Multiple Chemical Sensitivity Draft Report

Summary of Revisions

February 2010

In November 2008, NICNAS released a draft report on Multiple Chemical Sensitivity (MCS) entitled "A Scientific Review of Multiple Chemical Sensitivity – Identifying Key Research Needs". Public comment was invited on the report.

Given the uncertainty in relation to the mode(s) of action, diagnosis and effective treatment(s) of MCS, a number of studies and enquiries on MCS have occurred internationally, including in Australia. One consistent finding of such investigations has been the identification of the need for further research on MCS so as to enhance the understanding, prevention and management of MCS. However, these calls for further research have not specified priority areas for the research community. It is in this context that this report on MCS identifying key research needs has been released.

The call for comments on the draft MCS report attracted over 50 individual submissions. Comments were received on almost every section of the report. Different submitters often provided similar or identical comments on particular issues. However, also in many cases, different submitters expressed different views on particular issues and how these should be addressed in the report. Comments were received for content, as well as editorial issues.

All submitted comments have been considered in the review of the draft report. However, the substantial number of comments received has rendered it impractical to outline each comment and provide individual responses, explaining how each has been addressed in the revision of the review. However, NICNAS has prepared this summary of report changes outlining overall themes for changes across individual sections in the revised report.

In the revised report, paragraphs containing changes from the initial draft report other than for grammatical or editorial improvements, or inclusions of citations for additional data sources alone, are noted with a side bar.

General Issues

Many comments were received which were aimed at issues clearly outside the scope of the report. As noted clearly in the Preface of the report, the report is a technical document examining biomedical aspects of MCS, with the aim of examining current scientific and clinical research on MCS and identifying priority areas for further study to inform and engage the clinical and scientific research community.

Some comments requested that the report include discussion on disability access and accommodation for the chemically sensitive. Also, some comments requested inclusion of self management information including information on regional environmental pollution, water and air purifiers, sources of less chemically contaminated products and workplace modifications and alternative careers to reduce

chemical exposure. These social policy and wider chemicals regulatory issues are outside the scope of the review on key research needs of MCS.

Comments also requested that the report contain recommendations for the establishment of dedicated MCS treatment facilities, discussion on how to "heal the divide" between environmental and conventional medicine and also provide detail on how medical education on MCS could be facilitated. Public funding of environmental control units was also requested. These wider health and medical policy issues are also outside the scope of this technical review.

Some comments indicated a lack of distinction between well defined types of chemical sensitivities and MCS. There were comments suggesting inclusion of discussion on exposure to known allergens and sensitisers in MCS which were held as indicating a clear toxicodynamic process in MCS. However, the modes of action for these agents are well recognised, characterised toxicological responses in defined organ systems and do not conform to common definitions of MCS.

Similarly, some comments suggested inclusion of papers describing the known neurotoxicological effects of pesticides and solvents. Whilst neurological effects appear to be a common symptom of MCS, and pesticides and solvents are identified by some as common elicitants/triggers for MCS, their known neurotoxicological properties and effects on the nervous system occur via well characterised exposure doses and modes of action. The extent to which these well characterised effects and doses are relevant to MCS is questionable given MCS is defined as involving symptoms in multiple organ systems at levels far below those that are normally associated with effects in the normal population. As a result of such comments, brief discussion on environmental sensitivities and use of the term chemical sensitivity have been added to Section 2.1 to distinguish MCS from other environmental intolerances involving chemicals.

Some comments also requested inclusion of anecdotal observations of sensitivities in individuals or physiological changes from particular exposures. Deliberately, this review of MCS only includes published, peer reviewed information on sensitivities and symptoms.

The draft report contained references and citations from several overseas MCS workshops. For some of these, only interim or predecisional draft reports were available e.g. IPCS (1994); Interagency Workgroup (1998). Some comments advocated the citing of these reports and requested additional citations from these reports for certain sections of the MCS review. Other comments indicated that they should not be cited on the basis that the available reports were not finalised and do not represent final official views, or that workshop processes or their reporting contained significant inconsistencies or biases. In the revised report, the existence of these workshops is acknowledged but where possible, information or conclusions from these workshops was obtained from subsequent peer-reviewed publications.

There was a view expressed through some comments that the report reflected a psychological bias. Some comments requested deletion of discussion of psychological modes of action or deletion of discussion from particular authors who have published studies on the psychology of MCS. Some were of the view that discussion of

psychological modes of action risked further physiological research on MCS citing histories of false attribution of psychological mechanisms for many diseases that lacked well defined physiological modes of action.

In general terms, the use of language in different sections interpreted as biased commentary was unintentional and has been reviewed so as to preclude a suggestion of bias for particular modes of action. However, the revised report still contains commentary on studies suggesting psychological influences in the pathogenesis of MCS. The aim of the report is to provide a balanced reflection of the breadth of discussion and debate that exists within the scientific peer reviewed literature on modes of action in MCS. Moreover, the report now points out, importantly, that a lack of a characterised physiological mode of action is insufficient proof, in itself, of a psychological aetiology.

Changes to Specific Sections

Executive Summary and Findings

Comments on the overview directly reflected concerns with other sections of the review. The overview has now been revised to reflect changes made in other sections.

Section 2.1 What is Multiple Chemical Sensitivity?

Certain adjectives e.g. putative, controversial, and individual paragraphs containing overly subjective or insufficiently supported language have now been deleted or revised.

Discussion on environmental sensitivities and use of the term chemical sensitivity has been added to distinguish MCS from other environmental intolerances e.g. electromagnetic radiation and other recognised toxicological reactions and intolerances involving chemicals.

Discussion on clinical ecology are retained in this section as the term is still referred to in the scientific literature and in position statements on chemical sensitivities, and provides a background from which recognition of environmental illnesses arose. Origins of clinical ecology and environmental medicine are clarified and additional references added.

Comments requested exclusion of the term Idiopathic Environmental Intolerance from the text. The term Idiopathic Environmental Intolerance (IEI) is kept within the text as it is a common term used in the scientific literature. However, references to IEI being an outcome of the World Health Organization (WHO) workshop on MCS has been revised to indicate that use of this term was favoured by many, but not all workshop participants and to avoid the inference that IEI is an official WHO term. References to publications of outcomes of the workshop are also now included.

The paragraph on lack of agreement on the underlying cause and pathogenesis of MCS, and subsequent lack of agreement on an operational definition of MCS has now been deleted. The discussion on definitions highlights a level of consensus on MCS criteria in contrast to the incorrect implication of a universal lack of agreement on an operational definition. Also, additional discussion in the report importantly now distinguishes “causes” with “modes of action”.

Section 2.2 What are the symptoms of MCS?

Additional references are now included for literature sources of symptom profiles. Comments to the draft report included other symptoms to be included, but the symptom profiles discussed in this section were limited to symptom reports obtained from the peer reviewed literature.

A concluding paragraph is now included to indicate the difficulties with the lack of a validated characteristic symptom profile for MCS for diagnosis and investigation.

Section 2.3 Is MCS related to other syndromes or disorders

This section on relations between MCS and other syndromes is now relocated to the end of Section 2 (now Section 2.7) to improve the order of the discussion on the fundamental aspects of MCS.

Paragraphs in this section have been reordered to improve discussion flow and readability.

Additional information on multi-symptom conditions in Table 2 is now included. Statement on little evidence of exacerbation by ambient chemical triggers is not consistent with current data and has been deleted.

Section 2.3 What triggers the symptoms of MCS?

This section has now been retitled to "What chemicals trigger the symptoms of MCS" to note the focus on offending chemical agents and not physical agents or additional psychological or social factors. Reference to psychogenic components is now removed from this section as psychological factors are discussed in Section 3 under modes of action.

Additional triggering agents as well as literature sources are now added.

The separate concepts of initiation versus triggering are now also discussed.

Section 2.4 Can MCS be clinically defined?

This section focuses on agreed clinical definitions, not on individual physical abnormalities that may be present in MCS individuals. Anecdotal reports of individual symptoms suggested for inclusion have not been included on the basis that they do not inform discussion on clinical definitions of MCS. Physical abnormalities are discussed in Section 3 Mechanisms.

Some comments claimed that the review is politically naive because of a lack of discussion on vested industrial interests. 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.

References to WHO have been clarified to prevent implication of the term Idiopathic Environmental Intolerance (IEI) being an official WHO term. Publications containing outcomes of the WHO workshop in peer-reviewed journals are now included.

Section 2.5 Does MCS have a disease classification?

Discussion on whether, or not, listing by Germany in their national version of the International Classification of Diseases (IDC 10) represents "official" recognition of MCS has now been deleted. The background and interpretation of the status of listing is not sufficiently clear from personal communications from the German regulatory authorities and its official German status is of secondary importance to the observation in this section that MCS has not been commonly listed internationally as a classified disease.

For brevity, the reasons given in the personal communication from the National Centre for Classification of Diseases regarding rejection of a classification code for MCS for Australia is now summarised in a single paragraph.

Section 2.6 Do individuals with MCS share common characteristics?

This section is now retitled to reflect a wider discussion on demographic and socioeconomic profiles of MCS individuals which includes, but is not limited to, chemical exposure scenarios. Chemicals and chemical products implicated in MCS are explored in detail in Section 2.3.

Additional data sources are now included. The listing of individual groups most susceptible to MCS from Ashford and Miller on chemical sensitivity has been updated from their most recent 1998 publication. Demographic characteristics for these groups as noted by these authors have now also been included.

Additional brief information on race/ethnicity, geography, income and education levels and additional societal factors that may impact on the prevalence of MCS is also now included.

In line with the refocusing of this section on the demographics of susceptibilities to MCS, a concluding paragraph is now included to summarise overall the lack of a comprehensive defining demographic risk profile for susceptibility to MCS.

Section 2.7 Is MCS related to other syndromes or disorders?

This section has been reordered for readability. Additional references have been added. The first paragraph now notes similarities between MCS and a subset of multi-symptom disorders with established ICD classifications.

The general statement regarding the lack of evidence for exacerbation of other syndromes by ambient chemical triggers has been deleted. Additional genetic evidence for chemical susceptibilities for MCS and briefly Gulf War syndrome is now included in Section 3. Additional information on Sick Building Syndrome, Aerotoxic syndrome, Dental Amalgam Syndrome, and Electromagnetic Fields Sensitivity is now included.

The paragraph regarding heightened sensitivity to specific triggers in dental amalgam-induced mercury toxicity and electromagnetic fields extending to include other environmental triggers commonly associated with MCS has been deleted. This paragraph is of only marginal relevance to this section on symptom overlaps.

The observation of relationships between diagnosis of other multi-system illnesses and MCS is now moved to the last paragraph.

Section 3 Mechanisms of MCS

The revised title for this section now clarifies the emphasis of discussion on pathogenic mechanisms i.e. modes of action rather than the wider term "causes", which can be interpreted as involving both precedent (chemical exposures) and antecedent (physiological) events. Also, throughout this section and elsewhere in the revised report, use of the term "causes" has been revised to prevent, where appropriate, additional confusion between putative eliciting agents/events and symptom triggers.

This section also now more clearly notes the possibility of multiple modes of action.

The separate subheadings "Hypothesis" through this section have now been deleted as superfluous. The introduction now notes more clearly that only the most commonly discussed mechanisms are included and are NOT discussed in any particular order of relevance or plausibility. The basis for regulatory action is now clarified. The wording on regulatory action has been revised to reflect the role of understanding mode of action to inform regulatory decisions, not as required proof for regulatory action to occur.

Some comments suggested inclusion of papers describing the known neurotoxicological effects of pesticides and solvents. Such papers on neurotoxicological effects in normal individuals are regarded as only of marginal relevance to the extreme sensitivity seen in MCS (see General Issues).

3.1.1 Immune Dysregulation

Paragraphs within this section have been rearranged to improve readability and discussion flow. Additional information has been added including low level sensitisation animal model data. Some comments suggested inclusion of immune changes noted for single chemicals in normal individuals. However, the relevance to MCS of documented immunotoxicological effects in normal individuals from particular chemical exposures is not clear.

MCS case definitions are now included where appropriate. The research challenge conclusion is now expanded.

3.1.2 Respiratory Disorder/Neurogenic Inflammation

Paragraphs within this section have been rearranged to improve readability and discussion flow. Additional studies of neurogenic inflammation have been included.

Discussion on double blind placebo controlled challenge studies has been removed from this section and incorporated into Section 3.2. The Caccappolo study examining olfactory thresholds is now moved more appropriately to this section from limbic kindling/neural sensitisation section.

The mouse model of sensory irritation in MCS is now included.

The lack of explanation by this theory for reactions to non-inhaled chemicals is also now noted.

3.1.3 Limbic Kindling/Neural Sensitisation

Paragraphs within this section have been rearranged to improve readability and flow. Animal and human studies are now discussed separately and additional studies included. In particular, additional animal models of neural sensitisation are now included.

Some comments requested brain imaging studies of fibromyalgia (FM) to be included. Unfortunately, the extent of relevance of physiological changes in these studies to MCS is uncertain and so imaging studies solely on FM have not been included.

The Caccappolo study examining olfactory thresholds (i.e. ability to detect odours) is now moved more appropriately from this section to section on respiratory disorder/neurogenic inflammation.

The research challenge paragraph has now been revised to more clearly summarise the observations that support a neural sensitisation model for MCS and to more clearly indicate a research direction.

3.1.4 Elevated nitric oxide, peroxynitrite and NMDA receptor activity

Information from the latest Pall review of this hypothesis is now included.

The model is further described and section now includes the concepts of initiation and triggering phases, links with two other mechanisms for MCS – limbic kindling/neural sensitisation and neurogenic inflammation, and the origin of multi-organ symptoms from multiple local tissue reactions. Minor errors in descriptions of reactions are now corrected.

The research challenge more clearly acknowledges both the types of evidence in support of this theory as well as research directions required to provide additional support.

3.1.5 Toxicant-induced loss of tolerance (TILT)

Additional references are now included. Separate processes of initiation and triggering are included as part of the TILT theory.

The research challenge has now been expanded to include potential uses of environmental chambers to test chemical exposures and also to indicate the difficulties in testing this hypothesis in the absence of detail of a physiological mechanism.

3.1.6 Altered xenobiotic metabolism

This new section has expanded the discussion contained originally in the subsection on altered metabolism under the section Other Proposed Mechanisms. The section now incorporates additional human and animal information on gene variations in MCS. A research challenge section is also now included.

3.1.7 Behavioural conditioning

Additional references are now included. Relevant discussion on odour conditioning from the section "Odour Perception" has now been brought into this section. The section now includes further discussion of the shortcomings of the conditioning theory in terms of diversity of symptoms and symptom variations with time, susceptibilities also associated with non-odorous chemicals and an often lack of a toxic event that would constitute an unconditional stimulus.

The research challenge is now expanded to acknowledge the limitations of the behavioural conditioning theory. The challenge section also indicates the need for longitudinal studies of eliciting and triggering events (both physical and psychological) and behavioural systemic desensitisation treatments aimed at the extinction of conditioned responses.

3.1.8 Psychological factors

Additional references are now included. Relevant discussion on behavioural and social factors and psychiatric treatment approaches from the section "MCS as a Belief System" in the previous draft report have now been incorporated into this section, now entitled Psychological factors. The potential for neurotoxic effects of substances on mood and emotions are now noted. Further discussion on the difficulties with diagnoses of somatoform disorders is now included.

The research challenge section now notes the invalidity of interpreting a lack of evidence for a physiological cause as indicating support for a primarily psychiatric explanation. A focus on supporting and enhancing coping strategies rather than providing a cure is suggested as is longitudinal studies preceding symptoms of illness in high-risk populations.

3.1.9 MCS as a Belief System

This mode of action is now comparatively infrequently discussed in the MCS literature and there are aspects of belief influences that are complementary to other psychological mechanisms already discussed in the report. Consequently, this section has now been deleted and discussion relevant to behavioural and social factors and psychiatric approaches to treatment are now incorporated into section 3.1.8 Psychological factors.

Deleted Sections

In summary, several sections in the previous draft report have been deleted and relevant discussion incorporated into existing expanded sections.

The section Odour Perception has been deleted and discussion relevant to the role of odour in behavioural conditioning has been transferred into 3.1.7 Behavioural Conditioning. The section MCS as a Belief System has now been deleted and discussion relevant to behavioural and social factors and psychiatric approaches to treatment are now incorporated into section 3.1.8 Psychological factors. Under Other Proposed Mechanisms, the section Altered Metabolism has now been deleted and discussion transferred to an expanded section Altered Xenobiotic Metabolism. The section Commentary on the Proposed Models for Mode(s) of Action has now been deleted and relevant discussion has been incorporated into an expanded section on Further research for elucidating mode(s) of action.

3.2 Further research for eludicating mode(s) of action.

This section has been revised (including the addition of relevant discussion from the section Commentary on proposed models for mode(s) of action) to provide additional focus on data gaps to be addressed and methodologies to elucidate modes of action, rather than judgments on the comparative scientific weight of evidence for particular modes of action.

The section now notes the Hill criteria for distinguishing association versus causation in environmental diseases including MCS and suggests criteria for which additional information would be helpful in elucidating mode of action. Given discussion in the report on challenge studies, specific discussion on the difficulties with the conduct of challenge studies is also now included.

Additional discussion with more specific emphasis on research directions is also now included for particular modes of action identified as the most biologically plausible. Discussion is also now included on altered xenobiotic metabolism as a mode of action for investigation.

Section 4 Diagnosis, treatment and management of MCS

Overall, this section is now revised to reflect agreed criteria for MCS but also difficulties in diagnosis and treatment arising from the range of self-reported symptoms with which individuals present, differing views on the biological mechanisms by which MCS occurs, and the lack of an objective characteristic diagnostic marker.

Section 4.1 Diagnosis and prevalence of MCS

The section now more clearly underlines the difficulties in surveys of distinguishing different types of chemical sensitivity (see also section 2.1). Additional demographic data on MCS are now included from Australian state health surveys.

Some submitted comments questioned the international prevalence figures. Comment is now included on doubts for the prevalence figure from Kreutzer et al (1999) for medically diagnosed MCS in the absence of confirmatory self-reports of heightened chemical sensitivity. Comment on relative prevalence of MCS between US, Canada and UK based on the study of Reid et al. (2001) has been deleted as this study was only of British military personnel and does not allow international comparisons.

Section 4.2 MCS case definition and prevalence data

Difficulties with obtaining prevalence data from surveys are now highlighted in this section.

Discussion on challenge studies is now removed from this section because of marginal relevance of such studies in addressing prevalence. Discussion on challenge studies is now included in Section 3.2.2 and the issue with fluctuations in symptoms in challenge studies is now also noted in Section 3.2.3.3 where the advantages of individual longitudinal studies over group challenge studies are noted.

Section 4.3 Treatment facilities

For this section, some comments advocated discussion of the design of environmental control units. Such detailed discussion is outside the scope of this section which deals

with the current availability of facilities to treat the chemically sensitive, not their design detail or suitability to provide such treatment for these facilities.

Comments also requested recommendations in the report for the establishment of dedicated MCS treatment facilities, discussion on how to "heal the divide" between environmental and conventional medicine and detail on how medical education on MCS could be facilitated. Requests for public funding of environmental control units were also received. These health policy issues are also outside the scope of the current technical review of research needs.

The development of a South Australian hospital protocol for MCS by the South Australian Department of Health in consultation with the South Australian Interagency MCS Reference Group is now noted in this section.

Section 4.4 Treatment of MCS

The section has been renamed Treatment/Management Strategies and reorganised to firstly indicate the results of surveys of MCS therapies in the peer reviewed literature and then to focus on results from the Australian clinical survey on therapeutic approaches to MCS. The Australian clinical survey is also discussed in a new section 4.5 – Australian Clinical Approaches.

Some comments requested inclusion of information in the report on specific treatments that from personal experience were beneficial for MCS. Coincidentally, the therapeutic claims for chemical sensitivity made by one particular company recommended for inclusion in the report were recently challenged by the Australian Competition and Consumer Commission (ACCC). In general, anecdotal reports of benefit from particular therapies were not included in the report, which focussed primarily on therapies reported through surveys in the peer reviewed literature.

The benefits allegedly experienced by MCS patients from different treatments were also requested to be tabled in a similar manner to that of the HREOC recommendations in section 4.3. The current most detailed source for this information on treatments is already included in the report (Gibson et al., 2003), but the report now also includes a comment on the perceived benefits of therapies with regards to coping, as opposed to curing, MCS from this survey of treatments.

The small size of several separate studies on treatment of MCS are now acknowledged so as not to imply that comparative statistical data are available, as requested by some comments.

The paragraph on treatments noted by advocacy groups (also in Section 5.4.1) is now revised so as not to imply that these are advocated by all groups.

Comments indicated that the MCS Clinical Management Practices are held by some as likely to provide some support for patients, but by others as extremely medically conservative and that aim to trivialise MCS. Others claim that the management practices do not encourage GP's to monitor, evaluate and assess general health needs of those with MCS. However, these are a set of general principles useful for the management of MCS as agreed by general and specialist clinicians involved in the clinical review of MCS and are reported as such.

Some comments requested the report contain self management information including information on regional environmental pollution, water and air purifiers, sources of less chemically contaminated products and workplace modifications and alternative careers to reduce chemical exposure. These are outside the scope of the review.

Some comments also noted MCS advocacy websites which contain information on treatments with requests that such information be included. Some also requested inclusion of the potential benefits of non-conventional treatments. The existence of such information on advocacy websites is already acknowledged and both conventional and non-conventional treatments are referred to in this section as outlined in the comprehensive review of Gibson et al (2003).

Lastly, information on MCS in the Human Rights and Equal Opportunity Commission Guideline, *Access to Buildings and Services: Guidelines and Information* has now been moved from Section 4.4 Treatment Facilities into this section as this guidance is relevant to management.

Section 4.5 Clinical research needs

The first paragraph is revised to reflect differences (as opposed to difficulties) in approaches to clinical criteria for MCS from the clinical review.

Some comments requested the review recommend inclusion of MCS in the Australian International Classification of Diseases. This health policy recommendation is outside the scope of the review.

Information on dose-response revised in this section and in detail in section 3.2.1 to more clearly reflect an overall lack of information on dose-response.

Additional discussion is now provided in the statement regarding challenge studies in this section to emphasise the potential role of inhaled chemicals and odours in MCS. The report also now notes in other sections that inhaled chemicals are common but not the only elicitants/triggers for MCS (Section 3.1.2 and 3.2.3.2). Also, the need for challenge studies is now described more precisely in terms of exploring initiating/triggering agents/events and modes of action in MCS. Additional text clarifying the primary research needs is now included.

The last paragraph in Section 4.5.2 on public information to inform clinicians, workplaces and communities has now been deleted. Workplace and community education is outside the scope of this section on clinical research needs and education of clinicians is covered in the preceding paragraph. This paragraph has also been deleted from the Executive Summary.

Appendix 1 - A survey of Australian clinicians approaches to MCS

The initial paragraphs have been revised to more clearly elucidate the difficulties with current clinical practice with regards to MCS and to correct the implication of a universal lack of agreement on an operational definition of MCS. The opening paragraph now more clearly indicates that summaries of the findings in Appendix 1 have been incorporated in the body of the report in sections 4.4 and 4.5.

The identity of the consulting firm which prepared the report on Australian clinicians approaches to MCS is now included.

Comments were also received that the independence of clinicians and researchers reporting to this review should be assured. It is now noted in the report that initial contact lists provided to the clinical consultants to commence the survey included the identities of professional organisations as well as individuals who had experience in dealing with MCS. Moreover, the consulting firm has been requested to contact participants to the clinical workshop to obtain their approval for their identities to be included in the report.

Some comments requested additional information on why particular topics were not discussed at the workshop and how topics were chosen. Time constraints for the workshop only allowed for discussion of topics which centred on practical help for MCS patients and the challenges for clinicians in dealing with MCS. It is clear in the report that the identified topics have their origin from the initial interview processes and the outcomes of these discussions are as presented.

5.2 Problems encountered

The first paragraph is amended to indicate that the lack of authoritative research on MCS refers not to the body of literature on all aspects of MCS but to the specific issue of characteristic biological markers.

5.3 The Common ground

Comments queried why clinicians with limited clinical experience were involved (paragraph 1). This paragraph is amended to clarify that limited experience with MCS expressed by the clinicians is relative to total caseloads.

The third paragraph was revised ("respected medical organisations" deleted) to clarify the focus in this section on opinions from the clinical workshop.

Under 5.3.3 Prognosis and Treatment, the first paragraph was amended to indicate that insufficient (as opposed to no) evidence exists in the literature for any particular treatment for MCS, in contrast to views from particular medical practitioners.

5.4 Implications for treatment/management and 5.5 Recommendations

Some comments indicated that the clinical management principles and recommendation were regarded by some as vague and inadequate and that management information should include specific information on regional pollution, sources of less chemically contaminated products, workplace modifications and alternative careers to reduce chemical exposure. It should be noted that the management principles were those derived within this survey of clinical approaches from interviews, responses to the questionnaire and workshop comments.

Additional text clarifying the primary research needs is now included (section 4.5).

With regards to additional management information, these broader chemical regulatory issues were not specifically within the focus of the survey of clinical approaches to MCS and are additionally outside the scope of this current review of MCS.

Appendix 2 – Organisational Views

Given the technical nature of the review, Appendix 2 has now been reorganised to focus only on views and statements by key overseas health/medical organisations and federal regulatory bodies relevant to identifying MCS research needs. Consequently, commentary on MCS with respect to legal outcomes, social security or disability policy or local government chemical usage policy has now been deleted.

Government institutes and departments that support olfactory research, or deal with pesticide poisonings or finance, or housing departments that mention MCS were not included as these either do not relate specifically to MCS or provide little indication of a health or medical position on MCS that informs a review of MCS mechanisms.

Individual entries have been updated with more recent information where available and revised where descriptions of positions and opinions were regarded as incomplete or misleading. Entries have been also included for additional professional organisations that have sponsored significant MCS related conferences and publications. The entry for the National Centre for Environmental Health, CDC has now been deleted as it provided no specific information on MCS, reflecting a lack of activity on MCS for this organisation.

Repeated references to the report of the Interagency Workgroup have been removed on the basis of the report being a predecisional draft and a lack of clarity over its status as a formal representation of organisational views.