Supplementary Submission to the Senate Inquiry 'Investigation into the use of the quinoline antimalarial drugs mefloquine and tafenoquine in the Australian Defence Force.'

Associate Professor Jane C. Quinn

Major Stuart McCarthy (Rtd)

Affiliations:

The Australian Quinoline Veterans and Families Association,

The QVFA is lodging this supplementary submission in response to questions asked by the Committee at the Senate Inquiry hearings that took place in Brisbane on 30 August 2018.

Questions were raised around the role and engagement of the Defence/DVA Links Steering Committee (DLSC) in providing a mechanism for stakeholder engagement for veterans and their families affected by mefloquine as part of their ADF service.

DLSC is an inter-departmental government committee comprised only of senior Defence and DVA officials, not a forum for external stakeholder engagement. The DVA website states:

> *"The DLSC is responsible for implementing the strategic direction set by the DDEC and for monitoring both the progress of the MoU and the performance of the Support Continuum."*

The DVA website identifies the following officials as members of the DLSC:

- Chief Operating Officer, Department of Veterans' Affairs (Co-chair)
- Deputy Secretary, Defence People Group, Department of Defence (Co-chair)
- Deputy President, Department of Veterans' Affairs
- **Repatriation Commissioner, Department of Veterans' Affairs**
- Head, People Capability, Department of Defence
- Commander, Joint Health Command, Department of Defence
- First Assistant Secretary, Health and Community Services, Department of Veterans' Affairs
- Principal Medical Adviser, Department of Veterans' Affairs

The DLSC meeting summary of 1 November 2016 (attached) states in part that DLSC "received reports on a range of issues" including "the Mefloquine outreach program." QVFA was not invited to attend this meeting, nor did we have any input into any material presented to this meeting. In a separate submission we have identified the Repatriation Commissioner Major General (retired) Mark Kelly as a key witness to this inquiry, given his crucial role in representing the interests of veterans to DVA. General Kelly has never at any time spoken to us about the matters under consideration in this inquiry.

In May 2017 we were contacted by Melissa Davey from *Guardian Australia*, who provided us with an untitled, undated document which appears as if it *may* have been a briefing to DLSC from an unknown party (attached), seeking our comment for a forthcoming newspaper article. Ms Davey was quite excited about this document, explaining that it was the first time *Guardian Australia* had received a "leak" from a Government Minister's office. We believe this "leak" most likely came from the office of Veterans Affairs Minister Dan Tehan.

The backhanded manner in which this presumably official government document was provided to us again highlights the cynicism and disdain which a number of witnesses have described to the Committee.

We wish to note that QVFA was not consulted or requested to provide input to this document, nor were any other ESOs within ADSO to the best of our knowledge. This document therefore appears to represent the views of Defence and DVA alone.

Please note that this document **makes no mention of tafenoquine**.

This document notably includes the following false or misleading information in relation to **mefloquine**; with section headings align to those in the attached document:

Prescription of mefloquine in the ADF:

The focus of the information presented is on general use of mefloquine for antimalarial prophylaxis in travellers as per recommendations from the WHO and others, without taking into account the specific requirements for oversight of antimalarial medications in military populations.

The number of prescriptions globally and within the ADF. The scale of use globally, and relatively small numbers of prescriptions of mefloquine in the ADF in recent years are not, in themselves, a justification for, or proof of safety.

In section 9, and referring to information in section 8, the document addresses the question of how many ADF members were prescribed mefloquine. The document states '*These figures are contentious and advocates in this area claim that the real numbers – including those prescribed tafenoquine – are closer to 5,000.*' This statement is deliberately misleading. The numbers are not contentious but fact and as such, the numbers presented in this DVA-Defence Links Select Committee document are deliberately reduced to suggest that the actual number of ADF members prescribed mefloquine and tafenoquine are small. The actual numbers prescribed mefloquine and tafenoquine as part of ADF trials are shown below.

Year	Refs	Location	Purpose	Population	Study Cohort			Comparator Cohort		
					Drug	Dose	Subjects	Drug	Dose	Subjects
1998-1999	1-4	Bougainville, PNG	PEP	Peace Monitoring Group	Tafenoquine	400mg od[a] or 200mg bid[b] for 3d	374[d]	Primaquine, doxycycline	7.5mg tid[c] for 14d	210[d]
2000	1-4	East Timor	PEP	3 RAR, 5/7 RAR	Tafenoquine	400mg od[a] or 200mg bid[b] or 200mg od[a] for 3d	639[d]	Primaquine, doxycycline	7.5mg tid[c] for 14d	289[d]
2000-2001	1, 2, 5	East Timor	Prophylaxis	1 RAR	Tafenoquine	200mg daily for 3d, then 200mg weekly	492	Mefloquine	250mg daily for 3d, then 250mg weekly	162
2001-2002	6	Australia	Relapse prevention	Australian military	Tafenoquine	200mg daily for 3d, then 200mg weekly	31	Nil	Nil	Nil
2001-2002	1, 7	East Timor	Prophylaxis	4 RAR, 2 RAR	Mefloquine	250mg daily for 3d, then 250mg weekly	1,157	Doxycycline	100mg daily	388

[a] Once daily.
[b] Twice daily.
[c] Thrice daily for primaquine plus 100mg doxycycline daily.
[d] These figures are the totals of enrolled subjects administered each drug. A total of 239 of the enrolled subjects who were co-administered other drugs were excluded from the reported findings.

The total number who were given mefloquine and / or tafenoquine as part of ADF trials is 2,885 individuals. The numbers provided in this document by the DVA-Defence Links Steering Committee identify a further 137 individuals from 2010 only. The numbers prescribed between 1998 and 2010 are not provided but given that mefloquine was the second line antimalarial for the ADF during this time the numbers

are predicted to be between 500 and 1000 individuals. Given that we are aware that some ADF personnel were given mefloquine without this prescription being recorded in their central medical records, the numbers could be higher.

In section 11 this documents states *'Members are also advised to seek medical attention immediately if they experience particular symptoms and are monitored regularly while taking it'*. It has been our contention, and evidence to this Committee from multiple sources support this view, that this safety advice was routinely not provided and monitoring of symptoms did not occur effectively in deployed individuals taking this drug.

In section 12 the statement is made *'If mefloquine is the only suitable medication, and they do not want to take it, they will not be able to deploy'*. Although a necessary safety precaution, this statement indicates the level of pressure an ADF member may feel to take a drug that is potentially unsafe in order to be able to deploy to a malarious area with their peers.

Use of mefloquine in allied militaries:

'Third line agent' is not the same as *'drug of last resort'*. Both the UK and US militaries have relegated mefloquine to a 'last resort' option in their operational pharmacy, as have Germany and France. Only the Irish Defence force steadfastly retains mefloquine as a first line antimalarial, and this in the face of increasing pressure for them to follow the lead of other global military organisations. A drug of 'last resort' means that ALL other pharmaceutical possibilities have been exhausted, not that just the first two options have been considered and, if these have been ruled out, that mefloquine is the default. As such, the inference from these paragraphs that the ADF is in concert with the approach of other military organisations is incorrect and misleading.

Participation of ADF members in clinical trials involving mefloquine:

The sections relating to this area of the document do not address the concerns of veterans and their families in regard to these trials at all. They defer to information generated by the IGADF inquiry, an inquiry that was exceptionally limited in the number of individuals called to give evidence, and that did not engage independent third-party experts as part of its review process. The 'relevant subject matter experts' engaged to determine if the trials were conducted under appropriate ethical principles were the same investigators undertaking the trials, representing a clear conflict of interest, and negating the validity of this investigation. This conflict is not reported in this document. The IGADF's report therefore cannot be used as a justification of ethical scrutiny in this situation and this evidence should be disregarded by the Government.

In section 20, the ADF acknowledges the recommendations made by the IGADFs report that identifies ADF members as vulnerable subjects, but only states that it 'gives due consideration to such issues' is disingenuous. The safety of vulnerable subjects, and how their vulnerability is managed and mitigated, has been a requirement of ethical approval through all national HRECs since the time of the original trials. Therefore, the ADF has not changed its position at all in this context

and questions should be raised as to the governance of their human ethics review process in this regard that these considerations was not adequately taken into account at the time of the trials in question, or potentially beyond.

Adverse health effects:

Sections 21 – 26 state the argument that '*all medications have some side effects'* and that the mild – severe adverse event profile affects between 1-13% of individuals taking the drug dependent on the symptom. Although some of these figures are contested in the scientific literature, that the drug has a side effect profile including both common and rare adverse events is not contested.

In section 24, the document states *'In rare cases, side effects may persist for months or longer. In a small number of people, the effects may be permanent. Because mefloquine is long acting, it is possible for people to first experience side effects in the weeks after stopping mefloquine.'* This statement clearly acknowledges that Defence and DVA are aware that permanent side effects can occur from taking this drug. However, this has repeatedly been refuted by a number of witnesses to the inquiry, as well as senior DVA medical advisors and ADF officials, who have suggested that the debilitating health issues affecting mefloquine veterans are, dismissively, all related to drugs they took some years ago. Absolutely this is the case, and DVA and Defence acknowledge that in this document, yet continue to argue that these cases do not exist, or that they cannot be validly proven. This is clearly contradictory and this document has provided misleading and contradictory statements to the Government in this regard.

Adverse health effects among current and former serving ADF members

Sections 27 – 39 cover information related to the reported adverse health effects suffered by current and ex-service members who have been exposed to mefloquine as part of their ADF service.

Sections 27 – 29 report incidences of adverse events to mefloquine, tafenqouine and doxycycline as reported in the publications related to the AMI clinical trials. In my first submission to this Committee I provide extensive evidence as to how these adverse event profiles were underreported in the peer-reviewed publications relating to these trials, in comparison both between the trial cohorts and against other comparable trial reports. Defence DVA have no re-reviewed this information to confirm its validity or returned to the original trial records to determine if all AE's were reported in the trial publications, therefore these statements are both superficial and misleading.

Section 30 states that 'There have also been public reports that some suicides among former members of the ADF' are linked to the use of mefloquine yet section 31 reports that 'No suicides of serving ADF personnel have been linked to mefloquine use'. This is not an appropriate comparison. Only comparison of numbers of EX-serving ADF members in realtion to mefloquine prescription could address this question of suicide risk. As neither Defence nor DVA collect veteran's suicide data they are currently unable to address this question, for this reason. That is not stated in this document. The

statements made in sections 30 and 31 divert the reader away from the original question without addressing it at all.

Section 32 begins with the statement 'There is no evidence that mefloquine causes or triggers PTSD'. Why this question is being asked is not clear. At no point has any advocacy group suggested that mefloquine triggers PTSD, but that the symptoms of mefloquine toxicity can present with some similarities (in the absence of traumatic exposure). Therefore this section is presenting a misleading question which it then answers in the negative. This again diverts the reader from the central issue that some ADF members who have experienced side effects of mefloquine may have been incorrectly diagnosed with PTSD, and are therefore receiving inadequate or inappropriate treatment.

Again, and further to other submissions relating to the ethical requirements imposed by the ADF for re-review of existing trial data from this cohort – section 32 states *'A review of Medical Employment Classification outcomes of members involved in the Timor-Leste studies showed no significant differences in the incidence of those prescribed mefloquine becoming medically unfit for service or being diagnosed with PTSD compared with those taking another anti-malarial drug.'* Clearly a reanalysis of existing trial data has been performed without reconsent, clearly going against the ADFs own requirements that data linkage cannot be performed in any retrospective data analysis without re-consent from trial participants.

Section 33 states '*ABI is a broad term that covers a range of long term neurological symptoms from a variety of causes.* ***Defence and DVA are not aware of any globally accepted evidence that supports the suggestion that ABI can be caused by mefloquine'***. That Defence and DVA have already accepted that permanent neurological and other medical sequelae can result from exposure to mefloquine and tafenqouine, acceptance that is reflected in some of the existing RMA SOPs which identify permanent neurological changes in the brain (see section 35 - sensioneural hearing loss, trigeminal neuropathy, and recently retinal neuropathy can be added to this list) as well as neuropsychiatric disorders that can present as both temporary and lifelong in nature (epileptic seizure, bipolar disorder, depressive disorder, attempted suicide – and perhaps the most permanent neuropsychiatric side effect – completed suicide), the statement highlighted above is both contradictory and extraordinary.

The follow sections require scrutiny together:

'37. In its Inquiry report, the IGADF recommended that Joint Health Command consider a mechanism to ascertain whether any participants in the 2000-2002 AMI trials who took mefloquine may have had any history of a health condition that would have been a contraindication to mefloquine use. This aims to ensure that any previous health condition inconsistent with the prescription of mefloquine is identified and, where necessary, allow possible treatment to be provided through DVA or Defence.

38. This recommendation has been met by Defence with the establishment of a dedicated email address that allows any current or former serving members with

concerns to contact Joint Health Command directly and request a review of their case. Defence has, and will continue to, build awareness of this mechanism in its public statements and respond to requests for review.'

Section 38 is not a suitable or appropriate response to the recommendation identified in section 37. Section 37 asks for the medical records of all AMI trial participants to be reviewed to identify if any had a pre-existing medical condition that should have precluded them from being part of the trials, and that potentially those individuals be contacted for follow up. The DVA / Defence response in section 38 suggests that this has been achieved by '*establishment of a dedicated email address'* for trial subjects to request a review of their case history. This is not an appropriate response to this IGADF recommendation nor should have this been suggested to the Government to be so in this document.

The response to the IGADFs recommendation that all ADF health records be available to any clinical trial administrators utilising ADF members is also disingenuous. The Defence response states that using the new eHealth *'all Defence health practitioners to access records wherever they are in Australia'*. This will, of course, not cover trials undertaken overseas (such as the AMI trials in question) or provide sufficient access to medical record for ADF members being allocated alternative antimalarial medications with known risk, such as mefloquine and tafenoquine, when in a theatre of operations. This is therefore a superficial and misleading response.

Support available for current and former members of the ADF:

As the previous components of this document will testify, the statement in section 40 which suggests that the Department of Defence engage in 'An open and transparent approach to information sharing' must be viewed with some caution.

Section 41. The *'Malaria, mefloquine and the ADF' online resource'* contains numerous inconsistent and misleading statements. The content of this website was reviewed by the QVFA in 2016, at the request of the SGADF, but suggested changes to the wording in the website were not made.

Section 42 states that the website contains information on 'the support available to those with concerns'. A review of this website cannot identify any information on support available to affected veterans, other than the statement *'Any former ADF member who feels they may have health problems related to any aspect of their military service is encouraged to submit a claim to the Department of Veterans' Affairs (DVA).'* This is not 'support' specific to this cohort, nor are the national clinical guidelines or other resource documents present on this website an equivalent. Indeed, the DVA helpline established to provide information to veterans with mefloquine and tafenoquine-associated health issues is not even included in this information. As such, the 'support' inferred by Defence in this statement is simply not in existence.

Section 45 states 'Current serving Defence members who are concerned about the use of mefloquine are provided support as part of

Defence's comprehensive health system'. The QVFA are all too aware of the failures of this 'comprehensive health system', failures that have resulted in ADF members paying for their own specialist treatment, relying on support from ESOs and other charitable organisations to assist them get the healthcare they need, or simply having to forgo any appropriate necessary treatment and suffer as a consequence. This situation is clearly not articulated in this governmental consultation document.

Section 48 states 'From 1 July 2014, all former members of the permanent and reserve forces have been able to access a physical and mental health assessment from their General Practitioner (GP), whether or not they are DVA clients. This comprehensive assessment can be performed at any point after a member has discharged from the ADF, however, it is only available once in their lifetime'.

A 'once in a lifetime' GP assessment, where GPs are clearly not adequately informed about the risks and potential side effects of these drugs for ADF members is, at best, unhelpful, and at worst, useless. This is particularly the case as exposure to mefloquine or tafenouine as part of ADF-run clinical trials was NOT recorded in the members Central Medical Record – the medical record available to the member or GP on discharge – and to correlation of exposure with symptomology could not be investigated or proven unless the ADF veteran or member had specifically requested their AMI trial records. None knew they had to do this until early 2016. As such any GP review carried out to date simply will not have taken these exposures into account. This fact is clearly not articulated in this document.

Department of Veterans' Affairs

Section 50 states that *'DVA has established a dedicated mefloquine support team to assist current and former serving members of the ADF with mefloquine related claims'*. Experience of this 'dedicated support team' to date is that they do not have the specialist knowledge required to assist mefloquine and tafenoquine veterans access appropriate treatment, and in some cases, simply refer the veteran to their existing case worker. This has been an ineffective and inadequate response.

Section 51 refers to medical advice sent to GPs by the Chief Medical Officer from DVA. This information was not disseminated through local primary healthcare networks, or GP surgeries, but by a mailshot through the GP accrediting body in Australia. As such, it appears that the majority of GPs did not register this information and this process has not been repeated to ensure that this information has been widely disseminated to primary healthcare providers. This information is not provided in this document.

Election Commitments

Four election commitments are identified in this document:

1. 'Establish a formal community consultation mechanism to provide an open dialogue on issues concerning mefloquine between the Defence Links Steering Committee and the serving and ex-serving Australian Defence Force (ADF) community'

This Commitment has not been carried out. No formal consultation has been initiated and no dialogue between the Defence Links Steering Committee and those affected by mefloquine and tafenqouine has been initiated.

2. 'Develop a more comprehensive online resource that will provide information on anti-malarial medications'

The document states that this action has been completed. However, the inadequacies with the current Defence website have been identified above. The relevance of this election commitment is also in question as it is not information on antimalarial medications that is required but information on support and treatment for the health impacts of these medications on ADF members and their families.

3. Establish a dedicated Department of Veterans' Affairs (DVA) mefloquine support team to assist our serving and ex-serving ADF community with mefloquine-related claims, which will provide a specialised point of contact with DVA.

The document states that this action has been completed. The QVFA would argue that this is not the case, and continues to be so in 2018. This 'dedicated team' has not been actioned in any useful or meaningful way for mefloquine and tafenoquine veterans.

4. Direct the inter-departmental DVA-Defence Links Steering Committee to examine the issues raised, consider existing relevant medical evidence and provide advice to the Government by November 2016.

It is suggested that this document is the outcome of that inter-departmental review. The significant number of issues and flaws in the information presented within it indicate that any advice or recommendations made on this basis of this document would be potentially flawed.

Finally, the DVA-Defence Links Steering Committee document makes a series of recommendations. These included:

Outreach Centre

*'To provide easy access to information and assistance for former serving members of the ADF who have been administered mefloquine, it is recommended that a temporary outreach centre be opened in Townsville for up to one week'***.**

This 'outreach' activity was undertaken at very short notice in late 2016. It included a GP information session, undertaken by a senior ADF medical official who was involved in the AMI clinical trials, and the senior DVA medical advisor. Only a small number attended the meeting due to the short notice in advertising it, and some significant and misleading information was presented to these GPs at this event. Further information regarding this event can be supplied on request.

Additional 'outreach' sessions were advertised for ADF members and their families through the Townsville Bulletin. The description of these sessions was non-specific and a number of veterans attended these who were under the impression that they were general sessions for information on the process of making DVA claims. The sessions were, again, held at very short notice and at the start of the local education authority summer vacation period (second week in December as identified in section 62) when many veterans and their families had left Townsville for their summer holiday.

The QVFA was informed of the 'outreach' sessions only a week before they were to be delivered, offered to assist in developing the materials to be delivered at these sessions (an offer what was declined), and the majority of the membership were not able to attend them. This DVA 'outreach' event has not been repeated.

No 'evaluation' of this outreach event has been published despite this evaluation intimated in section 63. That the outreach event undertaken by DVA was, in the opinion of the QVFA, poorly designed and singularly unsuccessful, that this situation has not been reviewed is a cause for concern. Equally, that a well-designed and thoroughly research 'outreach proposal' was then subsequently rejected by the Minister makes this situation even more untenable. **No 'outreach centre' coincident with the description in section 64 – 67 has ever been established in Townsville.**

It is clearly identified in this document that consultation only occurred between Defence, DVA and the RMA on the delivery of this outreach activity (Section 70). This shows level the disregard to which this veterans population and their families have been held by these organisations that none of the veteran stakeholders were engaged in this discussion, despite the QVFA

being well known and easily accessible to those undertaking this planning process.

Community Consultation

The recommendation in section 71 states: *A report on the outcomes and issues raised at the outreach centre will be tabled at a future DVA-Defence Links Steering Committee meeting. This will be in line with the Government's commitment to establish a formal community consultation mechanism to provide an open dialogue on issues concerning mefloquine between the Defence Links Steering Committee and the serving and ex-serving ADF community.'*

If this has been carried out, the QVFA and their veteran membership are not aware of it.

In conclusion

The DVA-Defence Links Steering Committee document, tabled to the Government in late 2016, provided many false or misleading statements and suggested to have completed actions items that were either poorly delivered or simply not undertaken.

This key example of the failure of internal Defence and DVA committees to comply with the simple requirements of due process is a further example of the fundamental disregard that has been shown to mefloquine and tafenoquine veterans during this process.

The QVFA hope that the Committee will take these misrepresentations to Government most seriously and make recommendations from this Inquiry that the governance of this internal DVA-Defence Committee be reviewed and significant changes made to its operation in the light of this information.

Department of Defence / Department of Veterans' Affairs
Links Steering Committee

Summary of Meeting – 1 November 2016

The 38th meeting of the Defence DVA Links Steering Committee (DLSC) was held in Canberra on 1 Nov 2016. The following matters were discussed at the meeting.

Suicide Review

The Committee noted progress on the Suicide Review being conducted by the National Mental Health Commission. The interim report is due by the end of December 2016, and the final report by the end of February 2017.

Transition

The Committee received an update on transition and agreed the establishment of a Transition Taskforce to look further improvements to the process. A brief is to be prepared jointly by DVA, in consultation with Defence, for Minister Tehan.

Transformation Update

The Committee received an update on DVA's Transformation program.

Policy, Programme and Initiatives

The Committee was updated on progress of the Early Engagement Model which aims to establish a relationship between DVA and Defence members as early in their service as practical. Other updates were provided on Goal Attainment Scaling for rehabilitation outcomes, medical discharge rates and the Mefloquine outreach program.

Reports Back

The Committee received reports on a range of issues, including the Support Continuum Performance Report, Non-Liability Health Care, jet fuel exposure case file review, joint research activities and the GP Connect Project.

Other Business

Other issues discussed included the launch of the Prime Minister's Veterans' Employment Initiative and Ministerial priorities.

Background

1. The Government asked the inter-departmental DVA-Defence Links Steering Committee to examine the issues raised in respect of the use of mefloquine in the Australian Defence Force (ADF), consider existing relevant medical evidence and provide advice to the Government by November 2016.

2. Issues raised in respect to the use of mefloquine in the ADF can be categorised as concerns about:

- the prescription of mefloquine in the ADF;
- the participation of ADF members in clinical trials involving mefloquine;
- adverse health effects suffered by current and former members of the ADF which have been attributed to the use of mefloquine; and
- the support available for former members of the ADF who believe they have been adversely affected by mefloquine.

Prescription of mefloquine

Prescription of mefloquine in the general community

3. Concerns have been expressed about the use of mefloquine in the ADF, including allegations that members of the ADF were compelled to take mefloquine as part of clinical trials. In examining this concern, it is useful to remain mindful of the extensive use of mefloquine in the general community.

4. Mefloquine is an anti-malarial medication that can be used for both the prevention and treatment of malaria. The major advantage of mefloquine is that it only needs to be taken once per week. It is one of only three medications approved by the Australian Therapeutic Goods Administration (TGA) for malaria prevention and is currently used around the world. Mefloquine is included in anti-malarial guidelines published by:

- The World Health Organization International Travel and Health
- The US Centers for Disease Control and Prevention
- The Public Health Agency of Canada
- The United Kingdom Advisory Committee on Malaria Prevention.

5. Mefloquine is commonly prescribed for civilians travelling overseas to malarious areas and remains popular as it is taken as a once weekly dose rather than daily. Mefloquine was first registered with the TGA in 1988 for the treatment of malaria and in 1993 for malaria prophylaxis. Since then there have been over 35 million prescriptions of mefloquine worldwide. The TGA is responsible for monitoring and evaluating the safety and efficacy of therapeutic products and manages any risks associated with individual products. When registering mefloquine for use in Australia, the TGA noted associated side-effects and assessed that it was a safe and effective medication.

6. The following table shows how many prescriptions were written each year in Australia from 2010-2015 for mefloquine.

Australian Civilian Prescription Data

Anti-malarial	2010	2011	2012	2013	2014	2015
Mefloquine	14,149	16,512	13,674	14,030	13,770	12,713
(Source: Australian statistics on medicines)						

Prescription of mefloquine in the ADF

7. In the ADF, mefloquine is a third line agent, meaning it is only used when other medications are not appropriate for an individual. Prior to 2006, when Malarone was registered and introduced, mefloquine was the second line option for malaria prophylaxis. In such cases mefloquine is only ever prescribed by a qualified medical practitioner in accordance with both the TGA approved product information and Department of Defence (Defence) health policy. Defence health policy incorporates all TGA recommendations and builds on that advice to ensure that the ADF's medical protocols are appropriate for the military context and remain consistent with best practice.

8. The vast majority of ADF members have never been prescribed mefloquine. Centralised medicines dispensing information has only been available in the ADF since 2000 and records show that, between July 2000 and June 2015, approximately 1,979 ADF personnel have been prescribed mefloquine. Most of these prescriptions were as part of the Army Malaria Institute (AMI) studies in Timor-Leste from 2000-2002 (a total of 1,319 soldiers).

9. These figures are contentious and advocates in this area claim that the real numbers – including those prescribed tafenoquine – are closer to 5,000.

10. On average, less than 25 ADF members will be prescribed mefloquine each year. The following table shows how many ADF members were prescribed mefloquine from 2010-2015.

Number of ADF members prescribed mefloquine 2010-2015

Year	Number of ADF members
2010	25
2011	26
2012	13
2013	20
2014	35
2015	18

11. Deployment to any area of operations involves appropriate health protection, to minimise the chance of injury or illness. This will often include particular vaccines or medications. Deployment to malarious areas involves ADF members taking anti-malarial medication, and for a small number of individuals mefloquine will be the most suitable medication. In such cases Defence health policy requires ADF members be assessed for suitability and fully informed of the potential side effects of before it is prescribed for them. Members are also advised to seek medical attention immediately if they experience particular symptoms and are monitored regularly while taking it.

12. ADF personnel may refuse to take mefloquine. However, if they are deploying to a malarious area then they will be required to take an anti-malarial medication to protect them against malaria. If mefloquine is the only suitable medication, and they do not want to take it, they will not be able to deploy.

Use of mefloquine by allied militaries

13. Mefloquine is used in militaries around the world, including the United States (US) and United Kingdom (UK) armed forces.

14. The US military retains mefloquine as an option for malaria prevention and continues to use it when it is the only suitable anti-malarial for a particular individual. They describe it as a 'drug of last resort', which is synonymous with the ADF term 'third line agent'. In practice, this means both the US military and the ADF now only prescribe mefloquine when no other anti-malarial is suitable for an individual. Elements of the US Special Forces suspended the use of mefloquine in 2013 in response to updated US Food and Drug Administration (FDA) advice regarding side-effects associated with the drug. However, they have since resumed using mefloquine as a 'drug of last resort'.

15. The UK House of Commons Defence Select Committee recently completed an inquiry into the use of mefloquine by the British armed forces. The subsequent report recommended that any future prescribing of mefloquine to UK military personnel be restricted only:

- to those who are unable to tolerate any of the available alternatives;
- after a face-to-face individual risk assessment has been conducted; and
- after the patient has been made aware of the alternatives and has been given the choice between Lariam (trade name for mefloquine) and another suitable anti-malarial drug.

16. These recommendations are in line with existing ADF policy, which is quite restrictive when compared to the use of mefloquine by the UK armed forces and a number of other militaries. As discussed, in the ADF mefloquine is prescribed as a third line agent, meaning it is only used by personnel who demonstrate an intolerance to other medications or for whom the other medications are not suitable. Further to this, Defence health policy requires ADF members to be properly informed of the potential side-effects of mefloquine and the drug may only be prescribed by a qualified medical practitioner after the member has been fully assessed for suitability and fully informed of the risks and benefits.

Participation of ADF members in clinical trials involving mefloquine

Inquiry into trials conducted in Timor-Leste

17. In September 2015, the Inspector-General Australian Defence Force (IGADF) launched an inquiry into issues concerning Army Malaria Institute (AMI) studies of the drug mefloquine between 2000 and 2002 involving ADF members deploying to Timor-Leste. The subsequent report, released in October 2016, contains 72 findings and three recommendations.

18. The IGADF examined the circumstances of the use of mefloquine in studies conducted by Defence during 2000-2002 and determined, in consultation with a number of witnesses and relevant subject matter experts, that the use of mefloquine was reasonable and consistent with relevant health protocols and policies at this time. He also found that the trials were ethical.

19. The IGADF also examined the allegation that Defence members were compelled to take mefloquine during these studies, including the allegations that individuals were threatened with disciplinary action for expressing concerns about the effects of mefloquine. He found these allegations were not substantiated.

20. The IGADF did recommend that the ready acceptance by soldiers of advice or encouragement provided to them by military persons in authority, combined with a potential belief that participation in the trial was expected, is an issue worthy of further consideration in the conduct of any future medical trials, particularly in the context of a pre-deployment for an overseas operation. Defence has accepted this recommendation and current Defence policy requirements for human research gives due consideration to such issues.

Adverse health effects

Mefloquine side effects

21. Concerns have been expressed about the adverse health effects suffered by current and former members of the ADF due to the use of mefloquine.

22. All medicines may have some side effects and mefloquine is not suitable for everyone. Mefloquine has known side effects and precautions need to be taken in individuals with particular health conditions, including any mental health condition or seizure disorder. For most people taking mefloquine, side effects are minor and the medication is generally well tolerated. When taken for malaria prevention, the predominant side effects are neuropsychiatric – sleep problems, vivid dreams, anxiety, and depressive symptoms. Trouble sleeping and vivid dreams are the most common of these, occurring in around 13 per cent of people. When medication is ceased, these symptoms resolve in the vast majority of cases.

23. Uncommonly, people taking mefloquine can experience agitation, restlessness, mood swings, panic attacks, confusion, hallucinations, aggression, psychosis and suicidal ideation. These symptoms occur in less than 1 per cent of people taking mefloquine. Other short term neurological symptoms, such as dizziness and headaches are relatively common, occurring in up to 10 per cent of people. Uncommonly (less than 1 per cent), balance problems and seizures can occur. People who have, or have had, any mental health condition or seizure disorder should not take mefloquine.

24. Usually, if someone experiences side effects from mefloquine, it happens soon after starting it. This is one of the reasons it is given before deployment, so that this can be monitored and the medication stopped if necessary. Side effects usually go away within days or weeks after stopping mefloquine. In rare cases, side effects may persist for months or longer. In a small number of people, the effects may be permanent. Because mefloquine is long acting, it is possible for people to first experience side effects in the weeks after stopping mefloquine. New side effects have not been known to occur once mefloquine has completely left the body.

25. Both the TGA in Australia and the FDA in the US routinely issue warnings on medicines, as detailed in the product information for prescribers and the consumer medicine information for patients.

26. In 2013, the FDA updated its advice regarding neurological side effects of mefloquine. The FDA added a warning label to the medication stating that neurological side effects may persist or become permanent in a small number of people. These side effects include dizziness, loss of balance or ringing in the ears. The possibility of long term dizziness, balance problems and ringing in the ears was already recognised in product information published by the TGA.

Adverse health effects among current and former serving ADF members

27. As stated at paragraph 8 above, most ADF members who have taken mefloquine did so as part of the AMI studies in Timor-Leste from 2000-2002 (a total of 1,319 soldiers). The outcomes of the studies were published in peer reviewed medical journals. No permanent neurological adverse events were identified during the studies.

28. In the study comparing mefloquine and doxycycline, the most commonly reported adverse effects were sleep disturbance, headache, tiredness and nausea. The rates of adverse events were the same in both the mefloquine and doxycycline groups. Three serious neuropsychiatric events were reported in soldiers taking mefloquine and these soldiers were withdrawn from the study. Two of these individuals had undisclosed medical conditions that would have prevented the prescription of mefloquine if they had been known to medical staff.

29. In the study comparing mefloquine to tafenoquine, the most commonly reported adverse event was gastrointestinal upset. The only neurological adverse effect reported was headache. The rates of these events were similar in both groups. No psychiatric side effects were reported in either group.

30. Nevertheless, a small number of current and former serving members of the ADF have reported suffering adverse health effects which they attribute to mefloquine use, including posttraumatic stress disorder (PTSD) and acquired brain injury (ABI). There have also been public reports that some suicides among former members of the ADF are linked to the use of mefloquine.

31. No suicides of serving ADF personnel have been linked to mefloquine use. Defence maintains a list of ADF members known or suspected of having committed suicide while serving. This list has been cross checked against ADF prescribing data on mefloquine since July 2000 and none of those individuals were identified as having been prescribed mefloquine by Defence.

32. There is no evidence that mefloquine causes or triggers PTSD. In some cases, neuropsychiatric side effects from mefloquine may have some similarity to those of an acute stress reaction. However, a diagnosis of PTSD requires the exclusion of medications as a cause of symptoms. A review of Medical Employment Classification outcomes of members involved in the Timor-Leste studies showed no significant differences in the incidence of those prescribed mefloquine becoming medically unfit for service or being diagnosed with PTSD compared with those taking another anti-malarial drug.

33. ABI is a broad term that covers a range of long term neurological symptoms from a variety of causes. Defence and DVA are not aware of any globally accepted evidence that supports the suggestion that ABI can be caused by mefloquine.

34. The Repatriation Medical Authority (RMA) website details processes for eligible individuals and/or organisations to lodge a request if they believe there is a specific injury or disease which requires additional investigation to determine causal links.

35. Claims under the *Veterans' Entitlements Act 1986* and the *Military Rehabilitation and Compensation Act 2004* are assessed using the Statements of Principles (SoPs) regime. The RMA determines SoPs using sound medical-scientific evidence of a causal link between a factor (e.g. an exposure or consumption) and the particular injury or disease. At present, and based on the determinations of the RMA, there is sound medical-scientific evidence linking mefloquine and other anti-malarials by name, or via a more generally worded factor, as a potential causal factor in SoPs for 12 conditions:

- suicide and attempted suicide
- sensorineural hearing loss;
- tinnitus;
- epileptic seizure;
- peripheral neuropathy;
- bipolar disorder;
- psoriasis;
- heart block;
- myasthenia gravis;
- methaemoglobinaema;
- trigeminal neuropathy; and
- depressive disorder.

36. The RMA is currently conducting reviews of a number of SoPs with regard to mefloquine use, including panic disorder and anxiety disorder. These reviews will be completed in 2016.

37. In its Inquiry report, the IGADF recommended that Joint Health Command consider a mechanism to ascertain whether any participants in the 2000-2002 AMI trials who took mefloquine may have had any history of a health condition that would have been a contraindication to mefloquine use. This aims to ensure that any previous health condition inconsistent with the prescription of mefloquine is identified and, where necessary, allow possible treatment to be provided through DVA or Defence.

38. This recommendation has been met by Defence with the establishment of a dedicated email address that allows any current or former serving members with concerns to contact Joint Health Command directly and request a review of their case. Defence has, and will continue to, build awareness of this mechanism in its public statements and respond to requests for review.

39. The IGADF also recommended that for future medical trials involving Defence personnel, trial investigators be given access to the Defence eHealth System to enable any relevant medical history of contraindicators to be identified at the time of obtaining a Defence member's consent to participate in the trial. Defence has accepted this recommendation as the Defence eHealth System now allows all Defence health practitioners to access records wherever they are in Australia.

Support available for current and former members of the ADF

Department of Defence

40. An open and transparent approach to information sharing is a key component of Defence's response to this issue, which has resulted in the development of a dedicated online resource and a single point of contact for public enquiries (adf.malaria@defence.gov.au).

41. Launched in February 2016, the 'Malaria, mefloquine and the ADF' online resource (http://www.defence.gov.au/Health/HealthPortal/Malaria/) is designed to assist current and ex-serving members and their families who want to learn more about the use of anti-malarial medications in the ADF.

42. It contains comprehensive information on the range of medications used to prevent and treat malaria in ADF members, including specific details such as prescription numbers, possible side effects, clinical guidelines, and the support available to those with concerns.

43. Other important features include information on research conducted by Defence; links to national health bodies and guidelines; media statements, responses and presentations; numerous publications, including the outcomes of an independent IGADF inquiry into the conduct of past anti-malarial trials; and historical information about the impact of malaria and why it is considered one of the most critical public health issues worldwide.

44. In recent months, the 'Malaria, mefloquine and the ADF' online resource has been reviewed and updated regularly, with the latest additional content added on 4 October 2016.

45. Current serving Defence members who are concerned about the use of mefloquine are provided support as part of Defence's comprehensive health system.

GP Health Assessment

46. If any ADF member, past or present, is concerned that they might be suffering side effects from the use of mefloquine, they should present to their usual medical practitioner for assessment and treatment as appropriate.

47. From 1 July 2014, all former members of the permanent and reserve forces have been able to access a physical and mental health assessment from their General Practitioner (GP), whether or not they are DVA clients. This comprehensive assessment can be performed at any point after a member has discharged from the ADF, however, it is only available once in their lifetime.

48. A key objective of the assessment is to help GPs identify and diagnose the early onset of physical and/or mental health problems. A Medicare rebate is available for this assessment under health assessment items 701, 703, 705 and 707 on the Medicare Benefit Schedule. These item numbers include health assessments for a range of different groups.

Veterans and Veterans Families Counselling Service

49. Former members who are concerned about their mental health are encouraged to contact the Veterans and Veterans Families Counselling Service (VVCS). VVCS provides free and confidential, nation-wide counselling and support for eligible current and former serving members of the ADF and families. A family inclusive organisation, support is also available for relationship and family matters that can arise due to the unique nature of military service.

Department of Veterans' Affairs

50. DVA has established a dedicated mefloquine support team to assist current and former serving members of the ADF with mefloquine related claims. Any current or former members who feel that their health problems may be related to any aspect of their military service are encouraged to submit a claim to DVA. A number of ex-service organisations provide advocate services to assist members with the submission of claims for liability to DVA.

51. On 30 September 2016, DVA's Principal Medical Adviser wrote to all GPs in Australia to bring their attention to information that may assist in managing patients who took mefloquine. This included a link to Defence Joint Health Command's Clinical Guidelines for providing appropriate care to ADF members concerned about having been prescribed mefloquine and also explained the support available through DVA.

52. Under non-liability health care arrangements, DVA can provide access to treatment for the following mental health conditions:

- PTSD;
- depressive disorder;
- anxiety disorder;
- alcohol use disorder; and
- substance use disorder.

53. There is no need to establish that these conditions were caused by service. All current and former members with continuous full-time service are eligible for treatment under these arrangements.

Election Commitments

54. To address concerns relating to the use of mefloquine in the ADF, the Government committed to four actions as part of its 2016 election policy.

Establish a formal community consultation mechanism to provide an open dialogue on issues concerning mefloquine between the Defence Links Steering Committee and the serving and ex-serving Australian Defence Force (ADF) community

55. This action is considered at paragraph 71 below.

Develop a more comprehensive online resource that will provide information on anti-malarial medications

56. This action has been completed. As noted at paragraph 41, Defence has established a comprehensive online resource in the form of 'Malaria, mefloquine and the ADF'.

Establish a dedicated Department of Veterans' Affairs (DVA) mefloquine support team to assist our serving and ex-serving ADF community with mefloquine-related claims, which will provide a specialised point of contact with DVA

57. This action has been completed. As noted at paragraph 50, DVA has established a dedicated team to process claims in which mefloquine use is mentioned.

Direct the inter-departmental DVA-Defence Links Steering Committee to examine the issues raised, consider existing relevant medical evidence and provide advice to the Government by November 2016

58. This paper has been developed to assist the DVA-Defence Links Steering Committee fulfil this action. Recommendations are provided below for consideration by the Committee. The Committee may wish to consider using this paper and the recommendations as the basis for its advice to Government.

Recommendations

Outreach Centre

59. It has been suggested by those lobbying the Government to take action in relation to mefloquine that DVA or Defence should contact each individual who was administered mefloquine while in the ADF.

60. Outreach can take many forms. While Defence has a record of those who were prescribed mefloquine or tafenoquine, the vast majority are no longer serving and are unlikely to have any adverse health effects from its use. Defence and DVA may not have current contact details for these former members, and unsolicited offers of assistance or advice may cause distress and unnecessary anxiety in people who are well.

61. To provide easy access to information and assistance for former serving members of the ADF who have been administered mefloquine, it is recommended that a temporary outreach centre be opened in Townsville for up to one week.

62. It is proposed the outreach centre be held during the second week in December. The DVA-Defence Links Steering Committee understands that there may be an imminent announcement regarding a working group meeting on 7 December 2016 in relation to the suicide prevention trial site in Townsville. While the suicide prevention trial site is entirely separate to the proposed outreach centre, it would be preferable for the outreach centre to follow this possible working group meeting in Townsville and for the two activities not to be confused in the minds of stakeholders. The suicide trial site working group meeting is being arranged and coordinated by the Department of Health under the auspices of the Minister for Health and Ageing.

63. The temporary outreach centre could function as a trial centre and be evaluated afterwards to determine its effectiveness. Following the evaluation, consideration would be given to whether further outreach is required and the manner in which it should be delivered.

64. Townsville is suggested as the location for the outreach centre because this is where a large number of former ADF members who were administered mefloquine are now based. The deployments to Timor-Leste occurred from Townsville.

65. The proposed outreach program could provide targeted information sessions to current and former members of the ADF, advocates and pension officers, and GPs. It is envisaged that the outreach centre will have information sessions on the following:

- DVA to provide information on the claims process including how to lodge a claim and the information/evidence required, non-liability healthcare, the GP health assessment, and resources available through At Ease.
- VVCS to provide information about the services and support available through VVCS, where and how to get help, and what to expect in counselling.
- RMA to provide information on the role of the RMA, SoPs and current reviews concerning the use of mefloquine, and the process to request the RMA investigate a specific injury or disease.

66. Current and former members of the ADF who have been administered mefloquine will be able to visit the outreach centre for information and assistance. While current serving members will be able to access claims assistance through the outreach centre, their health care will continue to be provided by Defence and they will be referred back to their ADF heath centre.

67. To give individuals visiting the outreach centre flexibility and choice when attending sessions, sessions could be run every day, at different times throughout the week. Sessions will be accompanied by a handout that people can take with them.

68. Commander Joint Health and DVA's Principal Medical Adviser will brief GPs ahead of the outreach centre being run, so that they are able to better assist individuals presenting with symptoms or conditions attributed to taking mefloquine in the ADF. The briefing will cover mefloquine use in the ADF, long terms effects and the support available from DVA and Defence, including DVA's treatment card arrangements. GPs will be asked for permission to make their details available to those individuals attending the outreach centre.

69. DVA's Principal Medical Adviser could write to the Australian Medical Association, Royal Australian College of General Practitioners, Australian College of Rural and Remote Medicine and North Queensland Primary Health Network inviting GPs to attend the briefings.

70. The outreach centre proposal is currently being developed by DVA. A meeting was held on 27 October 2016 with stakeholders from DVA, Defence and the RMA to discuss and refine the proposal.

Community Consultation

71. A report on the outcomes and issues raised at the outreach centre will be tabled at a future DVA-Defence Links Steering Committee meeting. This will be in line with the Government's commitment to establish a formal community consultation mechanism to provide an open dialogue on issues concerning mefloquine between the Defence Links Steering Committee and the serving and ex-serving ADF community.