

1. **The single biggest issue** facing scientific progress on MCS is the high stakes involved and the politics and various overt and covert lobbying pressures and research distortions that result. Although this *is* the biggest issue likely to affect scientific progress and resulting patient treatment it **is not covered at all in the draft**. If the report is to adequately meet its stated objective “to examine current understanding and scientific research on MCS and to identify priority areas for further study and research to inform and engage the clinical and scientific research community” then it *must* cover this issue to ensure the accuracy, timeliness and appropriateness of the recommendations and to provide an accurate context and interpretation of the remainder of the report.

Discussion:

If/when it is eventually proved that many people are irretrievably damaged by exposures to common chemicals either as sensitisers (chemicals that affect the patient’s immune or related systems in ways not currently understood, making them sensitive to other concomitant chemicals) or direct irritants (chemicals that themselves cause symptoms at exposure levels below the level currently understood to be problematical), then the simplistic and popular government response would of course be to ban those chemicals. The potential costs of such restrictions (and of associated public anti-chemical hysteria) to industry, agriculture and government are enormous. Thus there is a strong motivation by various vested interests to ensure that this does not happen. As with tobacco, hemp and climate change there is no doubt that those with vested interests have and will continue to use legitimate and sometimes less legitimate means to devalue good research into the relevant issue as a means of avoiding the enormous costs they fear. This is undoubtedly happening with MCS. The fear needs to be eased.

NICNAS in this report should be raising the level of debate by, on the one hand, accepting that these pressures already exist and analysing and presenting the ‘research’ accordingly and, on the other hand, making it clear that the eventual response to MCS as a reality would not mean wholesale banning of every chemical known to cause a problem, but rather the establishment of an environment where :

- data collection related to offending chemicals is transparent and efficient,
- minimal legislated regulation is in place to ensure that avoidance, management and treatment are not only possible but well recognised and accepted, and
- identification of a particular chemical as an MCS concern is not a ‘death sentence’ for that chemical in terms of manufacture, IP value or use but in most cases only a trigger for useful and minimum-cost monitoring and control of its application.

Summary comment on this point:

- A. The report should acknowledge the political reality of MCS and that this has encouraged some biased ‘research’ and information papers which aim to generally denigrate MCS as a physical condition and more particularly to extend interminably the period of ‘controversy’ and the ‘doubt’ over physical vs psychological aetiology. It should attempt to distinguish between good and bad quality research and biased and unbiased research.

- B. The report should canvas the stakes involved on both sides and make some guiding statement as to possible reasonable and non-catastrophic approaches to dealing with the probably reality that some chemicals do cause MCS or symptoms of MCS. This should aim to raise the level of discussion from “commerce and government vs sufferers” to a progressive multi-partisan approach.
- C. The report should not fall into the trap of yet again extending indefinitely the process of research and eventual treatment. As it is written now it does nothing but adopt the industry line and propose yet more vague research with no priorities or timeframe stated, even in areas where dispassionate assessment makes it obvious that no more research is required.

2. The report as a whole concentrates on the areas of doubt and emphasises what is not known, or rather, what is disputed, instead of what *is* known. The harder facts and their socially responsible consequences are simple:

- MCS causes enormous suffering and economic consequence
- MCS is currently largely ignored by government, the medical mainstream and by Australian researchers.
- sufferers need immediate government and medical support and recognition, and the establishment of a combined treatment and research facility as well as updated protocols and advice to professionals.
- adequately funded unbiased research is needed and justified.

3. Other comments below are indexed by the relevant section numbers in the draft.

DR §1.1 and §4.5 and yet again §1.2.2 “Available reports suggest that MCS individuals do not show a typical dose-response reaction following exposure to triggering agents.”

This is simply not true. MCS individuals clearly show dose-response relationship but at much lower levels than are associated with the “normal” effects of these chemicals. Every MCS sufferer can recount having “slight” symptoms and being able to avoid offending chemicals to a greater or lesser extent with greater or lesser effects. Publishing this sort of nonsense devalues the whole report.

Further, it is completely inappropriate to include such an erroneous statement in the Exec Summary. Equally this statement does not belong, even if it were true, in §4.5 which is essentially the concluding recommendations.

4. DR §1.1 and §4.5 and again §1.2.2 “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.”

While some poorly designed studies may suggest this, it is clearly not true as a defining or even useful characteristic of MCS and the untruth can easily be demonstrated. There

are many MCS sufferers who have severe sensitivities to odourless chemicals and chemicals which are contacted via skin or gut. The report should rise above reporting such badly conducted studies or incorrect application of conclusions to areas beyond the scope of the study or extending a limited conclusion to MCS as a whole. The conclusions reported may be applicable in some behavioural study but are not applicable in determining the direction of research for MCS or, by strong implication, in a debate about the “reality” of MCS.

This pre-occupation with smell and odour pervades the report and is simply wrong. There are many MCS responses to odourless chemicals.

Again it is completely inappropriate to include such an erroneous statement in the Exec Summary. Equally this statement does not belong in §4.5 which is essentially the concluding recommendations.

*5. DR §1.1 “While numerous attempts have been made to define MCS, there is no unequivocal epidemiological evidence or quantitative or qualitative exposure data to distinguish individuals with **MCS** from others experiencing symptoms such as fatigue, headache, dizziness, lack of concentration or memory loss and labeled with diagnoses such as Chronic Fatigue Syndrome.”*

This is a meaningless statement when read carefully that casts doubt where none need exist. There is equally “no unequivocal epidemiological evidence or quantitative or qualitative exposure data to distinguish individuals with **pre-menstrual symptoms** from others experiencing symptoms such as fatigue, headache, dizziness, lack of concentration or memory loss and labeled with diagnoses such as Chronic Fatigue Syndrome”. But PMS symptoms are recognized and treated effectively. Epidemiological evidence is not a means of distinguishing an individual in any way, and it is not clear what “quantitative and qualitative exposure data” actually means in this context other than to be vaguely denigrating and imply rather than demonstrate a lack of evidence. There have been tests that show that MCS symptoms are caused by exposure.

DR§1.2.1 “Analysis of the scientific literature has identified that 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.”

There are many examples of MCS that do not involve smell i.e. olfactory pathways. Many would not agree this is the most credible mechanism, what is the basis for this statement? It needs to be removed or justified.

DR§1.2.1 “The scientific weight-of-evidence currently suggests that while physiological mechanisms may play a part in MCS, there may also be a psychological or psychogenic component in its pathogenesis. Medical/scientific opinion suggests that MCS has a multifactorial origin, involving physiological, psychological and social predispositions.”

This is an 'explanation' that has been discredited in the context of other previously unexplained chronic illnesses that are now adequately explained without invoking psych or social predispositions. It is convenient, lazy and entirely unsubstantiated proposition that has not proven accurate for any 'unexplained' illness to date. There is no evidence for it at all other than a lack of evidence to the contrary, which as any Philosophy 101 student can tell you, is not evidence.

DR §1.2.1 Finding 3. *"The development of a clinical education program be investigated."*

What sort of recommendation is this? The recommendation should be "A clinical education program should be established". The phrasing used here is reminiscent of much of the entire report and its transparent emphasis on delay, doubt and maintaining the status quo. Many parts of the report appear well and dispassionately written, but other sections carry apparent bias against MCS as a real illness or one worthy of serious research and treatment. It appears as though different authors with different agendas have written parts of the report.

DR §2.1 *"For this reason, the descriptor Idiopathic Environmental Intolerance or IEI is favoured by many, including the World Health Organization (WHO), because it does not make inferences with regards to causative agents. This reflects the lack of an agreed biological basis for MCS symptoms."*

The WHO does not favour this name. The name does not need to include a biological basis, and MCS does not imply any. MCS describes only the observable fact that there are sensitivity symptoms in response to exposures to multiple agents = chemicals. This is unarguable and does not suggest any particular biological basis.

DR §2.4 *"QUESTION: are there additional triggers identified in MCS?"*

Other well known triggers which are largely forgotten in this draft and some of which give a different emphasis to the problem are:

- plasticizers or other plastic components leaching into food and drink, or volatilised and airborne
- fabric treatments
- moulds and their toxins
- common component(s) of laundry detergents
- newsprint

DR §3.1 *"Using the **mode of action level of proof as the benchmark appropriate to trigger regulatory, clinical or other action on the causative agent(s) of MCS, a review of the available literature was undertaken to identify which scientific reports of the cause(s) of MCS are most discussed as reflecting biologically plausible and scientifically testable***

hypotheses. This analysis identifies those theories that warrant further research/testing including in the clinic."

Why is the "mode of action level of proof" required to trigger any action on this illness? No mode-of-action proof exists for autism or many other diseases that are recognized and have clinical or other actions in place but are not yet understood. What justifies this benchmark as appropriate for MCS? Why should sufferers of more complex chronic conditions be discriminated against and not receive any, let alone adequate, medical assistance? Why should a more recalcitrant illness (in terms of being understood) justify ignoring the needs of sufferers or hiding them behind a faux-worthy requirement for a more complete understanding of etiology?

DR §3.1.2 and §3.1.3 *"Hypothesis: Respiratory disorder/neurogenic inflammation suggests that MCS may be initiated by interaction of chemical irritants with sensory nerves. In essence, the theory suggests that inhaled chemicals bind to receptors on sensory nerve C-fibres in the nasal mucosa which trigger the local release of inflammatory mediators from nerve endings, leading to altered function of the respiratory system."*

Again, it needs to be pointed out that MCS exposures are not all inhaled, and digestive and contact sensitivities are well known. The emphasis on odour (especially §3.1.3) and inhaled chemicals is inappropriate and unjustified by the evidence. The simple fact that many sufferers are sensitive to odourless compounds should be enough to either remove these confounding research results, or at least to add a note that they are not representative of MCS as a whole. These proposed mechanisms should be moved well to the bottom of the list in terms of likelihood.

DR §3.1.3 *"In a study of odour thresholds and perceptions, Caccappolo et al. (2000) assessed odour detection thresholds to phenylethyl alcohol and an unpleasant-smelling pyridine. No differences were found between MCS subjects (n=33), CFS subjects (n=13), controls (n=27), and asthma patients (n=16). When exposed to suprathreshold concentrations of phenylethyl alcohol, MCS subjects reported significantly more trigeminal symptoms and lower aesthetic ratings of phenylethyl alcohol, but did not demonstrate lower olfactory threshold sensitivity or enhanced ability to identify odours (Caccappolo et al. 2000). This study reinforces the notion that MCS subjects do not have increased odour sensitivities compared to healthy individuals and that cognitive, non-sensory factors play a role odour perception (Dalton and Hummel, 2000)."*

This study is so foolish it should not be included. It is well agreed that MCS sufferers are susceptible to SPECIFIC substances to which they have been sensitized by an unknown mechanism. As stated many times in this draft, the substances to which sufferers react are individual and vary widely. As far as is known a sufferer needs to be exposed to a chemical to develop an MCS-type sensitivity to it. To test MCS sufferers with an arbitrary random chemical which is almost certain not to be one to which they are sensitive is not just poor science, it is plain misleading, and no useful conclusions *about MCS* can be gained from such an experiment. The MCS sufferers are almost certain to

respond to phenylethyl alcohol in exactly the same way as other subjects, but for a variety of obvious experiential psychological reasons will find it less pleasant than 'normal' subjects. The test did not deal at all with the phenomenon of an MCS-type response.

DR §3.1.6 *Behavioural conditioning.*

This study is mildly refuted in the report's last para of §3.1.6, but this does not mention the more obvious flaw – proof that behavioral conditioning exists is nothing to do necessarily with MCS, it only proves that behavioral conditioning exists. MCS and behavioural conditioning are more likely unrelated *as etiologies*, and only related by the fact that MCS sufferers are more likely than non-sufferers to develop behavioural conditioning due to their unfortunate and repeated negative odour-related experiences.

The report should be far more critical of the research it quotes especially when that research points away from rational and effective treatment and research.

DR §3.1.9 *Odour perception*

This section continues the unjustified and pervasive emphasis on odour as being an essential ingredient of MCS. This is not only incorrect but if maintained will inaccurately characterize the illness, will unnecessarily increase public, government, medical and research skepticism of MCS as a "real" illness, will perpetuate the 'uncertainties' surrounding MCS and will skew research efforts for years to come. It should be removed altogether or, at worst, should be demoted to a minor comment not a major recurring theme.

DR §3.2 *"Whether MCS is a disorder with an underlying toxicodynamic cause or a psychogenic cause, or is particularly the result of both is not clear from the analysis of the available scientific literature.*

The currently available toxicological information does not support the view that MCS arises solely from the toxic effects of low-level exposure to chemicals in the environment. Specifically, it does not explain the diverse symptoms affecting multiple organ systems or the diverse range of triggering agents. Furthermore, it cannot be explained why the same chemical trigger can induce different symptoms in different MCS patients. No currently known biological mechanisms, processes or anatomical alterations can adequately explain such divergent effects (Gots & Pirages, 1999)."

Once again the significance of the report for sufferers and other stakeholders adds additional importance on the need for accuracy of what and how information is presented, and in particular interpretative statements like this. The fact that available toxicological information does not explain MCS is not in ANY way a demonstration that MCS is or is not psychogenic. It provides *no* insight into the likelihood of psychogenic etiology at all, these are unrelated arguments which have been incorrectly aligned in these paras. The unjustified relationship between the first and second para needs to be removed.

“The currently available toxicological information does not support the view that MCS arises solely from the toxic effects of low-level exposure to chemicals in the environment” is a loaded and incorrect statement. “Does not support” is not the same as “supports the opposite view”, it only means that current information does not explain MCS. This is to be expected of a complex condition and if not true we would not have this report or the medical uncertainties surrounding the condition. It most particularly does not support the psychogenic alternative either, so no such implication should be made.

“Specifically, it does not explain the diverse symptoms affecting multiple organ systems or the diverse range of triggering agents. Furthermore, it cannot be explained why the same chemical trigger can induce different symptoms in different MCS patients. No currently known biological mechanisms, processes or anatomical alterations can adequately explain such divergent effects” does not mean that any alternative explanation is correct or even likely to be correct, it only means that we don't know the etiology.

The report is full of such logical errors and false implications which all lean in the same direction. It needs to be purged of these inaccurate implications because they will have a real and profound effect on the future of MCS research.

DR §3.2 *“Another important question in determining the aetiology of MCS is whether or not MCS patients are able to discriminate in double-blind placebo controlled challenge studies (using an olfactory masking agent) between reported environmental triggers and placebos...”*

Of course this is of pivotal importance. All the current studies seem to be faulty and any that involve odorous substances have no chance of eliciting usable information. It is very easy to design a well-blinded trial but my own search for such a trial has produced nothing. The first recommendation of this report should be for such a trial that if positive, would in one stroke remove 90% of the confounding arguments that have to date prevented useful research on MCS. Such a trial is in global terms easy to arrange and comparatively cheap and there is no argument at all for not initiating a good quality trial immediately.

The need for a trial should be highlighted by the report, and the reasons that such has not been performed to date should be discussed.

DR §4.1.1 *“In NSW, a 2002 survey of adult health conducted by the Department of Health, 24.6% of respondents (from a total of 12,491 individuals) answered “yes” to the question “Do certain chemical odours or smells regularly make them (or their children) feel unwell?”. Moreover, 2.9% answered “yes” to the question “Have you been medically diagnosed with a chemical sensitivity?” The severity of these health effects and their conformity to the 1999 Consensus Criteria (Section 1.2) are not known. Interestingly, the survey did not find significant variations in the proportion of people reporting diagnosed chemical sensitivity based on level of socio-economic disadvantage.*

In South Australia, two surveys were commissioned by the State Health Department (September 2002 and June 2004) to determine the prevalence of MCS and general chemical sensitivity. Combining both surveys, in 4,009 randomly selected adults, 16.4% of respondents reported sensitivity or adverse health effects from exposure to one or more chemicals, and only 0.9% reported a medical diagnosis of MCS”.

Once again the report seems to be promoting the confusing factors rather than the useful ones. There is a very clear distinction between ‘chemical sensitivity’ meaning that one chemical causes a reaction in a subject, and MCS, in which it is the multiplicity of causative agents as well as the low levels of exposure required that differentiates the latter from the former. The report should make it clear the difference between the two and not put forward the first quoted para as though it applies to MCS and as though the disparity in the figures casts doubt on the reasonableness of MCS as a condition. The final sentence correctly points out the actual comparative situation as though this is surprising (nb the gratuitous use of the word ‘only’), again without explaining the well-accepted difference between the two.

DR §4.1.2 *“The best overseas estimates for prevalence of MCS are from the United States where prevalence appears to be less than 1% (Reid et al. 2001)”.*

The figure “less than 1%” is again loaded information that betrays an apparent bias in the viewpoint of the writer, or in the impression the writer is trying to give. Why is the actual figure not given? Many serious and well-resourced diseases occur in ‘less than 1%’ of the population, and whether the incidence is 0.9% or 0.1% is highly relevant to any discussion of MCS. The “less than” is uninformative and apparently pejorative or at least dismissive.

DR §4.4 *“Psychotherapy, biofeedback and relaxation and other behavioural therapies are regarded as efficacious”*

Add ... “by some.” to make it accurate.

DR §5.3.3 *“No evidence exists for benefit from any medication, dietary supplements or other therapies despite support for some of the treatments by some clinicians at their interviews or in response to the questionnaire. “*

A note should be added that no evidence *will* exist until and unless MCS is well accepted by mainstream medical political and research areas and significant funds are made available for research. At present with the strongly polarized views on, and controversial nature of, MCS together with the high cost of properly controlled research and lack of patentable candidate treatments, it is almost impossible that any worthwhile research will be conducted on possible treatments. The lack of treatment evidence is not evidence for the non-physical etiology of MCS. The current phrasing carries the implication that lack of proven treatments indicates that MCS is not ‘real’ or not worth further research. The

real implication or correlation is that lack of proven treatments indicates that not enough effort is being expended on research.

DR §5.5 etc

The report's recommendations are disappointingly vague and appear to be designed to avoid coming to grips with MCS and avoid changing anything at all significantly i.e. they appear to be designed to make no waves. Given that the report is now subtitled "IDENTIFYING KEY RESEARCH NEEDS" (possibly in an attempt to weaken or reduce the scope of the original report) the reader is entitled to expect some hard-core research recommendations. Instead the recommendations amount to nothing more than collecting arguably useful data and *consideration* of a number of elliptically useful things.

Recommendations are currently spread between sections 4.5 and 5.5 and there is a lack of consistency between the two. The recommendations need to be highlighted, placed in one section and strengthened.

It is undeniable that there is a significant loss of productivity (i.e. significant economic cost) and a great deal of personal suffering in Australia resulting from MCS, no matter how it is defined. It is also evident that treatment of and research into MCS are woefully inadequate by any measure. The report should have as its first priority to end this unsatisfactory situation. It should conclude with a firm criticism of the current situation and at least several practical unequivocal recommendations for further research, as suggested by the subtitle. Some obvious needs are:

- Immediate establishment of a research and treatment facility.
- Immediate recognition as an illness under ANY definition to allow useful research to proceed. The only result of the present standoff and lack of recognition is to avoid and obfuscate useful research.
- Immediate funds from NHMRC for MCS research.
- Establish a joint industry, government and medical group to PROMOTE research into understanding MCS and guide development of appropriate strategies for policy, funding and research into MCS treatment, avoidance, management and minimization.
- Immediate development of treatment and management guidelines based on what is known to date (and not limited to what has been proven in controlled trials).
- Immediately setting up suitable controlled tests to determine the relative contributions of toxicodynamic and psychogenic mechanisms in the process of the disorder through the use of appropriately blinded challenge tests – as currently discussed in §4.5.

Any community risk with high potential costs and/or high likelihood requires risk management. MCS needs to be appropriately considered as a community risk and appropriate funds (proportional to the risk and existing and potential costs) need to be allocated towards understanding and mitigating this risk. The government, NHMRC and

OHS/NICNAS can not continue to sit on their hands and do little or nothing without incurring significant and increasing costs to the community.