

A SCIENTIFIC REVIEW OF MULTIPLE CHEMICAL SENSITIVITY: IDENTIFYING KEY RESEARCH NEEDS

Draft Report prepared by the
National Industrial Chemicals Notification and Assessment Scheme
(NICNAS) and the Office of Chemical Safety and Environmental
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SUBMISSION

by **Catherine McIver**
on behalf of

aessra

**Allergy and Environmental Sensitivity
Support and Research Association Inc.**

Reg. No. A0006141S ABN 32 386 589 943

P.O. Box 298, Ringwood, Vic 3134

www.aessra.org

The February 2010 Draft is a big improvement on the November 2008 Draft, but it is still seriously flawed and misleading. There are too many errors, apparent misunderstandings of important concepts and instances of biased language, and some important studies and other resources have been ignored.

WHAT IS MULTIPLE CHEMICAL SENSITIVITY?

It is worth contrasting the Draft Report 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), which is far more informative and objective:

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.^{212,1044} [Caress et al (2002), Miller and Prihoda (1999)].

On page 5 the February 2010 Draft Report says

A common theme reported by individuals is experiences of heightened responsiveness to chemicals at extremely low exposure levels.

“Heightened responsiveness to chemicals at extremely low exposure levels” is not “a common theme”; it is the defining characteristic of MCS.

The Draft Report says on page 8:

In terms of sensitivities involving chemicals, the terms “MCS” and “chemical sensitivity” (sometimes known as “chemical intolerance”) are often used interchangeably. However, “chemical sensitivity” in its wider context can describe several distinct types of reactions encompassing classical adverse toxicological reactions, immunological “allergic” sensitivities, individual chemical idiosyncrasies and intolerances through to aversions to particular odours. Broadly, on the basis of consensus criteria, MCS is distinguished from other types of chemical sensitivities or intolerances predominantly on the basis of reactions to multiple, diverse chemical substances, the wide spectrum of non-specific symptoms reported in multiple organ systems and the extremely low levels of environmental exposures linked to responses.

The Consensus Criteria don’t say anything about mechanisms and so don’t rule out “other types of chemical sensitivities or intolerances”. They don’t mention “the wide spectrum of non-specific symptoms reported in multiple organ systems”. You have invented this. ‘Multiple Chemical Sensitivity: A 1999 Consensus’ (Bartha et al. 1999) does say,

we recommend that MCS be diagnosed whenever all 6 of the consensus criteria are met, along with any other disorders that also may be present, such as asthma, allergy, migraine, chronic fatigue syndrome (CFS), and fibromyalgia (FM). 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.

The Draft Report says on page 8:

The initial concepts underlying MCS were developed by the allergist Theron G. Randolph who, in the 1950's, asserted that patients became ill from exposures to a wide variety of environmental, occupational and domestic substances at levels far below those that affect the majority of the population. Randolph and colleagues developed a conceptual framework of allergic reactions, masking and maladaptation to explain symptoms in individuals that resemble what is referred to most frequently today as MCS (Randolph, 1961).

Again, the Research Advisory Committee on Gulf War Veterans' Illness (2008:278-279) does it better:

Historically, persistent reactivity to low-level chemical exposures following an acute initiating exposure was described by Hans Selye in the 1930s.¹³⁸⁵ [(Selye 1936)] In the 1960s, Theron Randolph diagnosed a chemical maladaptation syndrome in patients whose diverse symptoms improved after living up to a week in a specially designed chemical-free environment.¹²⁵³ [(Randolph 1964)]

Saying that “the initial concepts underlying MCS were developed by the allergist Theron G. Randolph” makes it sound as if he invented MCS. He described it based on his observations. The concepts he and his colleagues developed underlay their methods of diagnosis and treatment, not MCS itself (Ashford and Miller 1998:19-20).

“Observed” would be a more accurate and less biased word than “asserted”.

Although you cite Randolph 1961 in your text, you don't include Randolph in your list of references. Randolph, T.G. (1952). Sensitivity to petroleum including its derivatives and antecedents. *J.Lab.Clin.Med* 40:931-932 and his other articles published in the 1950s about reactions to chemicals would be appropriate.

The Draft Report says on page 8

Reflecting a rise in the general recognition of environmental medicine, the Society for Clinical Ecology founded by Randolph and colleagues in 1965 changed its name in 1984 to the American Academy of Environmental Medicine.

Where is your evidence that this is the reason for the change of name?

The Draft Report says on page 8

Although MCS is the most common term, there have been many terms used in the scientific literature and public media to describe the condition encompassing a range of symptoms linked to environmental chemical exposures (Sears, 2007). 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)*
- Acquired Intolerance to Solvents*
- Total Allergy Syndrome*

You've wrongly cited Sears here. Her list titled, "Aspects of Environmental Sensitivities", is:

State of heightened reactivity to the environment
Total allergy syndrome
Toxicant-Induced Loss of Tolerance (TILT)
Multiple chemical sensitivity(ies) (MCS)
Multiple chemical hypersensitivity(ies)
Chemical intolerance(s)
Gulf War illness/syndrome
Idiopathic environmental intolerance
Environmental illness
Chemical injury/allergy
Toxic injury
Tight building syndrome
Sick building syndrome
Twentieth century disease
Chemically induced illness
Chemophobia
Electromagnetic (hyper)sensitivities/intolerance
Radiowave sickness

Your list comes from Read 2002. If these terms are to be listed in the final Report it would be helpful if you distinguished between terms currently in scientific use, terms used historically and terms invented by the media. You should have tried googling each term before including it.

Read's 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).

The Draft Report says on page 9:

Use of the descriptor Idiopathic Environmental Intolerance (IEI) was favoured by many, but not all, participants at an International Programme on Chemical Safety (IPCS) workshop on multiple chemical sensitivities organised by the United Nations Environment Programme (UNEP), the International Labour Organization (ILO) and the World Health Organization (WHO). The term was suggested on the basis that it does not make inferences with regards to causative agents (Anonymous, 1996; Lessof, 1997).

The IPCS 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 (Anonymous, 1996). One of the principal (but not unanimous) conclusions from the workshop was that use of the term MCS should be avoided because it makes an unsupported judgement on causation. Instead, use of the descriptor “Idiopathic Environmental Intolerances” was suggested (Anonymous, 1996; Lessof, 1997).

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.’

Although your Summary of Revisions (2010:4) says

The review discusses scientific controversy as relating to the technical aspects of MCS, but does not discuss the politics of MCS, neither from the viewpoint of proponents nor skeptics of the validity of the MCS diagnosis.

there is no escaping the politics of MCS. By using biased language and a biased selection of evidence, NICNAS is taking part in the politics of MCS. Pretending to ignore the politics at the same time makes this worse.

You should point out that it is wrong to say that Idiopathic Environmental Intolerance (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. Also, note that there is a growing body of evidence pointing to the cause(s) of MCS (Pall 2007) making the term IEI obsolete and inaccurate.

You should also point out that it is wrong to say that the term MCS “makes an unsupported judgement on causation”. The term MCS is descriptive: people with MCS are sensitive to multiple chemicals.

WHAT ARE THE SYMPTOMS OF MCS?

The Draft Report includes a list of common symptoms, but it is important to note that people with MCS also commonly suffer more serious and disabling reactions to chemicals such as migraines and asthma (Ziem and McTammey 1997). Anaphylaxis (Saunders et al. 1995) and seizures (Ziem and McTammey 1997) can also occur. Not mentioning more severe and disabling symptoms may lead readers to underestimate the seriousness of MCS.

CAN MCS BE CLINICALLY DEFINED?

The Draft Report says on page 13:

The following description (Cullen, 1987) is now the most commonly cited case definition within the MCS literature:

Where is your evidence that Cullen’s description “now the most commonly cited case definition within the MCS literature”?

DOES MCS HAVE A DISEASE CLASSIFICATION?

The Draft Report says on page 5:

At this time, worldwide, MCS is not an internationally classified disorder, with only one country (Germany), listing MCS in their national disease classifications.

and on page 15:

In Germany, MCS is included in the alphabetical index of the German version of the International Statistical Classification of Diseases and Related Health Problems (ICD-10-SGB-V) first published in November 2000 by the German Institute of Medical Documentation and Information (DIMDI). At this stage, no other country has followed the German listing.

and on page 64:

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

Austria uses the same WHO ICD-10 Code for MCS as Germany, according to a letter from the Bundesministerium für Gesundheit (Schlögel 2009). Japan is reported to have added MCS to its version of the ICD-10 on 1 October 2009 (Caballé 2009).

DO INDIVIDUALS WITH MCS SHARE COMMON CHARACTERISTICS?

Yes, many share a history of exposure to toxic chemicals and/or particular genes.

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).

Six genes that help determine the metabolism of chemicals have been found to influence susceptibility to MCS. See Pall 2009 and Pall's submission on this Draft Report.

MCS affects all age groups. A survey of Australians with MCS, which formed the basis of an article in *Health Issues* (McIver 2007), found that the 125 respondents who fitted the Consensus Criteria for MCS (out of 151 who returned questionnaires) ranged in age from 18 months to 88 years, and 47 (37.9%) were 60 or over.

IS MCS RELATED TO OTHER SYNDROMES OR DISORDERS?

See comments on Read's list of terms for MCS under 'What is Multiple Chemical Sensitivity?' above.

The Draft Report says on page 18:

The multiple subjective non-specific symptoms and timecourses associated with MCS have been reported to be noticeably similar to other multi-organ or multi-symptom conditions that have ICD classifications such as chronic fatigue syndrome (CFS), fibromyalgia (FM) and post-traumatic stress disorder (PTSD) (Aaron et al., 2001; Bornschein et al., 2001; Pall, 2002; Lacour et al., 2005).

The symptoms of flu are similar but this doesn't mean flu is related to MCS. You need to look at syndromes and disorders where symptoms are triggered by exposure to low levels of chemicals. For comprehensive and evidence-based lists of medical conditions linked to chemical sensitivity see Ashford and Miller (1998) and Rea (1996).

The Draft Report says on page 19:

Self-reported health complaints attributed to dental amalgam have been compared to MCS (Malt et al., 1997) and the evidence linking amalgam dental restorations to a wide variety of diseases has been reviewed (Dodes, 2001).

You should explain why self-reported health complaints attributed to dental amalgam have been compared to MCS. You should point out that there is no mention of MCS or chemical sensitivity in Dodes' review.

The Draft Report says on page 19:

The symptomatology of MCS is indistinguishable from that of other multi-system disorders which have established ICD classifications.

And on page 5:

The symptom profile of MCS is indistinguishable from other multi-symptom disorders.

What obviously distinguishes MCS from other multi-symptom disorders is that in MCS symptoms occur with low-level chemical exposure.

The Draft Report says on page 19:

Some are of the view that a diagnosis of these other multi-symptom disorders should exclude a diagnosis of MCS (Lacour et al., 2005).

You should explain why they are of that view. Bartha et al. 1999 say,

we recommend that MCS be diagnosed whenever all 6 of the consensus criteria are met, along with any other disorders that also may be present, such as asthma, allergy, migraine, chronic fatigue syndrome (CFS), and fibromyalgia (FM). 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.

MECHANISMS OF MULTIPLE CHEMICAL SENSITIVITY

The Draft Report gives the impression that the hypotheses discussed are alternative explanations for MCS, but this is not always the case. Several fit together and some others are not incompatible with each other.

The Draft Report says on page 20

the heterogeneity of symptoms has given ground for doubt as to whether MCS is a single nosological entity with a specific aetiology and pathogenesis (Altenkirch, 2000; Lacour et al., 2005).

It is important to note that there may be subgroups of people with MCS due to different causes.

The Draft Report says on page 6

While there are a number of proposed mechanism(s) that warrant further research consideration, based on biological plausibility, testability and known research gaps, the following modes of action for MCS are highlighted for further scientific research and investigation as priorities:

Elevated nitric oxide, peroxynitrite and NMDA receptor activity should be on this list.

Immunological dysregulation

The Draft Report says on page 21

Overall, a consistent pattern of immunological reactivity or abnormality indicative of a specific immunological deficit has yet to be found in MCS (Simon et al. 1993; Graveling et al. 1999; Labarge and McCaffrey, 2000).

Your evidence that “a consistent pattern of immunological reactivity or abnormality indicative of a specific immunological deficit has yet to be found in MCS” comes from studies from seventeen years ago, eleven years ago and ten years ago. You need to include more research. 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.” 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.” 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.”

Limbic kindling/neural sensitization and psychological cofactors

The Draft Report says on pages 46-47

An important research question relates to the extent to which psychological factors contribute not only to the initiation but also to continued disability in long-term MCS. This 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 Siegel and Kreutzer (1997), the use of balanced-placebo study designs for testing the power of expectation similar to those used in alcohol research 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.

Using “deception procedures” on people with MCS couldn’t 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.” This probably wouldn’t 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.

Elevated nitric oxide, peroxynitrite and NMDA receptor activity

This section has so many errors it’s hard to believe they are accidental. Other sections of the Draft Report mentioning Pall’s work also have serious errors. Please reread Pall’s work and act on his submission on this Draft Report.

Toxicant-induced loss of tolerance (TILT)

The Draft Report says,

Miller (1997) proposed another disease theory, TILT, to explain MCS pathogenesis.

It's important to note that Miller does not propose TILT to only explain MCS pathogenesis, unless you are using an extremely broad definition of MCS which you don't seem to be doing in the rest of the Draft Report. For example, Miller wrote in 2000:

TILT, or toxicant-induced loss of tolerance, bridges the gap between addiction and abidction and has the potential to explain a variety of illnesses, including certain cases of asthma, migraine headaches and depression, as well as chronic fatigue syndrome, fibromyalgia and "Gulf War syndrome".

The Draft Report says

No mechanism is proposed to account for the initial loss of tolerance or the apparent spread of sensitivity to other unrelated chemicals.

and

it is unclear to what extent they would elucidate the TILT theory for MCS as no particular physiological mechanism has been proposed to explain the chemical sensitivity.

This isn't true. Miller (2000) wrote

We do not know exactly how this breakdown in tolerance occurs. We do know that rats bred for sensitivity to organophosphate pesticides (the Flinders Sensitive Rat Line) are also intolerant of structurally diverse drugs, including nicotine and ethanol, and have increased gut permeability, which in humans is associated with food intolerance (Overstreet *et al.*, 1996). These rats also over-respond to inhaled methacholine, which causes bronchoconstriction mimicking asthma in humans, and to inhaled ovalbumin, which causes both bronchoconstriction and inflammation, resembling allergic asthma (Djuric *et al.*, 1998). These observations suggest that the tolerance breakdown may involve the cholinergic nervous system, which regulates vital processes throughout the body. Another possibility is that chemicals might disrupt or sensitize neural pathways that link the olfactory system with the limbic system in the brain, leading to depression and cognitive difficulties (Bell, Miller & Schwartz, 1992). Several investigators have proposed neural sensitization as a model for multiple chemical intolerance (Bell *et al.*, 1999; Sorg, 2000). Memory and addiction appear to be interrelated phenomena (Berke & Hyman, 2000), which may have some intersection with the memory difficulties caused by chemical exposure in susceptible individuals. The striking parallels between chemical intolerance and addiction suggest they may share the same underlying mechanism, one likely involving multiple neurotransmitters and genetic polymorphisms.

In addition Pall's NO/ONOO⁻ cycle theory (Pall 2007a, Pall 2007b, Pall 2009) can explain both the initial loss of tolerance and the spread of sensitivity to other unrelated chemicals.

The diverse symptoms associated with MCS is explained with use of a masking concept, with the specific response to a particular toxicant being masked by responses to other exposures still affecting the person (Ashford and Miller, 1998; Miller, 1996, 1997; 2000; Miller et al., 1997; 1999a, b).

No, “Masking hides the relationship between symptoms and triggers.” (Miller 2000)

Altered xenobiotic metabolism

You should include the study of UGT1A1 by Müller and Schnakenberg (2008).

You have either missed the significance of the genetic studies or decided not to tell people. Both options reflect badly on you. The genetic studies provide strong evidence that exposure to toxic chemicals can cause MCS in genetically susceptible people. Please take note of Pall (2009) and Pall’s submission on this Draft Report.

Behavioural conditioning

The behavioural conditioning hypothesis depends on people with MCS being able to smell the 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). People with MCS react to chemicals, not to the smell of chemicals.

Psychological factors

The APA is proposing to **combine somatization disorder, hypochondriasis, undifferentiated somatoform disorder, and pain disorder into a new category entitled “Complex Somatic Symptom Disorder” (CSSD) in DSM-5. The APA (2010) says, “This is a major change in the diagnostic nomenclature, and it will likely have a major impact on diagnosis. It clarifies that a diagnosis of CSSD is inappropriate in the presence of only unexplained medical symptoms.”**

As the symptoms of MCS can be explained medically (Pall 2009) somatization disorder and somatoform disorder are inaccurate and inappropriate diagnoses for people with MCS.

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).

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

Chemical initiators/triggers and biological gradients

The Draft Report says on page 41

overall, the identification of chemical species implicated in MCS is poor, relying mostly on identification of chemical uses or chemical products e.g. pesticides, solvents, perfumes, cleaning products, or biological material (e.g. mold) rather than identifying particular chemical species associated with cases of MCS. From a toxicological point of view, understanding mode(s) of action in MCS would benefit from detailed information on chemical functional groups shown to be implicated in MCS and how they interact with biological tissues.

This depends on government regulatory bodies requiring that ingredients of chemical products be listed and that the public be notified (eg with signs) that chemical products have been used, so that members of the public can know what they have been exposed to.

DIAGNOSIS, TREATMENT AND MANAGEMENT OF MULTIPLE CHEMICAL SENSITIVITY

The Draft Report says on page 5

Presently, a diagnosis of MCS is based on self-reported symptoms and chemical exposure histories.

This isn't true. It's common but far from universal. In Victoria hundreds of patients with MCS were diagnosed in the way Ashford and Miller (1998) recommended – in an Environmental Medical Unit (Environmental Control Unit). 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. Ashford and Miller (1998:129-135) discuss provocation-neutralization. Environmental Control Units have been used to diagnose MCS since the 1950s.

It also says on page 5

No laboratory tests currently exist for diagnosing MCS.

This is misleading because, although there is currently no single laboratory test that gives a definitive diagnosis of MCS, a number of laboratory tests find abnormalities in patients with MCS and can be useful in some circumstances.

The Draft Report says on page 50

For MCS, clinicians are confronted with a range of self-reported symptoms with which individuals present, differing views on modes of action for MCS, no characteristic diagnostic markers for the disorder and challenges in determining the types and levels of chemical exposures responsible for symptoms.

An Environmental Medical Unit/Environmental Control Unit (Ashford and Miller 1998:54-6, 305-308) makes the diagnosis of MCS straightforward. 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.

TREATMENT FACILITIES

The Draft Report says on page 54

Evidence given to the South Australian Parliamentary Inquiry indicated that in the past there were specific facilities in Australia catering for the chemically sensitive. However, particular facilities were closed because it was concluded that the treatments provided by the facility were not effective (Social Development Committee, 2005).

This isn't true and it is very misleading. The comment made to the South Australian Parliamentary Inquiry only referred to the Sydney facility, 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. This was pointed out in AESSRA's submission on the November 2008 Working Draft so there is no excuse for what you have written here. It looks as if you have some sort of not-very-hidden agenda.

TREATMENT/MANAGEMENT STRATEGIES

The Draft Report says on page 54

Pharmaceutical treatments for MCS currently do not exist.

Dextromethorphan has been successfully used to treat symptoms triggered by chemical exposures in MCS (Dudley 1998, Pall 2007:292). It has also been used to treat fibromyalgia (Cohen et al. 2006) which some consider a related condition.

The Draft Report says on page 55

Some advocacy and support group websites (both national and overseas) note a wide range of treatments that are, or have been, used 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. However, in terms of a specific

treatment, information from these societies and groups does not establish a consensus for the treatment of MCS other than management by avoidance of chemicals that cause symptoms.

and says on page 66

Some advocacy and support group websites note a wide range of treatments including intravenous vitamin C and other 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 doesn't appear to be true and is misleading. Googling the websites for the Australian advocacy and support group websites below revealed that none of them mention colonic irrigation. On some of these therapies any information most support groups would present would be negative. If you are going to include a list like this you need to provide references for each treatment listed. Otherwise it looks as if you just made it up and makes the accuracy of the rest of this report look even more doubtful.

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 Draft Report says on page 5

There are no standardised treatments for MCS. The most common management regime for MCS is avoidance of agents that trigger symptoms.

Avoidance *is* treatment, not just management. Avoidance measures were pioneered by members of the AAEM and are now recommended by most doctors treating people with MCS, apparently even the Australian doctors who took part in the survey in Appendix 1 and “considered MCS to be a psychopathological condition created, enhanced, and perpetuated by the law and its application, termed a “nomogenic” disorder.” (p. 65 of the Draft Report)

See the American Academy of Environmental Medicine Practice Guidelines (1980), which are followed by a large number of doctors, for standardised treatments for MCS. As well as doctors in the US, their website currently lists doctors in Australia, Brazil, Canada, Italy, Japan, Mexico, Norway, Switzerland and the UK.

Also see *Chemical Sensitivity Volume 4: Tools of Diagnosis and Methods of Treatment* by William Rea (1997), which describes the procedures in the American Academy of Environmental Medicine Practice Guidelines (1980) and other procedures used at the Environmental Health Center – Dallas in detail and draws on studies of more than 20,000 patients at the Environmental Health Center in Dallas. The chapter ‘Long-Term Follow Up’ (pages 2851-2874) shows the effectiveness of their methods and the barriers to effective treatment that people with MCS face.

CLINICAL APPROACHES TO MCS IN AUSTRALIA

The Preface of the Draft Report states

the review identifies current diagnosis and treatment practices

No, it doesn't. They are not listed in the Draft Report.

The Draft Report says on page 57

MCS Clinical Management Principles

Accept that the person with MCS feels ill and is affected 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 and in parts harmful to patients. It would have been much better to consider information from effective overseas clinics instead of just relying on the common ground of a small group of anonymous Australian doctors.

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.

Saying, "Clinicians need to accept the patient's issues as a debilitating and disabling illness irrespective of whether the clinician recognises or accepts the presence of a condition, in order to minimise patients seeking unnecessary referrals," (Draft Report p.67) is harmful to the patient.

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 and food challenges, 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 (McIver 2007); 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.

The MCS Clinical Management Principles don't recognise that some groups of people with MCS have special needs, for example, pregnant women with MCS, children with MCS, elderly people with MCS and people with MCS and other medical conditions.

They also fail to consider the fact that many people with MCS have limited ability to avoid chemicals because of lack of money. This is a common problem. A 2004 survey of Australians with MCS, which formed the basis of an article in *Health Issues* (McIver 2007) found that, of 106 people with MCS who were of working age, 38 (35.8%) received the Disability Support Pension and two (1.9%) received Sickness Benefit. Among the severe MCS group, 44 were of working age and 25 (56.8%) received the Disability Support Pension.

CLINICAL RESEARCH NEEDS

The Draft Report says on page 57

Some challenge tests of inhaled chemicals suggest that it is the odour of an airborne triggering agent, or an expectation of harm from exposure, rather than any pharmacological or toxicological properties per se that elicits MCS symptoms.

You should say which challenge tests are referred to here. There have been serious flaws in a number of them (Ashford and Miller 1998:218-223, Goudsmit and Howes 2008).

The Draft Report says on page 58

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

- *Standardising diagnostic criteria for MCS that are acceptable to, and utilised consistently by, clinical and scientific groups;*

- *Determining the prevalence of MCS, for both self-reported cases and those that are medically diagnosed using standardized criteria;*
- *Exploring initiating/triggering agents/events and modes of action in MCS through the use of well designed and conducted blinded challenge tests and longitudinal studies of illness course;*
- *Determining and documenting effective treatment/management protocols for MCS based on positive, long-term 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. Properly conducted challenge studies could be put to much better use studying the effects of exposure to low levels of chemicals on people with MCS, with baseline and after exposure neuropsychological tests, tests of lung function, blood pressure and other measures. 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.

A longitudinal clinical and sociological study may be used as 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 attitudes shown by some of the doctors who took part in the 2006 Survey (Appendix 1), and the bias and numerous errors in the Draft Report, would deter many people with MCS from taking part in a longitudinal and sociological study.

The Draft Report says on page 58

Prevalence estimates need standardised criteria and surveys of sufficient power to distinguish MCS from other types of chemical sensitivity. A recently developed and validated symptom profile inventory (the Idiopathic Environmental Intolerance Symptom Inventory) could be utilised for reliably and rapidly studying symptom prevalence in MCS (Andersson et al., 2009).

The Quick Environmental Exposure and Sensitivity Inventory (QEESI) would be a better choice. It is the most widely used screening inventory (Miller and Prihoda 1999). It has already been used in the U.S., Japan (Hojo et al. 2008, Hojo et al. 2009), Germany and Sweden (Nordin and Andersson 2010).

Education/Training

The Draft Report says on page 59

There is unlikely to be coverage of MCS within the current Australian medical curriculum given the relatively small amount of time devoted to minor specialties. There are also currently no guidelines available to assist practicing clinicians to provide appropriate care for MCS individuals.

Which specialty is MCS part of?

The Australasian Society of Clinical Immunology and Allergy (ASCIA) has a position statement (Australasian Society of Clinical Immunology and Allergy 2007) which includes MCS, but it certainly doesn't assist practicing clinicians to provide appropriate care for people with 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

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It should be noted that ASCIA's position statement is misleading doctors and the public about the nature of MCS and how people with MCS should be treated.

The Draft Report says on page 59

the development of a clinical education program should be investigated. 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, it's not 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).

APPENDIX 2. VIEWS OF NATIONAL GOVERNMENTS AND PROFESSIONAL MEDICAL ORGANISATIONS

The following should be added:

UNITED STATES

Centers for Disease Control and Prevention (CDC)

The CDC's June 2009 Indoor Environmental Quality Policy for its own buildings recognises chemical sensitivities and bans fragrances and scented products and requires less toxic products and practices for construction, cleaning and pest control. Reported by the Human Ecology Action League (2010).

Department of Veterans Affairs

The report, *Gulf War Illness and the Health of Gulf War Veterans: Scientific Findings and Recommendations*, by the Research Advisory Committee on Gulf War Veterans' Illness (2008) has a section on Multiple Chemical Sensitivity.

Environmental Protection Agency (EPA)

On its website the EPA defines **Multiple Chemical Sensitivity** as "A diagnostic label for people who suffer multi-system illnesses as a result of contact with, or proximity to, a variety of airborne agents and other substances." (U.S. Environmental Protection Agency 2006)

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).

Austria and Japan: ICD classification for MCS.

The Draft Report says on page 75

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

The International Programme on Chemical Safety (IPCS), established in 1980, is a joint programme of three Cooperating Organizations, the United Nations Environmental Programme (UNEP), the International Labour Organisation (ILO) and the World Health Organisation (WHO), implementing activities related to chemical safety. WHO is the Executing Agency of the IPCS, whose main roles are to establish the scientific basis for safe use of chemicals and to strengthen national capabilities and capacities for chemical safety. In February 1996, a workshop organised by the IPCS in collaboration with several of German federal health and environmental agencies met in Berlin to discuss multiple chemical sensitivities. Invited participants represented a range of scientific disciplines but focussed on occupational and environmental medicine and toxicology. 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:

- IEI cannot be recognised as a clinically defined disease;*
- Clinical assessment should be designed to exclude conditions requiring specific treatment;*
- There are no specific tests to diagnose the condition;*
- Effective treatment has not been validated in controlled clinical trials;*
- Approaches to care based on supportive care and understanding are necessary;*
- Interdisciplinary approaches should be sought for diagnosis and treatment.*

The recommendations of the workshop included challenge studies to distinguish psychogenic from toxicogenic origins and epidemiological research directed at the prevalence of relevant symptoms and correlates such as demographics and time trends and the concurrent presence of other unexplained disease states, such as CFS and Gulf War Veterans illnesses. The workshop also recommended that public information be based on established facts and not on speculation and that coordination occur between responsible health care systems, institutions and insurers in order to coordinate approaches to patients with IEI (Anonymous, 1996).

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.’

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