Multiple Chemical Sensitivity Report

Summary of Revisions

November 2010

In February 2010, NICNAS released a revised draft report on Multiple Chemical Sensitivity (MCS) entitled "A Scientific Review of Multiple Chemical Sensitivity – Identifying Key Research Needs". Public comment was invited on this draft report, revised in response to significant comment following release of an initial draft in November 2008. This most recent call for comments on the draft MCS report attracted 33 individual submissions.

All comments (including identical comments made for the previous draft report) have been considered for the revision of the draft report. As with the previous report, the number of comments received rendered it impractical to outline each comment and provide individual responses, explaining how each has been addressed for the revision of the review. However, this Summary of Revisions outlines the important changes made in each section.

General Issues

Several respondents commented that the report is now more comprehensive and that the revision of the draft report has been responsive to concerns. Views were expressed also that the report fairly assesses the current situation on medical issues, provides a good appraisal of the literature and identifies some important research needs. Others noted improvement over the previous draft, but considered the report still flawed and misleading.

As with the previous draft, some respondents were of the view that the report is biased towards a psychological view, that it unacceptably concludes MCS is a psychosomatic illness and questioned why psychological factors were being discussed in the report. Some respondents called for discussion on psychological factors and behavioral conditioning to be excised from any report on MCS. On the other hand, others questioned why psychological factors were being downplayed compared to the first draft report.

As with the previous draft, the report clearly does *not* conclude that MCS is a psychological or psychosomatic illness or that MCS is a physiological/toxicological illness. The aim of the report is to provide a reflection of the breadth of discussion and debate within the scientific literature on modes of action in MCS. With this aim, the report contains commentary both on biochemical/physiological/toxicological mechanisms and psychological/behavioral mechanisms as reflected in the literature.

Some respondents requested inclusion of papers on physiological responses to particular chemicals. However, subjects in these studies frequently are not described as suffering from MCS and so their contribution to understanding the pathogenesis of MCS, which by definition involves responses to multiple unrelated chemicals, is unclear. In this respect, respondents to the previous draft report also criticised inclusion of studies that did not sufficiently describe the MCS patient population and

the extent to which they corresponded to common MCS diagnostic criteria. In response, descriptions of MCS populations were included both in the previous draft and current draft report.

Some respondents requested that an indoor air quality questionnaire used by overseas public health agencies be included. However, the questionnaire does not specifically relate to MCS and so was not included in the report.

As with the previous draft, several comments were received which were aimed at including and canvassing public health policy issues relating to MCS. Health policy is clearly outside the scope of the report and have not been included. As noted in the Preface of the report, the report is a technical document examining MCS with the aim of identifying priority areas for further study to inform and engage the clinical and scientific research community.

Some respondents agreed with the particular need to identify clearly the chemical species responsible for MCS and, despite noting that this is not how individuals experience chemicals in real life, advocated double blind placebo controlled trials to assess causation. Some also noted that single subject approaches, in addition to cohort studies, are likely to be productive and should be adopted. Others expressed the view that challenge trials on MCS individuals testing the powers of expectation using deceptive procedures, or even challenge trials in general, are unethical.

There was a view expressed that the report is unscientific or biased, because all the evidence for chemicals acting as toxicants in MCS has not been included in the report. This particular criticism has also been expressed recently in the scientific literature directed against investigators of behavioral explanations of MCS. This misunderstands the intent of the current report which is to present a balanced overview of scientific research on MCS focusing on the range of different purported modes of action with a view towards informing and engaging the clinical and scientific research community. Additionally, the report examines diagnosis and treatment practices for MCS amongst Australian medical practitioners.

Deliberately, the report does not include a discussion of the merits or otherwise of every publication regarded as relevant by proponents of particular modes of action, but does include key references enabling an informed view of the breadth of current research on MCS and scope for potential future investigations. Moreover, the report does not support the notion of the value of reviews, or of particular modes of action, or generally of the strength of argument, based merely on the length of citation lists.

Changes to Specific Sections

Executive Summary and Findings

The overview has been revised to reflect changes made in other sections.

Section 2.1 What is Multiple Chemical Sensitivity?

Minor wording changes have been made to the description of Randolf's initial observations of environmental sensitivities.

Section 2.3 What triggers the symptoms of MCS?

Paints and excipients (such as cornstarch and lactose) have now been included in the list from Ashford and Miller (1998) of chemicals and chemical products that have been implicated in MCS.

Corrections have been made to the identification of chemical/chemical product types claimed by Pall (2009) as commonly implicated in MCS.

Section 2.4 Can MCS be clinically defined?

The description of MCS by Cullen (1987) has been clarified to note this as the description of the disorder made by this author without inferences as to prevalence of this description within the literature.

Section 2.5 Does MCS have a disease classification?

Information on Austrian adoption of the German International Classification of Diseases (ICD) which includes MCS has now been added.

Section 2.6 Do individuals with MCS share common characteristics?

Reference to the Australian Hazard Exposure Assessment Database (AHEAD) has been deleted as, Safe Work Australia, have advised that the AHEAD database has been discontinued. Instead, Safe Work Australia completed the National Hazard Exposure Worker Surveillance (NHEWS) survey in 2008. Analysis of the NHEWS survey data has made it clear that it does not provide information on occupational exposures that may initiate MCS as hazard exposure responses are not linked to self-reported health effects.

Section 3 Mechanisms of MCS

3.1.1 Immune Dysregulation

A recent study of metabolic and immunological markers in MCS has been added.

3.1.2 Respiratory Disorder/Neurogenic Inflammation

Recent studies on airways sensory receptors, sensory irritation, sensory hyperreactivity and studies of hyperreactivity responses in MCS individuals have been added. The research challenge section has been expanded to note the potential for broad chemical sensitivities observed in reactive airways disease being mediated by particular populations of airways sensory receptors that might also play a role in MCS. In this respect, also noted now are potential trials in MCS individuals examining the effects of agents which block TRPV1 and TRPA1 ion channels.

3.1.3 Limbic Kindling/Neural Sensitisation

A recent study of skin conductivity responses in MCS individuals has been added and additional early SPECT studies of neurotoxic responses have now been noted.

3.1.4 Elevated nitric oxide, peroxynitrite and NMDA receptor activity

The discussion now more clearly notes excess activity of NMDA receptors as the main action of chemicals in MCS according to this theory.

Corrections also have been made to the outline of the chemicals and chemical classes claimed to be implicated in MCS according to this theory.

Links with other modes of action for MCS are now more clearly noted – neural sensitisation responsible for central nervous system symptoms and local neurogenic inflammation responsible for peripheral sensitivities.

The research challenge section has been reworded to note more clearly the need to confirm the biochemistry implicated in this theory in MCS individuals.

3.1.5 Toxicant-induced loss of tolerance (TILT)

An additional comment by the proponent of this theory has now been included noting that tolerance breakdown may involve the cholinergic nervous system, neural sensitisation or multiple neurotransmitters and genetic polymorphisms.

3.1.6 Altered xenobiotic metabolism

Additional genetic studies plus also a recent study investigating plasma metabolic and cytokine indicators of enzyme function have now been included. Genetic studies now include the numbers of individuals studied.

3.1.8 Psychological/psychiatric factors

This section has been retitled psychological/psychiatric factors to better reflect the focus on studies of psychological disorders.

A more recent report of the prevalence of panic disorder-associated cholecytokinin B receptor alleles in chemically sensitive individuals has now been added. Another report has now been included commenting on the potential interactive role, in addition to pathological changes, of personal and societal influences for the reporting of symptoms in MCS.

The presentation of results from a survey of German environmental medicine clinic patients has been revised to clarify the low numbers of individuals for whom toxic chemical exposures were the probable cause of symptoms.

Section 3.2 Further research for elucidating mode(s) of action.

3.2.1 Chemical initiators/triggers and biological gradients

Initial discussion in this section has now been expanded to further note difficulties in identification of particular chemical species responsible for MCS.

3.2.3.2 Respiratory disorder/neurogenic inflammation

Discussion has now been expanded to note similarities between sensory hyperreactivity and MCS and the potential for characterising the expression and function of particular airways ion channel receptors in respiratory irritant responses in MCS.

Section 4.3 Treatment facilities

Section now clarifies that evidence given to the South Australian Parliamentary Inquiry regarding closure of dedicated facilities refers to clinics in Sydney.

This section also now notes the availability of MCS hospital protocols in both South Australia and Western Australia.

Section 4.4 Treatment/management strategies

The section now clarifies that *established* pharmaceutical treatments do not exist for MCS.

Reference to the Fragrance and Chemical Sensitivity Support Group has now been removed due to its disbanding.

Section 4.6 Clinical research needs

Report now notes the advantages of the recent Idiopathic Environmental Intolerance Symptom Inventory (IEISI) over previously used inventories for chemical sensitivity.

4.6.2 Education/Training

Section now notes the availability of MCS hospital protocols in both South Australia and Western Australia.

Section 5 – Appendix 1

5.1.4 Workshop

Identities of clinical workshop participants have now been added to this section.

5.2 Problems Encountered

Listing of MCS in the Austrian ICD-10 is now noted.

Section 6 – Appendix 2

6.2.3 Department of Veterans Affairs

Section now notes a report on the health of Gulf War veterans which examined MCS (Research Advisory Committee on Gulf War Veterans' Illnesses, 2008).