosphate. ... the FSL rats have been reported to exhibit increased sensitivity to a variety of other chemical agents. Pall (2007: 18-19,116,124) discusses available animal models for MCS. Pall (In Press: 23-25) devotes a chapter to reviewing Animal model data relating to MCS. Anderson and Anderson (2003) present a mouse model that appears to have similarities to MCS in humans. Abou-Donia et al (2002a, 2002b, 2004) have published extensive studies on a rat model of MCS. Animals have yet to be shown to have belief systems.

### **3.1.9 Odour perception**

- The Working Draft says on Pages 27,

*Healthy individuals can acquire somatic symptoms and altered respiration in response to harmless, but odorous chemical substances, especially if an odour has been previously perceived to be the cause of symptoms (Van den Berg et al. 1999) (see Section 3.1.6).*

Said elsewhere and the reference wasn't in the reference list.

### **3.1.10 Other proposed mechanisms**

#### ***3.1.10.1 Altered metabolism***

- The Working Draft says on Page 28,

*One case control study of MCS genotypes reported that individuals with higher hepatic cytochrome P450 isozyme CYP2D6 gene activity and NAT2 rapid acetylator gene activity are at greater risk of developing MCS (McKeown-Eyssen et al. 2004). However, a more recent cross-sectional study of gene variants in MCS revealed that self-reported chemical sensitivity cases were significantly more frequently of the NAT2 slow acetylator genotype (Schnakenberg et al., 2007). These contrasting results were explained by differences in case inclusion criteria (Schnakenberg et al., 2007)."*

*and*

*NOTE: Although the results from these studies appear to be contradictory, they may stem simply from differences in chemical exposures, as MCS is regarded as a disorder linked to exposures to multiple unrelated chemicals.*

The situation is not as simple as that at all. NAT 2 is known in cancer research to be associated with protection or risk, depending on the context. For example with exposure to benzidine it is associated with high risk, and with exposure to cigarette smoke it is associated with protection. There is a relationship between the gene and the environment. So these 'opposite direction' results may be utterly consistent, demonstrating that the behaviour of this gene is dependent on the context, on the particular type of exposure. There were differences in inclusion criteria, but it would be a mistake not to look deeper into the behaviour of NAT2. This sort of detail on NAT 2 is probably in text books, but an email to McKeown-Eyssen or Schnakenberg should get you a reference describing the NAT2 behaviour, if necessary.

Haley et al. (1999) is a major genetic study that needs to be included. McKeown-Eyssen et al (2004) and Schnakenberg et al (2007) should be re-read with Haley et al (1999) as

together they give a strong and statistically significant role to 5 genes in determining the susceptibility of an individual to MCS.

### **3.1.10.3 Serum and intra-erythrocyte biochemical changes**

- The Working Draft says on Page 29

*clinically unimportant case-control differences in means*

Clarify what this means. Is it the same as ‘not statistically significant’?

## **3.2 COMMENTARY ON THE PROPOSED MODELS OF MODES OF ACTION**

- The Working Draft says on Page 29

*3.2 COMMENTARY ON THE PROPOSED MODELS OF MODES OF ACTION*

We think you could delete the entire section of 3.2 without harm to the review. We couldn't discern boundaries between opinion and speculation and scientific discussion. It is loose and unfocused, lacks references and abounds with unsupported assertions. Any referenced scientific material from this section that you really want to keep should be tidied up into other more appropriate sections.

## **3.3 FURTHER RESEARCH TO IDENTIFY POTENTIAL CAUSATIVE MECHANISMS OF MCS**

- The Working Draft says on Page 31

*There is considerable debate as to what causes MCS. The literature describes numerous potential causative mechanisms many of which are amenable to further testing. The most credible physiological mechanism for MCS is limbic kindling/neural sensitisation which proposes that sensitisation of the olfactory, limbic, mesolimbic and related pathways of the central nervous system occurs as a result of, or in the context of, chemical exposure. 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. Recent medical/scientific opinion suggests that MCS has a multifactorial origin, involving physiological, psychological and social predispositions*

If you are going to claim that “The most credible physiological mechanism for MCS is limbic kindling/neural sensitisation” you need to explain why it is the most credible and provide supporting evidence.

References are also required for “Recent medical/scientific opinion suggests that MCS has a multifactorial origin, involving physiological, psychological and social predispositions”.

The Working Draft is not thorough enough to come to an honest conclusion about the scientific weight-of-evidence for the cause of MCS. The far more comprehensive and rigorous book by Ashford and Miller (1998) concluded that there was far more evidence for physiological mechanisms than for psychological ones. Since then the gap has widened, particularly with genetic studies pointing clearly to physiological mechanisms. It is worth looking at the approaches towards psychogenic theories about MCS in the reports by the Research Advisory Committee on Gulf War Veterans’ Illness (2008) and Sears (2007), which was written for the Canadian Human Rights Commission; in comparison, the biased way in which the Working Draft parts company with the evidence is very clear.

- The Working Draft says on page 32,

*The important research question relating to the extent to which psychological factors contribute not only to the initiation but also to continued disability in long-term MCS can be addressed by balanced-placebo challenge tests in which not only the putative eliciting substance(s) but also the expectation of adverse effects are directly assessed.*

*As noted by Weiss (1997), the use of balanced-placebo study designs for testing the power of expectation involves deception procedures in the administration of the study, but with appropriate management of ethical issues would be expected to further elucidate the role of psychological mechanisms in MCS. In addition, with appropriate ethical controls, such study designs incorporating the testing of expectation conceivably could be incorporated in longitudinal repeated studies in individuals.*

We do not think that using “deception procedures” on people with MCS could be done ethically. As Gibson (2005) said,

Those with MCS have generally received such poor treatment from medical providers that they may have anger and distrust toward representatives and practitioners of conventional medicine.

and we are concerned that this would not be given adequate consideration. This sort of testing could increase distrust of doctors and lead to someone missing out on medical

treatment they needed. If this sort of testing is made part of a longitudinal study it would put many people off participating.

- The Working Draft says on page 7,

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

- Immunological variables*
- Respiratory disorder/neurogenic inflammation*
- Limbic kindling/neural sensitisation and psychological cofactors*
- Elevated nitric oxide, peroxynitrite and NMDA receptor activity.*

We agree with the selection of the above scientific theories as priority areas for research, although we think consideration should be given to Pall's comments on the convergence of neural sensitization theory and NO/ONOO<sup>-</sup> cycle theory (Pall 2007:120-123).

We also believe the following to be priority areas for research into aspects of MCS:

- **Biomarkers:** There are a number of possibilities and further research may uncover more. Kimata (2004) concluded that “substance P, vasoactive intestinal peptide, nerve growth factor and histamine levels would be good markers of MCS, and they may be involved in the pathogenesis of MCS.” Millqvist et al. (2005) concluded that “The findings demonstrate that, in patients with airway symptoms induced by scents and chemicals, SHR [sensory hyperreactivity] is real and measurable, demonstrating a pathophysiology in the airways of these patients compared to healthy subjects.” Elberling et al. (2007) concluded that “Perfume induces a dose-dependent non-IgE-mediated release of histamine from human peripheral blood basophils. Increased basophil reactivity to perfume was found in patients with respiratory symptoms related to perfume.” Little et al. (1999) found that “the levels of T-cell antigen-binding molecules against the para-aminobenzoic acid conjugated to human serum albumin were elevated significantly in subjects sensitive to toluene.” Fukuyama et al. (2008) said, “All chemicals induced significant increases in number of lymphocytes and surface antigen expression of B cells. Our mouse model enabled the identification and characterization of chemical-related allergic reactions at low levels. This long-term sensitization method would be useful for detecting environmental chemical-related hypersensitivity.”
- **Genetic studies,** including a study of families with several members with MCS, to elucidate genetic and/or environmental factors.

- **Porphyriopathy** in MCS is worth further study for a number of reasons. There is a link with nitric oxide (Pall 2007:127). Daniell et al. (1997) state “Measurements of the status of heme synthesis, particularly measurements of excreted heme precursors, have potential field and clinical utility as biological indicators of chemical exposure and chemical effect on body functions.” The tests are readily available and in some cases porphyrin levels are significantly abnormal. This may have implications for management (eg avoiding sunlight or medication choices) There is also the possibility that a diagnosis of hereditary porphyria has been missed. When AESSRA reported on the studies linking MCS and porphyriopathy, two members said that their sisters had died of porphyria many years earlier. One of these members said her own skin blistered in sunlight but she had never been tested for porphyria. (About a third of AESSRA members report sensitivity to sunlight, but this can have causes other than porphyrin abnormalities.)
- **A trial of the Pall/Ziem protocol** (Pall 2007:311-314) or similar protocol designed to downregulate the NO/ONOO<sup>-</sup> cycle mechanism

### 3.3.2 Respiratory disorder/neurogenic inflammation

- The Working Draft says on Page 31,

*The major criticism for this causative mechanism is that altered nasal mucosa and other respiratory changes such as increased nasal resistance alone, even if found consistently, cannot account for the multiple organ system pathology reported in MCS.*

This is not appropriate in this section ‘FURTHER RESEARCH TO IDENTIFY POTENTIAL CAUSATIVE MECHANISMS OF MCS’. Delete.

### 3.3.3 Limbic kindling/neural sensitisation and psychological cofactors

- The Working Draft says on Page 32

*noting that an existing psychiatric condition prior to the onset of symptoms has been observed as a strong diagnostic predictor of MCS.*

Delete Already covered and isn’t relevant to this section.

- The Working Draft says on Page 32,

*Lehrer (1997) outlines several psychophysiological hypotheses and research*

*strategies that would be useful for exploring psychological factors contributing to MCS.*

Delete as uninformative or explain this research challenge more explicitly.

With the above deletions, and some wording changes, the last paragraph of Section 3.3.3 should read thus,

‘The important research question as to whether psychological factors contribute to the initiation and, or to continued disability in long-term MCS can be addressed by balanced-placebo challenge tests in which not only the putative eliciting substance(s) but also the expectation of adverse effects are directly assessed.’

### **3.3.4 Elevated nitric oxide, peroxynitrite and NMDA receptor activity**

- The Working Draft says on Page 32,

*Currently, there is no de novo scientific evidence to support this theory. However, Support for the direct involvement of nitric oxide, peroxynitrite and NMDA receptor.*

Delete, as this misinterprets the evidence (see Pall 2007, In Press), and has been said elsewhere.

- The Working Draft on Page 32,

Include a section Titles ‘3.3.5 Genetic Studies’.

This is a most important area of research

## **4 DIAGNOSIS, TREATMENT AND MANAGEMENT OF MULTIPLE CHEMICAL SENSITIVITY**

### **4.1 DIAGNOSIS AND PREVALENCE OF MCS**

- The Working Draft says on page 6,

*The diagnosis of MCS is currently based on self-reported symptoms.*

In Victoria hundreds of patients with MCS were tested in the way Ashford and Miller (1998) proposed. In our 2004 survey of members, of 91 in Victoria, 27 had been diagnosed in an Environmental Control Unit and 40 (with considerable overlap) had been diagnosed with provocation-neutralization. The rates in other states were lower, for example, of 23 members in South Australia none had been diagnosed in an Environmental Control Unit and four had been diagnosed with provocation-neutralization. Ashford and Miller (1998:129-135) discuss provocation-neutralization.

- The Working Draft further says on page 6,

*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.*

MCS can be diagnosed objectively using an Environmental Control Unit, as Ashford and Miller (1998) suggested and as doctors practising environmental medicine have done since the 1950s. There have been far more serious impediments, such as the refusal to consider or study treatments used by doctors practising environmental medicine doctors.

- The Working Draft says on page 6,

*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.*

What distinguishes people with MCS from others with the same symptoms is that people with MCS experience symptoms as a result of exposure to low levels of chemicals. Therefore testing in an ECU or with provocation-neutralization distinguishes individuals with MCS from others with fatigue, headache etc.

- The Working Draft further says on page 6,

*The need for objective clinical criteria to identify MCS subjects and overcome the shortcomings of self-diagnosis is critical.*

The Consensus Criteria have been around for almost ten years. Testing in Environmental Control Units started in the 1950s and is easily combined with objective tests to measure changes in lung function, blood pressure, blood glucose levels, balance, memory and other symptoms patients report.

- The Working Draft says on page 7,

*... enable discrimination between individuals with MCS and those with common aversions to smells and odours.*

This is not a problem. People with MCS experience symptoms when exposed to low levels of chemicals and people with aversions to smells and odours don't.

## **4.1.2 Studies on the prevalence of MCS in other countries**

- The Working Draft says on page 35,

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)

You should include references to these overseas estimates, not just a secondary source. You also need to explain why these are the best estimates. You should say whether these estimates are for the general population or a population subgroup.

## **4.3 TREATMENT FACILITIES**

- The Working Draft on Page 37,

*Importantly, the South Australian Parliamentary Inquiry heard that patients with MCS attributed the majority of the benefits they experienced to education, support and acknowledgement of the illness (Social Development Committee Report, 2005).*

The comment made to the South Australian Parliamentary Inquiry only referred to the Sydney clinic, not to the Melbourne Environmental Control Units. Many people who were patients in the Melbourne ECUs have benefited enormously from finding out exactly which chemicals and foods affected them and how.

Unless and until tests using biomarkers have been developed, testing in a publicly-funded Environmental Control Unit should be made available for all Australians whose health problems could be due to MCS.

## **4.4 TREATMENT OF MCS**

- The Working Draft says on page 2,

*a clinical consultancy has been undertaken to identify current diagnosis and treatment practices*

So, what are the current diagnosis and treatment practices? These should be included in the Working Draft.

- The Working Draft on page 6,

*There is currently no standardised treatment for MCS.*

See the American Academy of Environmental Medicine Practice Guidelines (1980), which are followed by a large number of doctors, and Rea (1997), which describes these and other procedures used at the Environmental Health Center – Dallas in detail.

- The Working Draft further says on page 6,

*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 MCS patients and is a hindrance to scientific analysis/investigation and clinical research efforts regarding MCS.*

A major reason for this lack of agreement is the influence of the chemical industry, like tobacco industry's influence. See McCampbell (2001).

- The Working Draft on Page 37,

*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)*

Efficacious for how many, how efficacious, what percentage, is this statistically significant? How many find these not efficacious?

- The Working Draft says on Page 38,

*Chemical Sensitivity, Victoria*

We have seen no evidence that this group exists.

- The Working Draft on Page 38 says,

*These groups provide support and guidance for MCS sufferers and also present information on a range of treatments. Advocacy and support group websites (both national and overseas) list a wide range of treatments including intravenous vitamins, nutritional supplements, detoxification, chelation therapy, colonic irrigation, desensitisation, use of medication to boost the*

*immune system, antidepressants, antibiotics, antifungals, homeopathy, acupuncture, mind-body therapy, psychotherapy and total or partial avoidance.*

This requires references for each treatment listed. We think this paragraph is misleading. Please explain what you mean by “present information on” and “list”. On some of these therapies any information most support groups presented would be negative. We are not aware of support groups that recommend some of these treatments. The two largest support groups in the world are the Human Ecology Action League (HEAL) and the Chemical Injury Information Network (CIIN), both of which are American but have members in Australia). CIIN gives no information about treatment on its website. HEAL (2007) says

The following steps can help you meet challenges of coping successfully and get you started on the path to better health.

**TAKE RESPONSIBILITY.**

Identify symptoms. Remove suspected triggering agents one at a time and observe the results. Consult a medical specialist if necessary.

**CLEAN UP SURROUNDINGS.**

Investigate and reduce sources of indoor air pollution, including those that may come from ...

scented products  
household cleaners  
tobacco smoke  
gas stoves  
heat and ventilation systems  
office machines  
construction materials

**REDUCE STRESS.**

Minimize all stresses, emotional and environmental, so that you can cope better with those that are inevitable.

**PROMOTE HEALTH.**

Exercise regularly and choose foods wisely. Minimize or eliminate foods containing pesticides and chemical additives.

- The Working Draft on Page 39, (truncated point form of material on page 48, Section 5.4.3) says,

*The MCS Clinical Management Principles:*

*Accept that the person with MCS feels ill and is disabled by the illness;*

*Provide an empathic relationship to offer understanding and support;*

*Encourage self-management rather than offering or seeking a cure;*

*Recognise and explain that no specific therapy has yet been proven to be of benefit;*

*Maintain a long-term positive approach.*

The MCS Clinical Management Principles are totally inadequate, we will deal with each heading in turn.

*Accept that the person with MCS feels ill and is disabled by the illness;*

This trivialises MCS. You wouldn't say, "Accept that the person with Multiple Sclerosis feels ill and is disabled by the illness."

If the doctor is ignorant of or refuses to accept the evidence that MCS has a physical basis, he or she should refer the patient with possible MCS to a doctor who diagnoses and treats MCS.

*Provide an empathic relationship to offer understanding and support;*

Australians who have had MCS for years or decades have often learnt to live without understanding and support from doctors. Also, for people with more severe MCS it's not worth getting sick from fragrance, disinfectant and other chemicals in the doctor's clinic just for understanding and support. And even if the doctor does provide an empathic relationship it can be depressing or scary visiting a doctor who knows even less about your medical condition than you do.

*Encourage self-management rather than offering or seeking a cure;*

The information patients need for self-management includes which areas of the city or state are most and least polluted and/or mould prone, pollution sources and prevailing winds, sources of indoor air pollution and what to do about them, the most appropriate water filters and air purifiers, sources of less chemically contaminated clothing, bedding and furniture, the least toxic building products, non-toxic cleaning and personal care products, possible workplace modifications to reduce chemical exposure and/or alternative careers that involve less chemical exposure. This is beyond the scope of most doctors.

Doctors could refer patients to support groups that can provide much of this information, but support groups cannot tell patients what they are most sensitive to and what home and lifestyle modifications will bring most benefit to them. (Few people can afford to change everything at once.) A patient needs a doctor who diagnoses how sensitive he or she is to various chemicals and can say for example, whether an activated carbon water filter would be good enough or a water distiller is needed, or whether moving out of the city would be beneficial.

People with MCS also need doctors who can write letters on their behalf, eg explaining to a school which products and activities a child with MCS will need to avoid.

Most people with MCS have food sensitivities, so their doctors should be able to supervise an elimination diet, interpret the results and give advice on whether, when and how to

reintroduce foods that have caused reactions in the past. Nutritional advice and supplements may also be needed, particularly for people with MCS who tolerate very few foods.

*Recognise and explain that no specific therapy has yet been proven to be of benefit;*

Many people with MCS feel that they can't afford to wait twenty years or more (or another twenty years or more) for the average doctor to be convinced that a dietary supplement or other therapy is worth trying, especially when so little research is being done into treating MCS. People with MCS are in pain and are missing out on life, and some can see that their health and quality of life are deteriorating further. A doctor who is well-informed could help patients make well-informed decisions about what to try. There are nutritional supplements and other specific therapies that help many people with MCS (Ashford and Miller 1998, Pall 2007, Rea 1997), even if they are not considered proven to be of benefit.

*Maintain a long-term positive approach.*

People with MCS often find it hard to feel positive about the future because the basics most Australians take for granted, such as safe food, water and housing, can be very difficult for people with MCS to access; they know there are no aged care facilities that cater for people with MCS; they rightly worry about having to go to hospital and being badly affected by fragrances, disinfectants, cleaning products and pesticides, as well as medications, anaesthetics and inappropriate food; and they are largely excluded from the community. So far most doctors have been part of the problem, not part of the solution, and it would take far more than the Working Draft's MCS Clinical Management Principles to change that.

Effective clinical management of MCS has to be centred on diagnosis, treatment and expert advice, not humouring patients and discouraging them from seeking real help elsewhere. It would be best provided by dedicated health centres with buildings and furnishings free of toxic chemicals and fragrance-free policies for patients and staff.

## **4.5 CLINICAL RESEARCH NEEDS**

- The Working Draft says on page 40,

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

- Establishing agreed diagnostic criteria that are acceptable to clinical and scientific groups;
- Determining the prevalence of MCS, for both self-reported cases and those that are medically diagnosed;
- Determining the relative contributions of toxicodynamic and psychogenic mechanisms in the process of the disorder through the use of appropriately blinded challenge tests;

- Determining effective treatment/management protocols for MCS based on positive therapeutic alliances and individual self-management.

An Environmental Control Unit would currently be the best way to diagnose MCS for research purposes. It is very important that studies of MCS use people who actually have MCS. This sounds basic but some researchers aren't particular about this, eg Staudenmayer et al. (1993), whose study was criticised by Goudsmit and Howes (2008). Similarly, some research into CFS has rightly been criticised for including people who only suffer from fatigue and don't meet the full criteria for CFS (Carruthers et al. 2003). Until greater knowledge allows the development of better criteria for MCS, it would probably be best to adopt an existing definition, such as the 1999 Consensus Criteria, instead of developing yet another definition.

Prevalence studies would be worthwhile, particularly if they were designed to make the results easy compare with overseas prevalence rates.

In the apparently unlikely event that the suggested challenge studies were conducted effectively they would still shed very little light on causative factors. Research and theories about mechanisms have moved on. The only point in conducting more challenge studies to determine the "relative contributions of toxicodynamic and psychogenic mechanisms" would be the hope of proving that MCS is psychological and that is not an appropriate starting point.

A facility to enable unmasking and inhalation tests could be put to much better use with baseline and after exposure neuropsychological tests, tests of lung function, blood pressure and other measures. These tests could also provide more convincing and useful evidence of whether MCS is physical or psychological. For example, Little et al. (1999) challenged patients in an Environmental Control Unit with 15 minute exposures to 15ppm toluene. They found "significant associations between T-cell antigen-binding molecule levels and (a) decreased performance on the STROOP (Colour Word) test, (b) a shift in focal length following toluene exposure, (c) clinical assessment of disability, and (d) longer histories of chemical exposure."

"Positive therapeutic alliances and individual self-management" are not an adequate basis for effective treatment/management protocols.

While we appreciate the value of a longitudinal clinical and sociological study we are concerned that it would be an excuse not to do anything about MCS for another ten years. While not ideal, it should be possible to find out similar information far more quickly using retrospective studies. Many people with MCS (and who used to have MCS) were diagnosed in an Environmental Control Unit in Melbourne in the 1980s and they could be followed up.

- The Working Draft pages 6,8 and 39,

*Some challenge tests suggest that it is the smell or odour of a triggering agent,*

*rather any of its pharmacological or toxicological properties per se that elicit MCS symptoms.*

The Working Draft doesn't say which challenge tests are referred to here (references are required), but there have been serious flaws in a number of them (Ashford and Miller 1998:218-223, Goudsmit and Howes 2008).

Goudsmit and Howes (2008) reviewed the challenge studies discussed by Das-Munshi et al (2006) (cited in the Working Draft) and examined the hypothesis that MCS is a result of expectations, beliefs and conditioning. Eight other papers cited in the Working Draft were discussed in both Das-Munshi et al (2006) and Goudsmit and Howes (2008). Goudsmit (a Chartered Health Psychologist) and Howes reported that "Our analysis revealed a number of methodological weaknesses which do not appear to have been given due consideration by the authors when interpreting the findings," and concluded that, "In light of these shortcomings, we believe that their conclusions may have over-stated the role of psychological factors in the aetiology of MCS."

The following are brief (and by no means exhaustive) comments on each of these eight papers and Das-Munshi et al (2006):

Das-Munshi et al (2006). Goudsmit and Howes (2008) say Das-Munshi et al "emphasized the evidence suggesting that MCS is a learned response." However, after Goudsmit and Howes (2008) analysed the methodologies and designs of the studies in Das-Munshi et al.'s review they came to the following conclusion, "In light of the various shortcomings described above, we concluded that the findings of the various studies should be interpreted with caution and, given that the theory attributing MCS to expectation, fear and conditioning is largely based on generalization and speculation, we consider it to be simplistic and unconvincing."

**Staudenmayer et al (1993).** Goudsmit and Howes (2008) concluded that "Given the lack of clarity regarding the diagnosis and the failure to elicit the reported symptoms, the findings of this study cannot be extrapolated to patients with MCS."

**Georgellis et al (2003).** Goudsmit and Howes (2008) suggest that the 'coffee' masking agent was not innocuous and that the assumption of Georgellis et al (2003) that reactions to coffee were because patients interpreted the 'coffee' as threatening was without scientific basis.

**Hummel et al (1996).** Goudsmit and Howes (2008) say "According to the researchers, these results suggest 'the susceptibility of MCS patients to experimental manipulations'. This may be true but, as the participants were not challenged with the chemicals known to trigger symptoms in daily life, this wasn't a study on MCS. A healthy control group might have reacted in a similar way."

**Osterberg et al (2003).** Goudsmit and Howes (2008) argue that 'discomfort' recorded in the chamber prior to exposure may have reflected a reaction to

materials in the chamber itself and that there is no clear basis to say the response was a sign of psychological factors.

**Van der Bergh et al (1997).** Goudsmit and Howes (2008) said that “these types of studies are generally interpreted as showing that MCS may represent ‘learned somatic symptoms’, a result of an association between an unpleasant odour and the sensations linked to toxic exposure or stressful event. However, the [findings of Van der Bergh (1997)] do not support such a generalization.” and “One might also question whether this chemical [ammonia] is an appropriate ‘neutral’ stimulus.”

**Devriese et al (2000).** Goudsmit and Howes (2008)note that one of the chemicals used on subjects was described by Devriese et al as ‘pure odour’ not acknowledging it as an irritant. However, Goudsmit and Howes found “the Material Safety Data Sheet for butyric acid lists negative health effects of inhalation, such as ‘tissue damage particularly on mucous membranes of eyes, mouth and respiratory tract’. The concluded that Devriese et al’s study “was an experiment to assess classical conditioning and the phenomenon of stimulus generalization, not the effects of provocation in patients with MCS.”

**Graveling et al (1999).** Goudsmit and Howes (2008) agree with Graveling et al in that “the nature and pattern of the elicited responses in experimental situations are not entirely consistent with those reported by patients with MCS., and go on to conclude “Although it cannot be discounted, conditioning does not seem to offer a substantive model.”

**Simon et al (1990).** Goudsmit and Howes (2008) criticise the study for being incomplete in that it did not include a follow-up to determine whether the treatments given the patients for their emotional distress, or the receipt of compensation alleviated their sensitivity to chemicals.

People with MCS react to chemicals, not to the smell of chemicals. There are people with MCS who have no sense of smell and many others who have reacted to chemicals they couldn’t smell. Millqvist et al. (1999) found that asthma-like and other symptoms could be induced by exposing the eyes but not the nose or mouth to perfume. There have also been studies that show responses to odourless chemicals such as capsaicin, such as (Millqvist et al (2005), Millqvist et al (2008) and Ternesten-Hasseus et al. (2002)

- The Working Draft says on Page 8,

*Such a program should be based on evidence currently available, utilise any findings from clinical research in Australia (such as a longitudinal investigation) and consider the practical guidance on approaches to MCS clinical management agreed by participants in the recent clinical review of MCS.*

It’s not acceptable to wait until a longitudinal investigation is completed before starting a clinical education program. Also, we don’t think it’s appropriate to give much weight to what was said by the participants in the clinical review of MCS, firstly, because they were anonymous and secondly, because what they agreed on doesn’t amount to practical

guidance. It would be more worthwhile to look at the most effective approaches to diagnosis and treatment overseas, eg at the Environmental Health Center – Dallas (see Rea 1997, particularly the chapter ‘Long-Term Follow Up’ pages 2851-2874) and Breakspear Hospital in the UK (Breakspear Medical Group Ltd 2004).

## 4.5.2 EDUCATION/TRAINING

While clinical education and public education are good ideas in theory, the amount of misinformation in this Working Draft suggests that they could be worse than useless. There is a need for better public information, but the main difficulty assisting those who may be affected to seek appropriate help and treatment is the lack of appropriate help and treatment available.

# 5 APPENDIX 1. A SURVEY OF AUSTRALIAN CLINICIANS APPROACHES TO MULTIPLE CHEMICAL SENSITIVITY

## 5.1 THE SURVEY PROCESS

### 5.1.1 Stakeholder contact

- The Working Draft on Page 42,

*Table 3. Summary of responses from key professional organisations*

<p><i>The Australian Psychological Society (APS)</i></p>	<p><i>The APS was unable to find a member with a specialisation or interest in MCS for interview or completion of the questionnaire, and was also unable to provide any information on the possible role of their membership with individuals with MCS.</i></p>
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There is an Australian psychologist, Louise Samways, who wrote a bestselling book on chemical sensitivities, *The Chemical Connection* in 1989. It’s still in many public libraries. Faye Simpson is an Australian neuropsychologist who worked in a Melbourne ECU and was a co-author of Little et al. 1999. It would not have taken much research to track down either of them, or you could have asked AESSRA.

The Australasian Society of Clinical Immunology and Allergy (ASCIA) is conspicuous by its absence. It has a position statement (Australasian Society of Clinical Immunology and Allergy 2007) which includes MCS:

#### **Clinical Ecology/ Environmental Illness**

Use: Treatment of a variety of illnesses, usually attributed to exposure to dietary or environmental toxins, and sometimes, electromagnetic radiation.

Method: Promoters of clinical ecology claim that much illness results from exposure to dietary or environmental toxins and sometimes Candida. These concepts arose in the first half of the 20th century, when many ill-defined conditions were attributed to "allergy", and well before the key components of the immune system were identified or their function understood. A variety of "diagnostic tests" are used to confirm "sensitivity" such as those alluded to above. Patients usually complain that a number of distinct and chemically unrelated substances may trigger symptoms, such as smells, natural foods, food additives, environmental chemicals and even electromagnetic radiation. Treatment involves major environmental avoidance strategies, dietary changes, and elimination of Candida using antifungal agents or special diets, and "neutralization" of chemicals in order to minimize exposure and strengthen the immune system.

Evidence: Level III-2

Comment: Patients with this diagnosis usually display physical and emotional symptoms (particularly fatigue) involving multiple organ systems. Conventional medical tests are generally normal, showing no evidence of organ dysfunction or disease. There is no evidence of immune dysfunction or immune deficiency in these patients. Similar symptoms are found in some patients suffering from anxiety and depression, and there is evidence that a substantial proportion of patients suffer from psychiatric disorders and benefit from appropriate treatment. Major lifestyle changes can impact on employment, social functioning and nutrition.

This is their biased and out-of-date list of references:

**Clinical Ecology/ Environmental Illness / Multiple Chemical Sensitivity / Idiopathic environmental intolerance**

Terr AI. Environmental sensitivity. *Immunol Allergy Clin North Am* 2003; 23 : 311-28.

Guglielmi RS, Cox DJ, Spyker DA. Behavioral treatment of phobic avoidance in multiple chemical sensitivity. *J Behav Ther Exp Psychiatry* 1994; 25: 197-209.

Staudenmayer H, Selner JC, Buhr MP. Double-blind provocation chamber challenges in 20 patients presenting with "multiple chemical sensitivity". *Regul Toxicol Pharmacol* 1993; 18: 44-53.

Clinical ecology. Executive Committee of the American Academy of Allergy and Immunology. *J Allergy Clin Immunol* 1986; 78: 269-71.

Terr AI. Environmental illness. A clinical review of 50 cases. *Arch Intern Med*. 1986; 146: 145-9.

Caress SM, Steinemann AC, Waddick C. Symptomatology and etiology of multiple chemical sensitivities in the southeastern United States. *Arch Environ Health* 2002; 57: 429-36.

Bornschein S, Hausteiner C, Zilker T, Forstl H. Psychiatric and somatic disorders and multiple chemical sensitivity (MCS) in 264 environmental patients'. *Psychol Med* 2002; 32: 1387-94.

Caccappolo-van Vliet E, Kelly-McNeil K, Natelson B, Kipen H, Fiedler N. Anxiety sensitivity and depression in multiple chemical sensitivities and asthma. *J Occup Environ Med* 2002; 44: 890-901.

Tarlo SM, Poonai N, Binkley K, Antony MM, Swinson RP. Responses to panic induction procedures in subjects with multiple chemical sensitivity/idiopathic environmental intolerance: understanding the relationship with panic disorder. *Environ Health Perspect* 2002; 110 Suppl 4: 669-71.

Levallois P, Neutra R, Lee G, Hristova L. Study of self-reported hypersensitivity to electromagnetic fields in California. *Environ Health Perspect* 2002; 110 Suppl 4: 619-23.

Black DW, Okiishi C, Schlosser S. The Iowa follow-up of chemically sensitive persons. *Ann N Y Acad Sci* 2001; 933: 48-56.

Otto T, Giardino ND. Pavlovian conditioning of emotional responses to olfactory and contextual stimuli: a potential model for the development and expression of chemical intolerance. *Ann N Y Acad Sci*. 2001; 933: 291-309.

Bornschein S, Forstl H, Zilker T. Generalization of acquired somatic symptoms in response to odors: a Pavlovian perspective on multiple chemical sensitivity. *Psychosom Med* 2000; 62: 751-9.

Devriese S, Winters W, Stegen K, Van Diest I, Veulemans H, Nemery B, Eelen P, Van de Woestijne K, Van den Bergh O. Psychological treatment of psychogenic idiopathic environmental intolerance. *Occup Med*. 2000; 15: 627-46.

Staudenmayer H. A nine-year follow-up of people diagnosed with multiple chemical sensitivities. *Psychosomatics* 2000; 41: 253-61.

ASCIA's position statement should be discussed in the Working Draft. Overseas position statements are included so this is a particularly odd omission.

The people who wrote and approved ASCIA's position statement clearly have a belief that MCS is psychological and have no interest in evidence suggesting otherwise. Their views have affected how many Australians with MCS have been treated by doctors and the general community so they should be scrutinised.

### 5.1.3 Interviews

We would like to know why the clinicians who were involved are not named.

- The Working Draft on Page 43,

*Interviews with representatives from MCS support and advocacy groups from most states were also conducted to provide additional background*

*information*

These groups should be named.

Because an ECU opened in Victoria in 1983, Victorians with MCS have had different experiences from people with MCS in other states and it is unfortunate that AESSRA Inc. wasn't one of the support groups that were interviewed.

- The Working Draft on Page 43,

*Germany is the only country in which MCS is a recognised ICD10 disease term*

This contradicts the pers comm. from page 15.

## **5.3 THE COMMON GROUND**

- The Working Draft on page 2

*a clinical consultancy has been undertaken to identify current diagnosis and treatment practices (p. 2)*

In this case current diagnosis and treatment practices should be listed.

- The Working Draft on Page 45,

*Responses to questionnaires demonstrated that individual clinical views were polarised, vigorously stated and defended, based mainly on individual belief and limited clinical experience.*

It is not clear why clinicians with “limited clinical experience” participated. It would have been more useful to look at methods used to treat MCS overseas. For example, *Chemical Sensitivity Volume 4: Tools of Diagnosis and Methods of Treatment* (Rea 1997) draws on studies of more than 20,000 patients at the Environmental Health Center in Dallas.

Part of the problem may be that doctors with little experience of MCS simply generalise from the few patients they have seen and don't understand how severe and disabling MCS can be. For descriptions of four levels of severity see the table from Gibson and Vogel (in press) in the Appendix.

- The Working Draft on Page 46,

*the following common ground was uncovered in the clinical review:*

This is as useful as the common ground between evolutionary biologists and creationists.

## 6.3 CANADIAN GOVERNMENT

The Canadian Human Rights Commission has published two reports on MCS: *The Medical Perspective on Environmental Sensitivities* (Sears 2007) and *Accommodation for Environmental Sensitivities: A Legal Perspective* (Wilkie and Baker 2007).

## 6.4 GERMAN GOVERNMENT

- The Working Draft on page 55,

*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)*

You need more than a pers comm. for a statement of such importance and contention. What Schopen says is counter intuitive to what one would think of a listing on an official German ICD, If this pers comm. represents actuality then get a published reference. What does being incorporated in the ICD-10-SGB-V actually mean? refs needed.

## 6.8 INTERNATIONAL PROGRAM ON CHEMICAL SAFETY (WHO/ILO/UNEP)

- The Working Draft on page 57,

*In February 1996, a workshop organised by the IPCS in collaboration with several of Germany's Federal health and environmental agencies met in Berlin to discuss multiple chemical sensitivities. Invited participants represented a range of disciplines involved in researching, investigating, and treating MCS and other environmental illnesses. The majority of the invited participants suggested that the term "idiopathic environmental intolerances" (IEI) should be used to describe MCS, because they concluded that the condition's pathogenesis is unclear, and a relationship between exposure to chemicals and symptoms was unproven. Other conclusions were:*

However, Ashford and Miller (1998:279-284) say of this workshop, 'The four "NGO representatives" were full-time employees of BASF, Bayer, Monsanto, and Coca Cola, the first three of which claimed affiliation with an industry-funded science institute (the European Centre for Environment and Toxicology).' Ronald Gots, director of the Environmental Sensitivities Research Institute, whose members included DowElanco, Monsanto, Procter and Gamble, and the Cosmetic Toiletries and Fragrances Association, was a participant and 'was also invited to give the "U.S. perspective" on MCS'. Various outside "observers", some of whom were involved in a lawsuit about "wood preservative

syndrome”, were involved in drafting and possibly voting on the recommendations. After certain participants wrongly claimed that IEI was now WHO’s official name for MCS and IPCS received a letter of protest from 80 prominent U.S. scientists and physicians, ‘IPCS clarified the status of the IEI name by issuing a notice stating that WHO had “neither adopted nor endorsed a policy or scientific opinion on MCS.”’ The report now contains disclaimers, including ‘that the document does not necessarily represent the decisions or stated policy of UNEP, ILO, or WHO, that it does not constitute a formal publication; and that it should not be reviewed, abstracted or quoted without the written permission of the Director of the IPCS.’

The Working Draft’s comments on this workshop are misleading and inappropriate. The statement that WHO favours the term “Idiopathic Environmental Intolerances” is incorrect. It is also wrong to say that “*Idiopathic Environmental Intolerance or IEI ... does not make inferences with regards to causative agents*”. Idiopathic means “of unknown cause” so it denies the possibility that MCS can be initiated by chemical exposure.

## GENERAL PROBLEMS WITH THE WORKING DRAFT

There are several problems that affect the entire document:

- Although the Working Draft says on page 9,

*some see MCS not as a single disease entity, but as a collective term describing a range of symptoms associated with environmental exposures (Alterkirch, 2000). This is an important concept as the search for single causative mechanisms and single treatment regimes will not be fruitful if there are a number of conditions existing under the general label of MCS.*

this observation does not appear to inform the rest of the document.

- There appears to be a double standard with regard to evidence: physiological theories are criticized for lack of evidence, but psychogenic theories are taken seriously on the flimsiest of evidence, eg “Psychotherapy, biofeedback and relaxation and other behavioural therapies are regarded as efficacious” (p. 38), or no evidence at all, eg “Other clinicians considered MCS to be a psychopathological condition created, enhanced, and perpetuated by the law and its application, termed a “nomogenic” disorder.”(p. 46) For balance and integrity you must seriously review the critical arguments against psychogenesis, psychiatric illness, belief systems etc as well.
- The Working Draft uses the phrase “lack of agreement” ten times and attributes serious problems to it, so there should be some explanation of who is involved in this “lack of agreement”, what their interests in MCS are and critical analysis of the evidence supporting their views. See Ashford and Miller (1998) for an example.
- **Referencing**

18 references in the text were not in the reference list, and 11 references in the reference list were not in the text. Some of these may be spelling errors in the author's names or date errors or other typos (which the reader should not have to assume to be errors), while there is no apparent reason for the others.

The report is inconsistent in its treatment of multiple authors, in both the text and reference list; sometimes it is 'A and B' and others it is 'A & B'. Choose one way.

Many multiple references in the text are incorrectly written and ambiguous; when multiple references are used for a passage of text be sure to use the correct separators to differentiate references (i.e. commas to separate papers by same author and semi colons to separate papers by different authors (otherwise it is not possible for the reader to determine whether all the references are correct and listed).

The references list is often not in strict alphabetical/date order (especially when the prime author has multiple entries). Look up Miller to see this problem clearly.

While reading the text, I often could not tell if a passage of text was related to a preceding reference or a following reference, or neither.

I have an enormous problem with the sheer volume of unsupported and unreferenced statements and assertions. It really brings the quality of this paper down. I would urge you to sort out as many of these as possible.

Is there a valid reason for using both Ashford NA & Miller CS (1991) and the second edition of the book; Ashford NA & Miller CS (1998).

Here is the reference for Theron Randolph (page 9), the first peer-reviewed paper on chemical sensitivity. Randolph, T.G. (1952). Sensitivity to petroleum including its derivatives and antecedents. *J.Lab.Clin.Med* 40:931-932

- Two Authors to Reconsider

- 1) S. Barrett.

For scientific integrity of your review we strongly urge you to consider very seriously the removal of all reference to material by S Barrett.

Before I (Harry Clark) read your review I had never heard of Barrett or Quackwatch. I was intrigued by the inclusion of a citation, in a scientific review, to a web site called Quackwatch. When I looked through the Quackwatch site I was thoroughly dumbfounded.

To be fair, I decided I needed to look into Barrett a bit more before I came to any conclusions. He is a very interesting character. I have included the reference details to a court case that Barrett reportedly brought and lost (State of Pennsylvania 2005). In this case, while under cross-examination he reportedly conceded that he was not a Medical Board Certified psychiatrist because he had failed the certification exam. What does this say about the scientific integrity of Barrett's words cited in your review? I strongly recommend you read up on this case.

Amongst other odd things, Barrett has called two times Nobel Laureate (1954 Chemistry and 1962 Peace) Linus Pauling a "Quack". Seriously, he called one of the stand-out scientists of the 20th Century a "Quack".

Moving onto specific difficulties I have with the works of Barrett's cited in your Review.

As for Barrett S (1998) and Barrett S (2000) I found them both on the Quackwatch site. These both appear to be personal opinion essays from an advocate/blog web site (Quackwatch), they appear not to be refereed papers or professional reports. And they are by an author who has himself reportedly said in a court of law that he was not a Medical Board Certified psychiatrist because he had failed the certification exam.

As for Barrett S (ed) (1994), while it was in your reference list I didn't find it in the text of your review. So should be removed for just that reason. However, I read the work and it is full of surprises. This again is an advocacy essay, its purpose appears to be to defend industry from litigation, I challenge you to find otherwise in the following extract ...

In immune dysregulation theory lawyers have found a gold mine, a profitable strategy in environmental damage cases." An even bigger gold mine is the "unsick plaintiff." In these cases, the plaintiff does not claim to be ill but merely claims damages due to exposure to an environmental chemical. Because there would be no one to sue if the chemical culprit were a naturally occurring substance, the problem is invariably traced to a nearby industry. The alleged damages may include fear of illness as well as chemically-induced immune dysfunction.

Whole industries are being affected by the specter of class-action suits in which plaintiffs blame chemical exposure for whatever disease they acquire. For example, the pulp and paper industry has spent about \$10 billion dollars in an effort to reduce dioxin content in its waste water. Though the campaign reduced dioxin levels to those found in nature, the pulp and paper industry is justifiably worried. With MCS theory, any exposure could affect the immune system, and any person who drank water downstream from a pulp and paper plant or ate a fish from the same river could sue for damages with at least some chance of winning.

## 2) R Gots

Gots's role in the MSC world is complex. I am troubled by the apparently uncritical use of Gots in your document and ask you to seriously reassess the use of Gots. I say this on the basis of the following:

It has been alleged (Ferrie 2002) that Gots has been strongly accused on stage during a formal debate on MCS, by one of his fellow debaters, of what amounts to scientific fraud and dishonesty. This was apparently in front of an audience of several hundred people at a public debate on MCS sponsored by the American College of Toxicology. The alleged accusation was that his "prestigious study was fictitious, the authors were fictitious and even the journal was fictitious". It would appear he never countered the accusation or perused redress. These alleged accusations are contemporaneous with the papers by Gots you have used.

It is apparent that Gots was the head of a group called Environmental Sensitivities Research Institute (ESRI) and that the chemical industry giants, DowElanco, Monsanto, Procter and Gamble, the Cosmetic Toiletries and Fragrances Association, and other companies and trade associations involved in the manufacture of pharmaceuticals, pesticides, and other chemicals, each paid \$10,000 per year to keep ESRI going. Also Gots apparently ran the National Medical Advisory Group, which provides expert witnesses to defend the chemical corporations in tort lawsuits. (Campbell 1998, McCampbell 2001)

Additionally Gots has been closely associated with Quackwatch and has co-written books with S Barrett (eg Gots and S Barrett (1998) *Chemical Sensitivity: The Truth About Environmental Illness*).

## **WORKS THAT SHOULD BE INCLUDED IN THE REPORT.**

We would like OCS/NICNAS to consider the articles and books we have mentioned in our submission. We think the following deserve extra attention:

Pall M.L. (In Press) *Multiple Chemical Sensitivity: Toxicological Questions and Mechanisms*.

Pall M.L., (2007) *Explaining "Unexplained Illness": Disease Paradigm for Chronic Fatigue Syndrome, Multiple Chemical Sensitivity, Fibromyalgia, Post Traumatic Stress Disorder, Gulf War Syndrome and Others*. Harrington Park (Haworth) Press.

This book explains the NO/ONOO<sup>-</sup> theory. It also has a critical discussion on psychogenic theories, and their fundamental flaws.

Goudsmit, E. & Howes, S. (2008) 'Is multiple chemical sensitivity a learned response? A critical evaluation of provocation studies' *J Nutr Environ Med*, 17(3):195-211

This article should be read because this subject comes up repeatedly in the Working Draft.

Rea, W.J. (1992) *Chemical Sensitivity Volume 1: Principles and Mechanisms*, CRC Press, Boca Raton, Florida

Rea, W.J. (1994) *Chemical Sensitivity Volume 2: Sources of Total Body Load*. CRC Press, Boca Raton, Florida

Rea, W.J. (1996) *Chemical Sensitivity Volume 3: Clinical Manifestations of Pollutant Overload*, CRC Press, Boca Raton, Florida

Rea, W.J. (1997) *Chemical Sensitivity Volume 4: Tools of Diagnosis and Methods of Treatment*, CRC Press, Boca Raton, Florida

Research Advisory Committee on Gulf War Veterans' Illnesses, 2008, *Gulf War Illness and the Health of Gulf War Veterans: Scientific Findings and Recommendations*, Washington, D.C.: U.S. Government Printing Office

[http://sph.bu.edu/insider/images/stories/resources/annual\\_reports/GWI%20and%20Health%20of%20GW%20Veterans\\_RAC-GWVI%20Report\\_2008.pdf](http://sph.bu.edu/insider/images/stories/resources/annual_reports/GWI%20and%20Health%20of%20GW%20Veterans_RAC-GWVI%20Report_2008.pdf)

Serious consideration should be given to the section on sensitivity to chemicals and MCS, and other sections where MCS is mentioned in this authoritative report. In Australia the publication of this report has led to the Repatriation Medical Authority reviewing its 2003 decision not to list Gulf War illness or syndrome as a disease under the Veterans Entitlement Act (Reported in *The Age* 15/1/09).

# APPENDIX

## CATEGORICAL GUIDELINES FOR LEVELS OF DISABILITY

### **Mild**

Able to work. Frequently has many symptoms, some of vague nature. May find petrochemicals and other environmental exposure such as auto exhaust, cigarette smoke and cleaning materials to be unpleasant or produce uncomfortable feelings, but able to work effectively.

### **Moderate**

Able to work at home or with controlled environment at work place. May have to use gas mask or charcoal mask and air purifier filter system. Exposure to inciting agents causes acute symptoms, which may alter functional capacity (severe headache, muscle pain, poor concentration, memory loss, etc.). May have to change job or work conditions if environmental pollution is severe enough.

### **Severe**

Unable to work effectively, even with environmental control, using avoidance, masks or filters. On some days, may be able to work 30 to 60 minute shifts several times a day if in a very controlled environment. Reacts to chemicals such as insecticide, phenols, chlorine, formaldehyde, perfume, petrochemicals, etc. Has severe mental and physical symptoms which may or may not clear. Public exposures such as church, post office, movie, or shopping are not tolerated. Visitors to home much clean up significantly. Can usually care for self in a home situation. May be able to drive if automobile made free of inciting agents, sealed and has charcoal air filters. Has difficulty with other family members of guests in home who bring in aggravating exposures on clothing, printed material, hair, etc. Adversely reacts to many medications. May have to move if existing home has uncontrollable outdoor pollution, is new and has not outgassed, or has other significant problems of mold, flooring, or other incitants. Requires a clean room, carpet-free, cleared of inciting agents, special heating and air filtering. Must wear natural fiber clothing specially laundered.

### **Totally Disabled**

Requires assistance to function in rigidly controlled home environment. Reactive symptoms have spread to virtually all environmental agents including chemicals, foods, pollens and molds. Has mental and physical symptoms that are incapacitating, although frequently not structurally described. Total and very restrictive environmental control required in home and vehicle. Cannot tolerate family or help who have outside exposures with even small contamination of clothing or hair with odors. Visitors usually are too toxic to be tolerated indoors. Usually requires several moves to different areas of the country to find tolerable climate, which is also chemical free. May require unusual and extensive measures to make a tolerable clean refuge area to sleep in. Has difficulties with virtually everything in environment (universal reactor).

From 'E.I. Disability Classification', 1987, *The Human Ecologist*, No. 35, P. 13. Material relating to food sensitivities was deleted.

Reprinted in Gibson, P.R., & Vogel, V.M. (in press). Sickness related dysfunction in persons with self reported multiple chemical sensitivity at four levels of severity. *Journal of Clinical Nursing*.

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Australasian Society of Clinical Immunology and Allergy (2007) *Unorthodox Techniques for the Diagnosis and Treatment of Allergy, Asthma and Immune Disorders* (updated, November 2007, accessed 29 January 2009) <http://www.allergy.org.au/pospapers/unorthodox.htm>

Breakspear Medical Group Ltd (2004) [http://www.breakspearmedical.com/files/multiple\\_chemical\\_sensitivity.html](http://www.breakspearmedical.com/files/multiple_chemical_sensitivity.html)

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