

## **A review of the ethics of the National Health and Medical Research Council (NHMRC) focus on homoeopathy, 2010-2015 - Part 2**

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### **Abstract**

On 11 March 2015, the National Health and Medical Research Council (NHMRC) published its report on the Review of the evidence on homoeopathy, which concluded, 'there are no health conditions for which there is reliable evidence that homoeopathy is effective'. NHMRC assured the public that it assessed the evidence using "standardised, accepted methods for assessing the quality and reliability of evidence for whether or not a therapy is effective for treating health conditions", "developed by Australian experts in research methods".

Part 1 predominantly focused on the period 2010 to 2012. Part 2 tells the story of the NHMRC Homeopathy Review from the early termination of a first review process in 2012, to publication in March 2015 of the review produced by the second reviewer. It explores whether NHMRC fulfilled its obligation to fairly and objectively assess the evidence on homoeopathy, according to accepted scientific administrative standards and guidelines, suggestive of research fraud and misconduct.

Following is Part 2 of a two-part series examining ethical issues associated with the National Health and Medical Research Council's (NHMRC's) focus on homoeopathy between 2010 and 2015. Part 1 predominantly focused on the period October 2010 to mid-2012; Part 2 focuses on events that occurred from mid-2012 to March 2015 (publication of the final report), presenting key findings of a formal stakeholder investigation into NHMRC's procedures and methods spearheaded by the Australian Homoeopathic Association (AHA), Complementary Medicines Australia (CMA) and the Australian Traditional Medicine Society (ATMS), with scientific support from the Homeopathy Research Institute (HRI).

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### **Introduction:**

Between October 2010 and March 2015 the National Health and Medical Research Council (NHMRC) conducted an investigation into homoeopathy, to inform the Australian community on the "effectiveness of homoeopathy", as part of its responsibilities to 'advise the community' under section 7(1)(a) of the *NHMRC Act 1992* (1). This included a formal review of the evidence on homoeopathy (the 'Review') conducted between 2012 and 2015 under two separate contractors.

NHMRC's assessment was that for the 61 health conditions covered by the Review:

*"... no good-quality, well-designed studies with enough participants for a meaningful result reported either that homeopathy caused greater health improvements than placebo, or caused health improvements equal to those of another treatment"*

NHMRC's overall conclusion, based on this assessment was:

*"...there are no health conditions for which there is reliable evidence that homeopathy is effective."* (2)

NHMRC claimed:

*"The conclusion is based on the findings of a rigorous assessment of more than 1800 papers"* (3)

As a result of its findings, the NHMRC Statement on Homeopathy recommended:

*"Homeopathy should not be used to treat health conditions that are chronic, serious, or could become serious."* (4)

NHMRC presented its findings in 944 pages of report documentation, consisting of an Information Paper (presenting the Review's findings to the community), Statement on Homeopathy, an Overview Report (the technical analysis conducted by the contractor, OptumInsight), Reports of the review of additional evidence submitted by external stakeholders, an Administrative Report, Frequently Asked Questions and Expert Review Comments documents.

The NHMRC is a respected, publically funded government institution with a statutory responsibility to provide 'independent, high quality advice to assist the public in making decisions about their health care'; healthcare providers, researchers and decision-makers also rely upon its advice. It is therefore essential that this advice results from a fair and objective assessment of the evidence and employs standardised and accepted methods of scientific inquiry.

Part 2 explores the story of the NHMRC Homeopathy Review from mid-2012 onwards, in the context of whether NHMRC indeed ethically and objectively assessed the evidence according to accepted methods.

### **The 'first' NHMRC homoeopathy review:**

**NHMRC has withheld from public disclosure that between 4 April and early August 2012, it contracted a first reviewer to assess the research evidence on homoeopathy.** The start of the first review process coincided with commencement of the term of the Homeopathy Working Committee (HWC) on 2 April 2012. The latter was disclosed on the NHMRC website; the former was not.

Since NHMRC did not reveal the existence of the first review, its findings, methodology, reasons for its termination and taxpayer expenditure was not disclosed. Its existence was revealed during a process of discovery undertaken by stakeholders (5).

### **The first reviewer - an Australian expert in health evidence review:**

The NHMRC Information Paper (p.9) assured the public that:

*“When evaluating health evidence and drafting health advice, NHMRC uses a rigorous approach that has been developed by Australian experts in research methods.”*

The first reviewer was one of these ‘Australian experts’, having extensively published systematic reviews and co-authored a number of handbooks to support organisations in the development of evidence-based clinical practice guidelines for the NHMRC.

These include those commissioned by NHMRC to guide authors when developing clinical evidence based guidelines (6,7), using a standardised methodology that has since become NHMRC’s accepted protocol for reviewing evidence and guideline development to ensure quality standards are maintained (the NHMRC ‘dimensions of evidence’ assessment framework). The reviewer had co-authored numerous publications or were an NHMRC advisor covering specific conditions applying the NHMRC guidelines they had co-developed. NHMRC directly referenced these guidelines and methodology against the Homeopathy Review (8,9).

This, alongside the reviewer’s long list of publications in the field of allied health evidence, demonstrates their experience and expertise in conducting high quality, ethical scientific research.

### **NHMRC terminates first reviewer’s contract:**

Freedom of Information (FOI) documents reveal that the first reviewer submitted their final Draft Report at the start of August 2012 and that “*following discussions with the reviewer on Friday 3 August*” NHMRC decided to terminate their contract (10). No reasons were provided.

It is **highly unusual** to suddenly terminate the contract of such a respected and credentialed reviewer, particularly under circumstances where they had delivered on their contract and submitted a completed draft report for consideration. Under normal circumstances, it would have taken considerable time to properly review and assess the quality of the report, let alone come to the momentous decision to abruptly terminate the reviewer’s contract. Indeed, FOI documents indicate that it was the Office of the NHMRC that made the call, in the absence of consultation with the working committee (11).

NHMRC has refused to release a copy of the final Draft Report or any details of its methodology under FOI (12). Thus the public and researchers have been denied access to a publically funded report for scrutiny and debate. When challenged, NHMRC’s official response to stakeholders was (13):

*“An unfinished, incomplete draft report was provided on August 2012. This was developed as part of an iterative process that had not concluded before the contract commissioning the work was terminated. The draft report was not finalised by*

*the contractor and consequently did not undergo NHMRC’s quality assurance processes of: methodological review; expert review; consideration by the HWC; or consideration by NHMRC’s Principal Committee and Council.”*

The phrase “*iterative process*” is misleading: the AHA-led investigation into NHMRC’s conduct of the Review has revealed that the parameters of the first review’s research protocol were in fact continuously adjusted along the way, due to NHMRC having little familiarity with the homeopathic research evidence base. As well as exposing the process to risk of bias, it also demonstrated how the exclusion of homeopathy subject/ research experts, in breach of mandatory NHMRC standards, impacted the process (see Part 1).

Part 1 also outlines how from the outset, the Homeopathy Review was exposed to risk of bias resulting from the HWC, Health Care Committee (that the HWC reported to) and NHMRC Council containing Supporters of the anti-homeopathy advocacy group Friends of Science in Medicine (FSM). These conflicts remained undisclosed and unmanaged for the duration of the Review.

Part 1 also details explicit anti-homeopathy public statements made by the Chair of NHMRC Council (who in 2011 assured the public that NHMRC “*does not support homeopathy*”) and the CEO, who personally instigated, guided and signed off the Review while declaring the sector to be “*charlatans*”, “*snake oil merchants*” and “*dishonest people wanting to take your money*” (14).

### **Expert feedback on first review process:**

Information in documents released under FOI indicates that the first reviewer objectively assessed the evidence, using the accepted NHMRC methodology they co-authored and that the work was of high methodological quality:

In July 2012, the reviewer submitted a Draft Report for consideration by the HWC at its next meeting. HWC member Prof Fred Mendelsohn provided his following overall expert feedback on the July version of the draft report (15,16):

*“I believe that the assessment of secondary literature has been performed very well with careful systematic analysis and the results are supported factually with strong supporting material.”*

...

*“I am impressed by the rigour, thoroughness and systematic approach given to this evaluation of the published reviews of efficacy and side effects of homeopathy. The decision to restrict the evaluation to particular conditions is sensible.*

*The methods and criteria for various decisions are covered very well. The analysis of the included reviews seems to have been done in a careful systematic manner and there is ample detail to enable those who wish to do so to read and evaluate the original material.”*

Prof Mendelsohn’s overall assessment of the medical conditions he was allocated to comment on (headache, asthma, fibromyalgia and otitis media) was:

*"The summary of the methods is good, given that a fixed format has been used for all of the analyses, which is a positive feature of the overall report."*

*"Overall, the consistent use and reporting of the same criteria for each of the evaluations is a strength and reveals the careful systematic approach that has been brought to these evaluations."*

### **Feedback of this kind is not consistent with a review so deeply flawed it warranted being terminated so shortly thereafter.**

The premature termination of what appears a good quality, publically-funded report produced by a highly respected and experienced reviewer suggests that it was the report's findings, not its quality, that played a role in its demise.

The 1 September 2012 update to the NHMRC 'Complementary Medicines' webpage provided details of the Homoeopathy Review and the HWC's terms of reference, but made no reference to the fact that the evidence had already been assessed by a first reviewer.

### **The second (Optum) NHMRC homoeopathy review - methodology:**

From October 2012, NHMRC contracted a second reviewer, OptumInsight (Optum), to review the evidence on homoeopathy (17). Given that the first reviewer would almost certainly have applied accepted NHMRC methods for reviewing health evidence (that they co-authored), what approach was to be adopted for the second review process?

### **NHMRC's assurance - use of 'standardised, internationally accepted methods':**

The cornerstone of the Optum review's integrity rests upon the NHMRC's assurance that the evidence on homoeopathy was assessed using (18):

*"standardised, accepted methods for assessing the quality and reliability of evidence for whether or not a therapy is effective for treating health conditions."*

NHMRC reiterated this quality assurance throughout its published documentation; for example, the NHMRC March 2015 media release emphasised that the findings:

*"was the result of a rigorous examination of the evidence and used internationally accepted methods for assessing the quality and reliability of evidence for determining whether or not a therapy is effective for treating health conditions."*

The 'internationally accepted method' NHMRC adopted was the 'Overview' method, referenced against Chapter 22 of the *Cochrane handbook for systematic reviews of interventions* (19). Conducting an Overview meant that of the 176 studies included in the Overview, **no original studies were retrieved or assessed** - a major methodological limitation of the Review.

### **Use of an inappropriate method:**

Cochrane Overviews are intended primarily for summarising the results of Cochrane Intervention reviews or systematic reviews (SRs) **of an equivalent standard**. In themselves, SRs are summaries of original studies, thus for an Overview to be meaningful (since it is a 'summary of summaries'), it customarily

only examines SRs of the highest standard to provide a reliable 'overview' of the research.

The Overview identified 57 SRs covering 61 health conditions. Optum rated only 7 out of the 57 SRs as being suitably robust for the Overview method (20), **yet included all 57 of them, irrespective of their quality/ suitability**. An expert reviewer noted this, advising NHMRC (21):

*"An explanation on why the NHMRC chose to conduct the review based on systematic reviews instead of conducting its own systematic reviews based on original clinical studies, particularly when "the systematic reviews (included in this assessment) varied in quality" is required."*

NHMRC's response was, *"The HWC maintains that the overview method was justified, given the unfeasibility of conducting a full systematic review of the scope required by the NHMRC review."* This pertains to NHMRC's **choice** to adopt this unprecedented method, which the response indicates was likely adopted to save time and money (thereby making it 'feasible').

### **Findings of the SRs dismissed:**

NHMRC's unique and unusual interpretation of the Overview method was also highlighted by its **dismissal of the findings of the 57 SRs**, several of which reported positive conclusions. This was incongruous with the method prescribed by the Cochrane Handbook referenced, which stipulates that the **purpose of an Overview is to summarise the findings of SRs** (22).

Bizarrely, NHMRC/ HWC instead decided to re-review the original studies, using the secondary information included about them in the SRs that had already reviewed them.

NHMRC acknowledged the "limitations" of this approach on p.25 of the Information Paper, since SRs are secondary sources meaning that essential information about the original studies was incomplete and/or missing (let alone accurate). Brushing this off as a mere 'limitation' is an understatement when one realises the major extent to which it impacted the Review.

NHMRC **ignored and withheld** disclosure of extensive critique of its chosen approach by one of its expert reviewers in 2014 (after release of the Draft Information Paper). FOI documents reveal that the expert reviewer advised NHMRC (23):

*"What is not clear is how systemic or not the NHMRC review was of high quality RCTs. [...] I do not agree that considering random evidence provided by interest groups offsets this deficiency (p18). High quality RCTs with narrow confidence intervals (Level 1 evidence) should have been searched for and included in this review."*

*Systematic reviews (SRs) have considerable weaknesses as reliable sources of evidence. Personally, I would prefer a much more reserved approach to their use as Level 1 evidence. For example, we know that SRs can come to quite contrasting conclusions pending the grading RCT scale they adopt. (See Juni et al, JAMA, 1999 [http://rds.epi-ucsf.org/ticr/syllabus/courses/18/2009/04/16/Lecture/notes/Hazards\\_of\\_quality\\_scoring.pdf](http://rds.epi-ucsf.org/ticr/syllabus/courses/18/2009/04/16/Lecture/notes/Hazards_of_quality_scoring.pdf)). Some systematic reviews conclude homeopathy is more than placebo (Cucherat et al 2000; Linde & Melchart 1998; Linde et al 1997; Kleijnen 1991; and*

many of the reviews in the Swiss report found a trend in favour of homeopathy). It is probably unreasonable to discount this evidence on the basis that good quality trials did not show such strong evidence of efficacy, if the quality rating scale for trials is not well justified for use in homeopathy.”

This, and other extensive feedback provided by the reviewer, was **withheld from public disclosure**, despite NHMRC publishing a dedicated ‘Expert review comments’ document alongside the final report.

### **Heterogeneity bias - mixing ‘apples and oranges’:**

A major limitation of NHMRC’s approach was lack of differentiation between different, incompatible homeopathic intervention methodologies - known as ‘heterogeneity bias’.

Of the 176 studies included in the Overview, 119 studies tested the efficacy of individual medicines/ complexes against a specific disease (pathological prescribing) and 57 studies tested the efficacy of individualised homeopathy (classical prescribing) for a specific condition (24).

The HWC could not differentiate between these incompatible clinical approaches for the simple reason that all but one of the 57 SRs did not differentiate between them and the HWC did not assess any original studies (hence could not independently group the studies appropriately).

**In its own right**, this critical methodological flaw (‘mixing apples and oranges’) rendered the entire approach and its findings entirely meaningless.

### **NHMRC’s ‘standardised methodology’ abandoned mid-way through the Optum Review:**

While the NHMRC Information Paper boldly assured the public that NHMRC used ‘standardised, accepted methods developed by Australian experts’, it **did not report that NHMRC had to abandon its ‘standardised, accepted method’ for reviewing health evidence** (as stipulated in the original research protocol) **mid-way through the Optum Review** (25). This was a direct consequence of the limitations of the approach adopted.

This was **not disclosed** in the NHMRC Information Paper; it is only mentioned on p.20 of the Optum Overview Report (the technical document), which explains:

*“Studies that were identified during the systematic review of Level I evidence were not assessed according to the NHMRC dimensions of evidence as planned in the research protocol. These dimensions were originally developed for use in assessing primary studies. It became apparent during the evidence review that they would not be appropriate for overviews, as study-level data was often incompletely reported in the systematic reviews (e.g. primary outcomes were often not specified, effect estimates and confidence intervals were rarely reported).”*

### **Conduct of the Optum homeopathy review - Dec 2012 to Oct 2013:**

Following is an exposé of NHMRC’s procedures and methods in reviewing the evidence on homeopathy under the second contractor (Optum) between December 2012 and October 2013. This has been revealed through a formal investigation spearheaded by the Australian Homoeopathic Association (AHA) and Complementary Medicines Australia (CMA), with scientific support from the Homeopathy Research Institute (HRI). All information presented is supported by FOI documents referenced against key facts.

In considering the findings of the investigation, it is important to note that for each of the 61 clinical conditions evaluated, NHMRC included an evidence statement framework comprised of three ELEMENTS (26):

1. **Body of evidence** - a description of the body of evidence, which included the number of participants and a ‘quality rating’ for each of the included studies.
2. **Level of confidence (LOC)** rating for the body of evidence as a whole, using an ‘adapted GRADE’ tool that was specifically created for the Review.
3. **Conclusion** - a concluding statement that described the effectiveness of homeopathy as a treatment for a particular condition, compared with either placebo or other treatment(s).

### **Dec 2012 - original research protocol agreed and finalised:**

FOI documents reveal that the ‘original research protocol’ (referred to above) was **agreed and finalised between the ONHMRC, the HWC and Optum in late December 2012** (27). **It was never published.** FOI documents reveal that the originally agreed protocol included an evidence statement framework specifying: there ‘is an effect/ no effect where there is sufficiently powered, consistent evidence’; or that there ‘may be an effect where there is evidence of an effect but there is a slight concern over consistency or underpowering’; or ‘the effect is uncertain where there is little evidence available or where the evidence is conflicting or underpowered’.

This protocol **bears no resemblance to that ultimately used**, as outlined below.

### **March 2013 - Optum completes evidence assessment:**

After finalisation of the research protocol in December 2012, Optum began its evidence assessment on 3 January 2013 and completed it by March 2013. The minutes of the 18 March 2013 meeting of the HWC record (28):

*“Optum noted that the approach taken when developing draft evidence statements did not align with the approach proposed in the research protocol as the evidence statement for all conditions would have stated that the effect was uncertain.”*

This shows that a decision was made to deviate from the agreed research protocol in order to alter the results of the Review and reach more definitive conclusions - **a clear indication of bias**.

Concluding that an effect is 'uncertain' or 'inconclusive' - consistent with the original protocol - leaves open the possibility that the reported effect may in fact be positive, with future research shedding light on the issue. Importantly, this accords with accepted scientific reporting protocols. Apparently, the HWC/ ONHMRC were resistant to allowing any 'uncertainty' in the reported findings, leaving open the possibility that homeopathy *could* have positive effects.

**April to June 2013 - HWC Sub-Group established to refine the protocol:**

After Optum completed the evidence assessment and the HWC met in March 2013 to discuss the findings and evidence statement protocol, the ONHMRC established a HWC Sub-Group. The existence of this process was not disclosed. The specific purpose of the Sub-Group was to further refine the research protocol and evidence statement framework used for the Review (i.e. **to modify the research protocol**).

**During this time, all the elements of the evidence statement framework and its component criteria (which underpinned the Review's published findings) were developed and applied to the data.** The original protocol did not include any sample size or quality rating exclusion thresholds, no 'null hypothesis approach' or 'adapted GRADE' tool - all of which underpinned the Elements of the Review's framework for 'reliable evidence'.

Table 1 on the following page summarises the changes made to the research protocol during the HWC Sub-Group process and the impact it had on the Review's findings and conclusions:



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Date	Post hoc changes to the Optum review research protocol	Impact on the review	Disclosed/ reported?
22 Dec 2012	Research protocol for Optum review agreed and finalised.	Pre-agreed criteria to be applied to the assessment.	No FOI (29)
Jan-Mar 2013	Optum completes evidence assessment.	Evidence assessment completed according to agreed research protocol; evidence of attempt to modify the protocol.	No FOI (30)
Apr-Jun 2013	HWC Sub-Group process established to further refine the research protocol.	All Elements and criteria of the Review's published evidence statement framework are created during this process.	No FOI (31)
29 Apr 2013	ONHMRC/ HWC Chair (Prof Paul Glasziou) proposes that the 'null hypothesis' approach be adopted.  Approved by HWC early May 2013.	From this point, homeopathy is ' <i>assumed to be ineffective unless reliable evidence proves otherwise</i> '.  The criteria underpinning the concept of 'reliable evidence' do not yet exist.	No FOI (32)
29 Apr - May 2013	ONHMRC develops an 'adapted GRADE' tool for providing a 'level of confidence (LOC)' rating of the evidence ( <b>Element 2</b> of the evidence statement framework).  Applied by ONHMRC, since Optum is ' <i>unfamiliar with the tool</i> '.	The 'adapted' tool does not pass either round of independent methodological peer review (see below).  GRADE calculations are not published, despite use of a novel tool.	No FOI (33)
6 May 2013	" <i>Conclusive statements</i> " added as a component of <b>Element 3</b> of the evidence statement framework.	Original protocol stipulated that the purpose of the Overview was to ' <i>inform the community of the evidence</i> ' and ' <i>not draw conclusions</i> '.	No FOI (34)
24 May 2013	ONHMRC proposes an N=200 trial sample size threshold for whether a trial is 'adequately powered' ( <b>Element 1</b> of the evidence statement framework).	Does not pass ACC peer review (see below).	No FOI (35)
9 Jul 2013	First round of independent methodological peer review by the Australasian Cochrane Centre (ACC).	ACC advises NHMRC/ HWC that linking sample size to 'trial power' is not scientifically valid  ACC notes critical flaws of the 'adapted GRADE' tool.  ACC also questions the overly definitive nature of the draft evidence statements conclusions.	No FOI (36)
11-12 Jul 2013	HWC approves an N=150 trial sample size exclusion threshold for whether a trial is 'reliable'.  Modification to <b>Element 1</b> of the evidence statement framework.	Dismisses the results of 146 out of the 176 trials (83%) from their results being considered 'any further' in the Review's findings.	No FOI (37) Expert analysis, HRI (38)
Late Jul/ Aug 2013	New criterion added to <b>Element 1</b> of the evidence statement framework: a trial now ALSO had to be rated 5/5 using the Jadad (or equivalent) rating scale to be 'good quality' and hence 'reliable' i.e. 100% quality.	Dismissed 25 out of the 30 remaining trials from their results being considered 'any further' in the Review's findings.	No FOI (39) Expert analysis, HRI
30 Aug 2013	Second round of ACC methodological peer review feedback to ONHMRC/ HWC.	ACC advises that: <ul style="list-style-type: none"> <li>The definitive nature of the Review's findings '<i>does not accurately reflect the research</i>'</li> <li>The 'quality rating' criterion is "<i>problematic</i>" and a "<i>poor predictor of quality</i>"</li> <li>Key flaws of the 'adapted GRADE' tool have not been addressed (advice ignored)</li> </ul>	No FOI (40)
October 2013	Optum Overview Report finalised.  ONHMRC prepares Draft Information Paper for public comment.	Original research protocol not published; protocol changes and their impact on the analysis not reported.	N/A

**Table 1: Post hoc changes to the Optum review research protocol and their impact on the evidence assessment**

### **Post hoc modification to the research protocol dismisses 97% of the evidence from consideration in the findings:**

The retrospective creation and application of these criteria directly resulted in **the results of 171 of the 176 (97%) of the Overview trials being dismissed from “any further consideration” in the findings** (41).

NHMRC thereby gave the *impression* that these trials were ‘included’, whereas their results were in fact **excluded from any consideration in the findings at all** on account of being ‘unreliable’; i.e. because they had less than 150 trial participants and/or did not meet the unusually high 100% quality rating cut-off.

Both the ‘N=150 trial participants’ and ‘5/5 Jadad (or equivalent) quality rating’ thresholds are entirely **arbitrary criteria that are not recognised by any scientific standards and have never been used before or since by any other research group**, including NHMRC. NHMRC also did not disclose that both criteria were **post hoc modifications to the research protocol**.

### **Positive ‘reliable’ trial omitted from Table 1 of NHMRC Information Paper:**

Of the remaining 5 trials deemed to be ‘reliable’ according to NHMRC’s own definition, 1 trial was positive (Stam 2001) (42). This trial compared a homeopathic gel (*Sprioflor SRL*) with a Capsicum-based product (*Cremor Capsici Compositus*) and reported, “*both products [were] equally effective but the homeopathic gel had less adverse effects*”. The trial had 161 participants and was rated as ‘good quality’.

This positive trial was excluded from Table 1 of the NHMRC Information Paper that reported the findings of the Optum Overview to the public, being **substituted with a negative trial** in the same clinical condition that was not considered as part of the Overview. Whether or not this was deliberate, it is the only one of the 176 Overview trials omitted from Table 1.

### **Lack of transparency - changes to the research protocol not reported or justified:**

Table 1 (above) shows that the specific criteria that were developed during the Sub-Group process did **not exist as part of the original research protocol**.

The Optum Overview Report (pp.20-21) included a ‘Changes from the research protocol’ section, **yet did not disclose/ report any of the key changes to the research protocol** outlined in Table 1. The NHMRC Information Paper also failed to disclose this critical fact - only hinting in a footnote on p.33 that ‘the criteria applied were not universal rules or principles, but were unique to the Homeopathy Review’. One has to delve deep into the Optum Overview Report Appendices, where on p.270 it is stated:

*“The criteria in this document were not developed a priori, but rather were developed by the HWC with the assistance of the evidence reviewer over a number of months following the completion of the overview” .*

Even here, **none of the actual changes to the research protocol were disclosed or justified**. NHMRC described its approach to developing the evidence statements as “*transparent*” (43).

### **NHMRC erroneously cites BMJ paper to justify the N=150 sample size threshold:**

In attempting to authenticate the N=150 sample size threshold, NHMRC correctly identified the homeopathic trials it identified as ‘*continuous outcomes studies*’ (44) and cited a *BMJ* paper (45). However, the *BMJ* paper, which makes no link between trial size and ‘reliability’, also emphasises that its findings:

*“cannot be extrapolated to trials assessing continuous outcomes.”*

NHMRC uses this citation of the *BMJ* study against the N=150 threshold multiple times across the final report documents released to the public, who would not question that an expert body such as NHMRC would make such a fundamental error and/or intentionally publish misleading information. NHMRC regularly funds and collaborates on research trials with fewer than 150 participants, which are not judged as ‘unreliable’.

### **NHMRC’s findings do not pass independent peer review:**

As identified in Table 1, independent methodological reviewer feedback provided to NHMRC on 30 August 2013 by the highly respected ACC **advised that the definitive nature of the findings do not accurately reflect the research evidence** (revealed through FOI) (46):

*“If the intent is to provide general statements about the effectiveness of homeopathy, then ‘no reliable evidence’ may not adequately reflect the research. For example, when a substantial proportion of small (but good quality) studies show significant differences, [...] ‘no reliable evidence’ does not seem an accurate reflection of the body of evidence.”*

This was initially flagged by the ACC in its first-round July 2013 advice (36), further strengthened in its August advice since the issue remained unaddressed. NHMRC also ignored and withheld feedback from another expert reviewer, who in 2014 similarly advised NHMRC (47):

*“The dismissal of positive SRs compounded with the lack of an independent systematic review of high quality RCTs leaves me uncertain of the definitive nature of the Report’s conclusions. [...] if I were to dispassionately consider the evidence of efficacy, I am still left with niggling doubts that there are unanswered questions around the evidence.”*

### **Conduct of the Homeopathy Review - Apr 2014 to Mar 2015:**

After finalisation of the Optum Overview Report in October 2013, in April 2014 NHMRC released a Draft Information Paper for public consultation. In May 2014, NHMRC appointed a different contractor to assess additional evidence submitted by stakeholders and the public.

### **Homoeopathy stakeholders not informed of release of the Draft Information Paper:**

The 'NHMRC Service Charter' assures, *"We treat our stakeholders with dignity and respect and inform our stakeholders about decisions that may affect them."*

On 9 April 2014, on the eve of World Homeopathy Awareness Week, NHMRC released a Draft Information Paper for public comment. Homoeopathy stakeholders (including the AHA) were not informed of its release during the embargo period. Such conduct did not uphold the principles espoused by the Service Charter.

### **Anti-homoeopathy advocacy groups receive advance notification:**

On 8 April 2014, **the day before the official release** of the Draft Information Paper, FSM published an open letter on its website 'congratulating' the NHMRC CEO on its findings, signed by seven of FSM's founding members.

It included a personal message from FSM's co-founder and Vice President, Prof Alastair MacLennan, urging that Australians not be *"sold snake oil"* - a phrase **reiterated by the NHMRC CEO**, who in April 2015 declared the sector *"snake oil merchants"* (48). The significance of this is further highlighted below.

### **NHMRC appoints research group with FSM conflicts to assess public consultation evidence:**

Between May and September 2014, NHMRC contracted the Australian Research Centre for the Health of Women and Babies (ARCH), Robinson Research Institute (RRI), University of Adelaide to assess 40 studies (almost a quarter of the total evidence considered for the Review). The ARCH notably had no expertise that was relevant to understanding and interpreting homeopathic evidence.

Moreover, the ARCH **contained FSM Supporters, one of whom NHMRC contracted to perform the work, without declaring or managing the conflict** (49). The seriousness of this conflict is further amplified by the FSM Supporter in question being directly affiliated with FSM's co-founder and Vice president, Prof MacLennan (and long-term NHMRC grants recipient), who on 8 April 2014 directly lobbied NHMRC against homeopathy (as outlined above).

The RRI had also officially awarded Prof MacLennan its 'Skeptic of the Year Award for Friends of Science in Medicine' in 2012 and 2014 (i.e. during the Review period) for his anti-complementary medicine FSM activism (50).

### **NHMRC conducts sham public consultation process:**

NHMRC reported that the 'risk' of missing single trials not captured in the Overview Report was 'offset' by inviting submissions from homeopathy interest groups (in 2012) and via a formal public consultation (in 2014). NHMRC inaccurately states that this externally submitted evidence was, *"...assessed using a similar method to that applied in the overview"* (51) but *"did not alter the overall findings of the assessment of the evidence"* (52).

In fact, external submissions **were assessed entirely differently and separately** from the rest of the evidence base, in a way that meant that it was **never possible** for any externally submitted evidence to alter the results of the Review. Thus, of 49 submitted trials that NHMRC considered suitable (around a quarter of the data), **the number that entered the Overview Report was 0**. This made a sham of NHMRC's apparent attempt at external co-operation and transparency; also critiqued in undisclosed expert peer reviewer feedback (as outlined above).

However, how these extra trials were assessed is actually a **moot point**, since 27 of the 49 'suitable' trials submitted by external parties were entirely dismissed as being 'self-selected samples'; the remaining 22 were 'downgraded' for the same reason. This was not mentioned at all in the Information Paper, which only emphasised throughout that NHMRC 'considered submissions of evidence from external parties'. Further, this 'bias' could easily have been removed by NHMRC carrying out a systematic literature search for all other trials on the same topic as those submitted, **which NHMRC chose not to do**.

### **NHMRC retrospectively describes the Review as a 'Health Technology Assessment':**

NHMRC's final report documents refer to the Review as a 'Health Technology Assessment' (HTA). FOI documents reveal that this descriptor was **retrospectively adopted in mid-2014**, for the specific purpose of providing a justification for excluding subject experts from the HWC, based on widespread criticism received during public consultation (53).

The disingenuous basis of this descriptor is evidenced by the fact that **four out of five customary HTA parameters were entirely excluded from scope**, including 'effectiveness' (observational studies), 'cost-effectiveness', 'quality' and 'safety'. Thus the public has been misinformed that the NHMRC Statement, *"People who choose homeopathy may put their life at risk"* (54) is based on the Overview's findings, when it is not: it is **opinion, not evidence-based**.

Moreover, NHMRC has been clear in stating that the HWC conducted an 'Overview' under its Terms of Reference - not a HTA - using a method derived from Chapter 22 of the Cochrane Handbook. These are entirely different research processes conducted for entirely different purposes.

### **NHMRC publishes final report - 11 Mar 2015:**

On 11 March 2015, NHMRC published its final report, assuring the public that:

- *"The assessment of the evidence used standardised, accepted methods for assessing the quality and reliability of evidence for whether or not a therapy is effective for treating health conditions"* (Information Paper, p.5)
- *"When evaluating health evidence and drafting health advice, NHMRC uses a rigorous approach that has been developed by Australian experts in research methods"* (Information Paper, pp.9-10)

- “The evidence was identified and reviewed in a robust and transparent manner” (Information Paper, p.15)
- “The conclusion is based on the findings of a rigorous assessment of more than 1800 papers” (NHMRC media release), whereas only 176 were included in scope
- All changes to the research protocol were disclosed and justified (Optum Overview Report, p.20)
- Conflicts of interest were declared and managed (Administrative Report, p.5)

In response to concerns expressed to NHMRC by stakeholders in 2015 relating to whether the Review was conducted ethically and transparently, the new NHMRC CEO, Prof Anne Kelso, officially ‘stood by the Review and the processes that underpinned it’, stating (55):

*“I believe that the Information Paper and Statement on homeopathy, which is based on the current available evidence, have fulfilled this role.”*

In learning of the homeopathic community’s challenge to the NHMRC Homeopathy Review in February 2016, the HWC Chair and co-architect of the Review’s criteria, Prof Paul Glasziou, further vilified the homeopathy sector on the basis of the process he oversaw (56):

*“I can well understand why Samuel Hahnemann—the founder of homeopathy—was dissatisfied with the state of 18th century medicine’s practices, such as blood-letting and purging, and tried to find a better alternative. But I would guess he would be disappointed by the collective failure of homeopathy to carry on his innovative investigations, but instead continue to pursue a therapeutic dead-end.”*

### Conclusion:

The NHMRC Funding Rules stipulate, “NHMRC expects the highest levels of research conduct and integrity to be observed in the research that it funds” (57).

Research fraud involves the intentional falsification and/or fabrication of research and the misleading reporting of its findings, from the intent to deceive for personal gain or to cause damage to another party (58). Such improper and unprofessional conduct in clinical research has been shown to waste taxpayer money and harm public health (59).

Based on the evidence presented in Parts 1 and 2 to this article, it would be difficult for a fair-minded person to reach any alternative conclusion other than NHMRC’s conduct of the Homeopathy Review represents research fraud and misconduct, in both its scientific and administrative aspects.

The public, health professionals and decision makers rely on the advice of respected institutions such as the NHMRC, which evaluate the evidence on a particular topic, to determine which treatments are effective and safe. Since these are matters relating

to public health and safety, the integrity of processes undertaken by such institutions must be above reproach.

The evidence presented in Parts 1 and 2 to this paper indicates that the NHMRC undertook an ideological, not a scientific approach to assessing the research evidence on homeopathy.

Such processes can no longer be trusted if they are marred by such factors. This is an issue of momentous gravity, since NHMRC is a taxpayer-funded government institution with a statutory responsibility to ethically and impartially advise the community on matters relating to health. NHMRC’s conduct of the Homeopathy Review raises broader questions concerning the community’s ability to trust the integrity of other processes it has conducted.

NHMRC’s premature termination of a good quality first review process and the systematic, post hoc modification of the research protocol of the second (Optum) review, well after the assessment had already been completed, strongly indicates an agenda to report findings of a predetermined nature. Numerous other issues such as the adoption of unique and arbitrary criteria (e.g. the N=150 sample size cut-off for trial ‘reliability’), post hoc modification of the research protocol, undisclosed/ unmanaged conflicts of interest and misleading and inaccurate reporting lend further weight to this conclusion.

NHMRC demonstrated a consistent lack of regard for conflicts of interest policies and legislation designed to safeguard government processes from actual and perceived conflicts of interest, compromising the community’s confidence in the ability of the APS to act impartially and ethically (principles upheld by the *Public Service Act 1999*).

Of 104 placebo-controlled RCTs into homeopathy published in peer-reviewed journals by the end of 2014, 41% were positive, 54% inconclusive and only 5% negative (60) - a similar proportion to that observed in published conventional medical research (61). This basic research fact remained undisclosed in over 944 pages of NHMRC report documentation. Why?

Notably in this context, advice from NHMRC’s own methodological peer reviewer, the ACC, confirmed that “a substantial proportion of small (but good quality) [homeopathic] studies show significant differences”, which NHMRC ignored and withheld from public disclosure.

Why would NHMRC have gone to such extraordinary lengths to reduce the entire research evidence base on homeopathy to a blanket statement of ‘no reliable evidence’ - inventing an arbitrary framework and flouting accepted research methods and its own administrative standards and guidelines in the process?

The answer appears to lie in NHMRC’s ideological opposition to homeopathy, influencing a process where ‘the ends justified the means’. NHMRC had already pre-announced its position on homeopathy well before the Review commenced. In the first instance, this was evidenced by the explicitly biased process it undertook in developing a draft position statement in 2010/11, which proclaimed homeopathy to be “implausible”, “placebo”, “inefficacious”, “unethical” and its practitioners “deceptive” (see Part 1, *Similia* Vol 28, no 2, December 2016).

Before the formal evidence assessment commenced in 2012, the NHMRC website pre-emptively *reiterated* these same themes, alongside its Chairman 'assuring' the public in July 2011 'that NHMRC does not support homeopathy', openly adversarial public remarks of the CEO and the extensive involvement of undisclosed conflicts of interest.

In light of such factors, a fair-minded person would reasonably question whether NHMRC could allow itself to report any positive findings under its banner. Allowing the reporting of positive evidence for homeopathy *in even one area* would have represented an admission by Australia's peak scientific medical research body that homeopathy is not just 'plausible', but may actually be 'efficacious'. Even a suggestion of this possibility could have been seen to legitimise homeopathy's place in Australian healthcare and would have placed NHMRC at odds with its own preformed view, already definitively expressed in the public domain by its most senior officials, website and former NHMRC Council-approved draft position statement.

It also would have placed NHMRC at odds with the skeptics lobby, active supporters of whom were involved in the Homeopathy Review process at multiple levels, without observance of conflicts of interest policy. NHMRC and the skeptics lobby are not mutually exclusive groups, but belong to the same extended medical research community. Anti-homeopathy vested interests such as FSM have a strong presence amongst the research community that NHMRC draws from and supports; their Supporters are to be found in NHMRC's Principal Committees and Council. The current NHMRC Chairman, for example, is a FSM Supporter (Prof Bruce Robinson).

The systematic redefinition of the Review's research protocol throughout 2013, well after Optum had completed its evidence assessment is a clear sign of research misconduct. Research protocols are an important safeguard used to reduce/prevent reporting bias in scientific studies. Before a study begins, a protocol is created which outlines in detail all essential aspects of the project, such as the research question being asked, methods of data retrieval, criteria used to determine which studies will be included or excluded from the review, and how the included data will be analysed to produce the final results. If any changes to the protocol are required, they must all be fully disclosed and justified.

In the Optum review, **none** of the key changes to the research protocol were disclosed or justified, despite their forming the very basis of the Review's published evidence statement framework and overall conclusions.

It is inconceivable that NHMRC would have executed such a process in reviewing conventional healthcare treatments, where subject and research experts from the target discipline were deliberately excluded in favour of personnel with ideological opposition to the topic under inquiry. Justifiably, there would have been an outcry from the medical research and Australian community had this been publically known. Why then did NHMRC deem its approach acceptable in the case of homeopathy and why is NHMRC still seeking to defend such a deeply flawed process?

NHMRC describes itself as, "*an established leader in the development of high quality, evidence-based health advice*" (62).

Bearing in mind such expertise and the fact that multiple research experts sat on the HWC, the HWC/ ONHMRC would have been fully aware of how unusual their methods were in conducting the Review. Furthermore, the HWC/ ONHMRC would have understood the direct impact their decision-making and procedures would have on the results.

This raises the spectre of misfeasance, the wrongful exercise of lawful authority, not unintentional scientific error.

Research fraud and misconduct undermines the public's trust in science and results in loss of trust in public institutions. It endangers the health of millions, who are denied access to accurate information on clinical interventions relevant to their health and wellbeing.

### References:

1. NHMRC *Information Paper – Evidence on the effectiveness of homeopathy for treating health conditions*, p.6. CAM02A. National Health and Medical Research Council, 11.03.2015
2. NHMRC *Statement on Homeopathy*. CAM02. National Health and Medical Research Council, 11.03.2015.
3. NHMRC media release, 11.03.2015
4. NHMRC *Statement on Homeopathy*. CAM02. National Health and Medical Research Council, 11.03.2015
5. Research strategy employed by the first reviewer. NHMRC FOI 2014/15 021-05
6. NHMRC *Additional levels of evidence and grades for recommendations for developers of guidelines 2009*: NHMRC
7. Hillier, S. et al (2011). *FORM: An Australian method for formulating and grading recommendations in evidence-based clinical guidelines*. BMC Medical Research Methodology. 2011, 11:23. DOI: 10.1186/1471-2288-11-23
8. NHMRC Official Order - Contract & Statement of Requirement of first contractor, 04.04.2012. NHMRC FOI 2014/15 021-04.
9. NHMRC *Information Paper – Evidence on the effectiveness of homeopathy for treating health conditions*, p.9-10. CAM02A. NHMRC, 11.03.2015
10. Email between ONHMRC & the HWC Chair (Prof Paul Glasziou) re termination of first reviewer's contract. 13.08.2012. NHMRC FOI 2014/15 021-10.
11. Ibid.
12. Complementary Medicines Australia (CMA) FOI request to NHMRC re. final Draft Report of the first contractor. 07.10.2015. NHMRC FOI 2015-16 006.
13. NHMRC response to CMA/AHA re. Sep 2015 stakeholder submission of complaint to NHMRC, 22.12.2015.
14. National Press Club Speech, NHMRC CEO, Prof Warwick Anderson. 15.04.2015.
15. HWC member (Prof Fred Mendelsohn) expert feedback to ONHMRC on the July 2012 version of the first reviewer's draft report. 12.07.2012. NHMRC FOI 2014/15 021-08
16. HWC member (Prof Fred Mendelsohn) expert feedback to ONHMRC on the July 2012 version of the first reviewer's draft report. 12.07.2012. NHMRC FOI 2016/17 016-13
17. NHMRC *Administrative Report*, p.6. CAM02B. NHMRC, 11.03.2015
18. NHMRC *Information Paper*, p.5. CAM02A. NHMRC, 11.03.2015
19. NHMRC *Administrative Report*, p.7. CAM02B. NHMRC, 11.03.2015
20. Optum *Overview Report Appendices*. NHMRC CAM02H, 08.04.2014

21. NHMRC *Expert Review Comments*. NHMRC CAM02E. 11.03.2015
22. *Cochrane handbook for systematic reviews of interventions*, Chapter 22
23. Expert methodological reviewer feedback to NHMRC, 10.05.2014. NHMRC FOI 2014/15 004-62
24. Mathur, M. & Gupta, V. K. (2016) NHMRC report on homeopathy; mixing apples with oranges. Letter to the editor. *Homeopathy* (2016) **105**, 126-127. <http://dx.doi.org/10.1016/j.homp.2015.09.001>
25. Original research protocol for the Optum Homeopathy Review. NHMRC FOI 2014/15 004-58
26. NHMRC *Information Paper – Evidence on the effectiveness of homeopathy for treating health conditions*, p.33. CAM02A. NHMRC, 11.03.2015
27. Original research protocol for the Optum Homeopathy Review. NHMRC FOI 2014/15 004-58.
28. Homeopath Working Committee (HWC) meeting minutes, 18.03.2013. NHMRC FOI 2015/16 007-03
29. Original research protocol for the Optum Homeopathy Review. NHMRC FOI 2014/15 004-58
30. HWC face-to-face meeting minutes (final endorsed). 18.03.2013. NHMRC FOI 2015/16 007-03
31. HWC and HWC Sub Group meeting minutes, 2013-2014. NHMRC FOI 2015/16 008.
32. 2013.04.30 - Email from ONHMRC to HWC members re. approach to homeopathy evidence statements. 29.04.2013. NHMRC FOI 2014/15 021-11
33. HWC Sub Group teleconference meeting minutes. 29.04.2013 - NHMRC FOI 2015/16 008-03 & 06.05.2013 - NHMRC FOI 2015/16 008-03
34. HWC Sub Group teleconference meeting minutes. 06.05.2013. NHMRC FOI 2015/16 008-03
35. HWC Sub Group teleconference meeting minutes. 24.05.2013. NHMRC FOI 2015/16 008-07
36. First round Australasian Cochrane Centre (ACC) methodological peer review. NHMRC FOI 2015-16 008-13
37. HWC face-to-face meeting minutes. 11-12.07.2013. NHMRC FOI 2015-16 008-06
38. Homeopathy Research Institute (HRI). Independent expert analysis of NHMRC's methods, unpublished
39. Australasian Cochrane Centre (ACC) follow-up methodological peer review. 30.08.2013. NHMRC FOI 2015-16 007-05
40. Ibid.
41. Homeopathy Research Institute (HRI). Independent expert analysis of NHMRC's methods, unpublished
42. Stam, C., Bonnet, M. S. & van Haselen, R. A. (2001) The efficacy and safety of a homeopathic gel in the treatment of acute low back pain: a multi-centre, randomised, double-blind comparative clinical trial, *The British Homoeopathic Journal*, **90**:21-28
43. NHMRC response to CMA/AHA re. Sep 2015 stakeholder submission of complaint to NHMRC, 22.12.2015
44. NHMRC *Information Paper*, p.35. CAM02A. NHMRC, 11.03.2015; *Frequently Asked Questions*, p.11. CAM02C. NHMRC; *Optum Overview Report Appendices*, p.274. NHMRC CAM02H, 08.04.2014
45. Deschartres et al (2013). Influence of trial sample size on treatment effect estimates. *BMJ* 2013;346:f2304. [www.bmj.com/content/346/bmj.f2304](http://www.bmj.com/content/346/bmj.f2304)
46. Australasian Cochrane Centre Follow-up Methodological Review, 30.08.2013. NHMRC FOI 2015-16 007-05
47. Expert methodological reviewer feedback to NHMRC, 10.05.2014. NHMRC FOI 2014/15 004-62
48. National Press Club Speech, NHMRC CEO, Prof Warwick Anderson. 15.04.2015
49. NHMRC Decision Letter to Complementary Medicines Australia (CMA). NHMRC FOI 2016/17 016
50. Robinson research Institute (University of Adelaide) Annual Reports, 2012 and 2014
51. NHMRC *Information Paper*, p.8. CAM02A. NHMRC, 11.03.2015
52. NHMRC *Information Paper*, p.25. CAM02A. NHMRC, 11.03.2015
53. HWC meeting minutes, 30.07.2014. NHMRC FOI 2015/16 008 09-11
54. NHMRC *Statement on Homeopathy*. CAM02
55. Letter from NHMRC CEO (Prof Anne Kelso) to CMA CEO re. 30 Sep 2015 CMA/AHA submission. 22.12.2015
56. Glasziou, P. (2016) *Paul Glasziou: Still no evidence for homeopathy*. BMJ Blogs, 16 Feb 2016. <http://blogs.bmj.com/bmj/2016/02/16/paul-glasziou-still-no-evidence-for-homeopathy/>, accessed 31 May 2017
57. *NHMRC Funding Rules 2016 - 9.1. Responsible Conduct of Research and/or Incomplete, False or Misleading Information*. <https://www.nhmrc.gov.au/book/nhmrc-funding-rules-2016/9-researcher-responsibilities-and-considerations>, updated 13.11.2015.
58. Gupta, A. (2013). *Fraud and misconduct in clinical research: A concern*. *Perspectives in Clinical Research*, 4(2), 144-147. <http://doi.org/10.4103/2229-3485.111800>
59. Marusic A, Wager E, Utrobicic A, Rothstein HR, Sambunjak D. (2016). *Interventions to prevent misconduct and promote integrity in research and publication*. *Cochrane Database of Systematic Reviews* 2016, Issue 4. Art. No.: MR000038. DOI: 10.1002/14651858.MR000038.pub2
60. Faculty of Homoeopathy (UK), <http://facultyofhomoeopathy.org/research/>
61. El Dib RP, Atallah AN, Andriolo RB. Mapping the Cochrane evidence for decision making in health care. *J Eval Clin Pract*, 2007; **13**(4):689-92
62. NHMRC response to CMA/AHA re. Sep 2015 stakeholder submission of complaint to NHMRC, 22.12.2015.



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