Responses to the LDAA comments on the Scoping Study

Response to the Executive Summary.

Paragraph 3. I think it is important to recognise that the scoping study was meant to be a scientific study to investigate the research needs for 'an investigation into whether a causative tick-borne microorganism (*Borrelia*) for Lyme disease exists in Australia'. I am not clinically qualified and did not attempt to distinguish between clinical symptoms or syndromes, other than the need for the correct specimens for subsequent laboratory investigation. With respect to the 'people' dimension, I fully accept and believe that there is some 'Lyme-like' disease affecting many Australians, and that it is important to discover the cause of this disease syndrome, whether it be infectious, tick-borne, or a non-infectious cause. Thus I do NOT believe any person suffering from this syndrome should suffer any stigma or other prejudice, but they should be treated justly, sensitively, and with respect, and the treatment offered should try to alleviate the symptoms while seeking the actual cause.

Paragraph 4. I concede that there has been insufficient contemporary research into vector-borne diseases, other than mosquito-borne diseases, as Australia has been relatively lucky in not having most of the tick-borne, phlebotomus fly-borne, louse-borne or Culicoides-borne classical human diseases. This has changed substantially in recent years as more efforts are now being made to investigate tick-borne diseases, such as irwin's group at Murdoch, but other groups too are becoming aware of the need to undertake greater research efforts on tick-transmission. I do not accept that there is any evidence to indicate inadequate and inconsistent testing processes in Australia – all our major laboratories are able to consistently detect and diagnose *B. bergdorferi* infections acquired abroad, and if there is another indigenous *Borrelia* species in Australia causing disease, then it is probably not *B. bergdorferi*, as currently all the various *B. bergdorferi* s.l. members can be diagnosed.

I have absolutely no problem with 'necessary inclusion of more patient-focused outcomes' but, as stated elsewhere, I am not a clinician and the areas addressed in the scoping study were diagnostic, not focused on patient treatment or outcomes.

Responses to points in the Introduction

Page 4, para 4 '*Patients have also expressed concerns that the Study appears to rely heavily on United States (US) sources for its expertise and guidance.'* This scoping study referred to work in the US and Europe principally as this is where almost all the research has been done. This is not surprising as Lyme disease is endemic in these areas. Indeed internationally, the Infectious Diseases Society of America Lyme disease guidance document is the internationally accepted guidance document by the Health Departments of US, UK, Germany, ECDC, etc. However, I took greater note of the European workers and especially those in Austria, Germany, France and the UK.

Page 5, Table 1. This table is very strange – the scoping study was designed to seek evidence of *Borrelia bergdorferi* in Australian ticks, as per the TOR. The column of remarks on 'not finding *Borrelia* in indigenous ticks is ludicrous. A negative finding merely indicates that it was not possible to find the agent, and that it might be that a Lyme-like disease occurs which has yet to be identified – in fact a good reason to refer to the disease as 'Lyme-like'.

Page 5, final paragraph. This has moved on since the scoping study was prepared with more information by the Murdoch group and others that have been unable to find any evidence of *B. bergdorfer*i in any Australian ticks. I made every attempt not to trivialise or to invalidate Australian patients with a Lyme-like illness. I believe that there is a Lyme-like syndrome affecting many

Australians, but from my reading of the literature and from my experience with arthropod-borne viral diseases, I don't believe it is caused by *B. bergdorferi*. Its cause remains an enigma, and requires much more research, both in terms of other possible organisms and in other transmission cycles.

Page 6, first paragraph. I undertook the scoping study at the request of the CMO, and fulfilled the TOR, speaking to those indicated, which included patients on the CMO's Clinical Advisory Committee. I was asked to undertake the study, I believe, because of my expertise on arthropod-borne diseases, but I am not a clinician and I don't pretend to know or fully understand some of the clinical nuances.

Page 8 and onwards. Comments on the Scoping Study

Page 8, study 1, comment (a). There is still, in my view, no good scientific evidence to demonstrate the presence of *B. bergdorferi* in Australia.

Page 8, study 1, comment (b). Spirochaetes are not hard to demonstrate by any good microbiologist, and some of the best microbiologists in Australia have not been able to detect *B. bergdorferi*, except in cases acquired overseas.

Page 8, study 1, comment (c). I have no problem with this suggestion, but if so, the only suspect tick species, *Ixodes holocyclus*, does not occur in all areas, and not usually outside a narrow ~100km wide coastal strip in eastern Australia. Thus other species might have to be considered, but very few are known to bite humans.

Page 8, study 1, comment (d). I don't have a problem with this. However, it should be noted that all B. bergdorferi have only been found in certain tick species, never from other hematophagous arthropods. One form of relapsing fever can be transmitted by lice, but that is another *Borrelia* species.

Page 8, study 1, comment (e). I don't have a problem with this, and indeed the Murdoch group are doing just this. We know certain Rickettsia species can be transmitted by ticks.

Page 8, study 1, comment (f). *B queenslandica* was mentioned/discussed in the scoping study on page 14.

Page 9, study 2, comment (a). Spirochaetes from other insects have little relevance to this study – there are many spirochaetes and indeed other potential bacteria, rickettsia, viruses etc. To follow up on all these would be an enormous task!

Page 9, study 2, comment (b). I don't know of any reputable evidence that Australians are infected with one or more species of Borrelia, except those who have acquired either *B.bergdorferi* or relapsing fever *Borrelia* species from overseas.

Page 9, study 2, comment (c). We do not have any *Borrelia* species associated with relapsing fever in Australia, although a related species has recently been described by Irwin and colleagues. This species could be studied as suggested.

Page 9, study 2, comment (d). It is difficult to isolate a Borrelia species from wildlife unless there is a specific disease or unless it can be found in blood specimens in which case it is like looking for a needle in a haystack, and would be extremely expensive and time consuming to do. It would perhaps be more profitable to utilise arthropods obtained from wildlife – ticks, lice, etc. I would support such a study, and I understand this is proposed by Irwin's laboratory.

Page 10, study 3, comment (b). I am unaware of any *Borrelia* species being isolated in Australia by any private laboratory, and if true, those isolates should be shared with other laboratories – not to do so is counter-productive and against normal practice, and the isolation and other details be published in reputable, peer-reviewed journals. Sophisticated PCR and deep sequencing technologies are commonly undertaken by all major microbiological laboratories in Australia, and almost certainly those attached to medical schools will be doing so with greater sophistication than private laboratories would have access to.

Page 10, study 3, comment (c). I find this comment rather insulting. Westmead is recognised internationally as being one of the two most capable laboratories in Australia. To suggest that it uses sub-optimal procedures is a very ignorant view. I agree with the concept that a review of laboratories is needed, but this should be done particularly for unaccredited laboratories in Australia who are involved in clinical diagnoses.

In particular, the use of an international panel of specimens should be used for QA/QC is an essential step, and any putative positives should then be investigated fully in collaboration with the laboratory which has made the positive claim, and in parallel and together with an accredited public health reference laboratory to substantiate the claim.

Page 10, study 3, comment (d). The DOH should indeed urgently liaise with overseas laboratories which claim to find positive results to ensure they participate in a QA/QC assessment, and to ensure this is carried out properly, an international accredited and unaligned laboratory such as the UK Institute for Biological Standards and Control should be engaged to oversee the conduct and interpretation of the QA/QC results.

I think it is crucially important to also understand that diagnosing Lyme disease, or *B. bergdorferi* infection, is not a simple exercise, such as diagnosing Ross River disease or Salmonella food poisoning. This is compounded by the fact that there are many spirochaetes that infect the human body naturally, such as *Treponema* species in the mouth and others in the gut, with former responsible for periodontal disease, and they as well as other pathogenic species have serologically cross-reacting antigens. I would stress, therefore, as I did in both the scoping study and when I appeared before the Senate Committee last week, that it is essential that a QA/QC is undertaken with both the Australian Public Health and Clinical Laboratories, as well as the three private laboratories in Sydney, San Diego, and Germany, to ensure that all testing for *B. bergdorferi* is done correctly and specifically. To ensure that these are indeed done correctly, a third party should be responsible for the QA/QC, such as the UK National Institute for Biological Standardization and Control, an internationally recognised and independent validator of QA/QC programmes. In addition, where there are cases and/or differences, they should be explored in joint studies so that all tests are validated and confirmed. The three private laboratories conducting tests and finding evidence of *B. bergdorferi* must demonstrate in joint studies the veracity of their results. The LDAA accept the results of the three private laboratories, but not those of the major clinical diagnostic laboratories in Australia. It is important therefore for all that the findings of all laboratories are shown to be correct and are fully confirmed.

Pages 11-13. These comments are better addressed to a clinically qualified person. I would furthermore suggest that the best person to comment would be Dr B Hudson, and ID physician who has much experience in this area.