Australian Defence Human Research Ethics Committee (EC00101)
Adverse Event and Serious Adverse Event Report

It is a condition of ethical approval that Adverse Events (AEs) and Serious Adverse Events (SAEs) are reported to the Australian Defence Human Research Ethics Committee (ADHREC).

This report must be used to notify the ADHREC of AEs or SAEs that occur during a research project. For SAEs, the Chief Investigator (CI) must submit this report to ADHREC **within 72 hours.** For AEs, the CI must submit this report within 30 days.

Researchers will also need to include details on AEs and SAEs in their progress and final report.

Completed reports are to be emailed to human.research@defence.gov.au.

Notes: To check a box electronically, right click on the box, and select "Properties" then mark the "Default value" as "**Checked**".

If changes are recommended to the protocol or the Participant Information and Consent Forms the Chief Investigator will need to submit a request for modification and the revised forms (where appropriate).

PROJECT DETAILS	
ADHREC Protocol Number:	760-14
Project Title:	The role of the family in Australian Defence Force member's rehabilitation.
Name of CI:	S47F (Sponsor completed the form – JHC DG MHPR David Morton)
CI contact details:	S47F
Name of Supervisor/s (for student research):	N/A
Supervisor contact details:	N/A

EVENT DETAILS	
Date:	
Description of event (including location and number of participants affected):	JHC Research officer sent letters to sample of ADF members selected from the ADFRP database to participant in the study 'The role of the family in Australian Defence Force member's rehabilitation.' This sample contained six people who were deceased and letters were sent to five of these people accidently. One person was removed from the mail out as it had been notated that the person was deceased.
Has the CI reported the event to the sponsor?	☐ Yes ☐ No ☒ N/A If no or n/a applicable selected, please indicate why the sponsor was not notified of the event. CI had no involvement in the incident.
Relationship:	☒ Suspected related ☐ Probably related ☐ Unlikely related ☐ Not related
Immediate action taken:	Notification of incident through chain of command. Apology phone calls made to the next of kin, followed by letters

Subsequent action taken and/or required:	Dataset is checked again before sent to CI for any further deceased personnel. Sponsor is linked into the suicide database for duration of the study for notification if any further participants die by suicide during the course of the study. This information can then be passed on to the CI.
Outcome:	Improved screening for deceased personnel before and during research projects.

IMPLICATIONS

Does this event raise any additional safety concerns for participants? ☐ **Yes** ☒ **No**
If yes, please provide details. If no, please explain why.
Participants have not been directly affected by this incident.

Will there be changes to the research protocol as a result of this event? ☐ **Yes** ☒ **No**
If yes, please provide details.

Will there be changes to the Participant Information Sheet or Consent Form as a result of this event? ☐ **Yes** ☒ **No**
If yes, please provide details. If no, please explain why.
Participants have not been directly affected by this incident.

Are there any other issues raised by this adverse event that may have wider implications?
☒ **Yes** ☐ **No**
If yes, please provide details and explain how you will address them.
Wider implications for research in Defence to implement processes to ensure all participant samples only include living members.

Declaration made by Chief Investigator *(please circle)*:
I advise the following:

Change to the Protocol* (*please advise*)	Yes / No
Change to the PICF*	Yes / No
Previously enrolled participants to be notified	Yes / No
The Study to be stopped	Yes / No
Action required (*if yes then specify*)	Yes / No

Name: Jess Murray Signatur s22 [redacted]
Date: 4/11/14

+Sponsor & PI have been notified.

HREC Acknowledgement (Office Use Only)
Name: _____ Position: _____
Signature: _____ Date: ___/___/___

Comment:

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Researchers will also need to include details on AEs and SAEs in their progress and final report.

Completed reports are to be emailed to ADHREC@defence.gov.au.

Notes: To check a box electronically, right click on the box, and select "Properties" then mark the "Default value" as "**Checked**".

If changes are recommended to the protocol or the Participant Information and Consent Forms the Chief Investigator will need to submit a request for modification and the revised forms (where appropriate).

PROJECT DETAILS	
ADHREC Protocol Number:	767-14
Project Title:	The effect of moderate and high intensity exercise on cardiovascular health and cardiac remodelling.
Name of CI:	S47F [redacted]
CI contact details:	
Name of Supervisor/s (for student research):	
Supervisor contact details:	

EVENT DETAILS	
Date:	5th of March 2015
Description of event (including location and number of participants affected):	A study participant was found to have a bicuspid aortic valve and a mildly dilated aorta during the conduct of the research echocardiogram.
Has the CI reported the event to the sponsor?	☒ No If no or n/a applicable selected, please indicate why the sponsor was not notified of the event. I have reported the event to the Senior Medical Officer at Kapooka Health Centre and I have referred the member to see a Defence Doctor for referral to a Cardiologist. Depending on the outcome this will be referred through the Chain of Command and the event sponsor. The member is continuing training until review.
Relationship:	☒ Not related
Immediate action taken:	Notified the Senior Medical Officer and the member.
Subsequent action taken and/or required:	Referral letter sent to a Defence Medical Officer at the Recruit Clinic for referral to independent Cardiologist.
Outcome:	Awaiting review by an independent Cardiologist.

IMPLICATIONS

Does this event raise any additional safety concerns for participants? ☒ No
If yes, please provide details. If no, please explain why.

The finding of a congenital bicuspid valve and a mildly dilated aorta does not raise any safety concerns related to the study per se. This finding does however have potential implications in terms of medical fitness for service. This is a congenital condition and it is important for the member and his family to be aware of the condition from a medical point of view. The specific issue of bicuspid aortic valve was addressed in the ethics submission. The patient information sheet and consent form states there is a risk of unexpected results of less than 1% if the member has progressed through the Army's routine medical screening. The patient information sheet does raise the issue that if an unexpected result is found they may need referral to a specialist.

Will there be changes to the research protocol as a result of this event? ☒ No
If yes, please provide details.

Will there be changes to the Participant Information Sheet or Consent Form as a result of this event? ☒ No
If yes, please provide details. If no, please explain why.

Are there any other issues raised by this adverse event that may have wider implications?
☒ No
If yes, please provide details and explain how you will address them.

No new issues that were not already addressed in the ethics submission.

Declaration made by Chief Investigator *(please circle)*:
I advise the following:

Change to the Protocol* (*please advise*)	Yes / (No)
Change to the PICF*	Yes / (No)
Previously enrolled participants to be notified	Yes / (No)
The Study to be stopped	Yes / (No)
Action required (*if yes then specify*)	(Yes) / No

- review by independent Cardiologist

Name: s47F _____ Signature s47F _____

Date: 30/3/2015

HREC Acknowledgement (Office Use Only)
Name: _____ Position: _____
Signature: _____ Date: ___/___/___

Comment:

JOINT HEALTH COMMAND

Army Malaria Institute

MINUTE

AMI/OUT/2014/O7861024

ADHREC

PROGRESS REPORT: ADHREC PROTOCOL 649-11

References:

A. ADHREC/OUT/2012/R10959318 dated 6 March 2012
B. AMI/OUT/2013/O6672818 dated 18 October 2013

1. The objective of the study entitled, "Pharmacokinetics and ex vivo antimalarial activity of methylene blue combined with artesunate and amodiaquine in healthy Vietnamese volunteers" is to determine whether methylene blue (MB) can enhance the blood stage activity of artesunate-amodiaquine (ASAQ) (Reference A). If so, the triple drug combination may be a potential option to treat artemisinin resistance malaria infections, which is currently present in several Southeast Asian countries (e.g. Cambodia, Myanmar and Vietnam). ASAQ is the second most widely used artemisinin combination therapy for the treatment of uncomplicated *P. falciparum* malaria and the addition of MB could extend its useful life.

2. Previously, for Cohort 1 of the randomized cross-over study design no adverse events were reported in eight subjects administered ASAQ alone (Reference B). However, of the eight subjects administered ASAQ+MB, six had gastrointestinal disturbances such as nausea and abdominal pain and one subject experienced hypotension and sweating. One subject also vomited ASAQ+MB and was withdrawn from the study. The clinicians evaluated the intensities of the nausea, abdominal pain, diarrhoea and sweating as mild and self-limiting. For Cohort 2, where the alternative medication was given, none of the 15 subjects reported adverse events. We have no explaination for the difference in adverse events reported between the two Cohorts. As expected all volunteers given ASAQ+MB had bluey-green stools and urine, which disappeared 24 and 72 hours, respectively, after dosing. There were no complaints received from the volunteers.

3. The collection of plasma samples for the study was completed in October 2013. Serial plasma concentrations of artesunate and amodiaquine and their active metabolites have been measured in 15 healthy volunteers who participated in Cohort 1 (samples collected June-July 2013) of the study. A LC/MS method for the measurement of methylene blue is currently under development. Analysis of these analytes in plasma samples collected from the same 15 healthy volunteers (Cohort 2; September-October 2013) will be done over the next several months. We plan to complete the measurement of the antimalarial drugs and ex vivo antimalarial activity assessment of the plasma samples by the end of 2014.

4. Documentation for the study (i.e. consent forms, case report forms, tolerability data, blood chemistry results and blood collection times) are secured at Central Military Hospital 108 in Hanoi and raw data has been entered into an Access database.

5. Please feel welcome to contact the undersigned for any further information or clarification.

s22 [redacted]

M.D. EDSTEIN (MSc, PhD)
Head, Department of Drug Evaluation

AMI
Bld K10, Gallipoli Bks
ENOGGERA QLD 4051
Tel: (07) 3332 4930

24 June 2014