DEPARTMENT OF CLINICAL MEDICNE
Faculty of Medicine and Health Sciences

MACQUARIE University
SYDNEY·AUSTRALIA

2nd July 2020

Loes Slattery
Senior Research Officer

PFAS Sub-committee
Joint Committee on Foreign Affairs, Defence and Trade
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Dear Ms. Slattery,

Thank you for your invitation to provide a submission to the PFAS Sub-committee of the Joint Standing Committee on Foreign Affairs, Defence and Trade (JSCFADT) regarding an update on work being done under the MFB and Macquarie University's PFAS Blood Trial, **"A randomised controlled trial examining the effect of blood and plasma donation on serum per- and poly-fluoroalkyl substances (PFAS) levels in Metropolitan Fire Brigade staff."**

Trial summary:

Whilst PFAS levels do appear to slowly drop over time once the source of exposure has been eliminated, their potential adverse health effects indicate the importance of developing an intervention to bring down elevated levels at a faster rate.

This is a randomised, controlled trial of current and former Australian Firefighters in the Metropolitan Fire Brigade (MFB) and contractors, with previous occupational exposure to PFAS and elevated PFOS levels. The study investigates whether a simple intervention over 12 months (whole blood donation every 12 weeks or plasma donation every 6 weeks) might alter levels of PFAS in MFB staff's blood. The trial also includes an observation group.

Participants have PFAS blood tests scheduled at Screening, Baseline, Week 52, and Week 64. The Baseline and Week 52 PFAS level differences shall inform our Endpoints, while the final PFAS blood test at Week 64 shall be compared to Week 52 PFAS blood test. This information shall allow examination of whether PFAS levels, after cessation of intervention at Week 48, either increase or continue to fall as per natural clearance levels established in the study's first two PFAS tests and in the observation group.

The trial also includes biochemistry analysis. Biochemistry samples shall be taken at Screening and Week 52 and shall assess the following biomarkers: urea and electrolytes, liver function, lipid levels, full blood exam and thyroid test.

If whole blood or plasma donation significantly reduces serum PFAS levels, this may inform strategies to reduce the potential health risks associated with occupational PFAS exposure.

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Approvals and registration:

The trial is registered with the Australian New Zealand Clinical Trials Registry (ANZCTR). Reference: ACTRN12619000204145.
http://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12619000204145

The trial has been approved by Macquarie University Human Research Ethics Committee (Medical Sciences), 17 Wally's Walk, Macquarie University, NSW 2109. Approval date: 17/12/2018. Ethics approval number: 3855

Funding:

The study was funded by the Metropolitan Fire Brigade.

Co-Primary Endpoints:

To identify whether there is a significant change in serum PFOS and/or PFHxS levels after 12 months of whole blood or plasma donation.

Secondary Endpoints:

1. To identify whether there is a significant change in serum levels of other PFAS chemicals (PFOA, PFBS, PFPeS, PFHpS, PFDS, PFBA, PFPeA, PFHxA, PFHpA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeDA, 4:2 FTS, 6:2 FTS, 8:2 FTS, 10:2 FTS, FOSA 10, MeFOSA, EtFOSA, MeFOSE, EtFOSE, MeFOSAA, EtFOSAA) after 12 months of whole blood or plasma donation.

2. Difference in serum PFAS (PFOS, PFOA or PFHxS) levels between whole blood and plasma donation.

3. Changes in serum PFAS (PFOS or PFHxS) levels in each group from post-test to 3-month follow-up.

4. Changes in serum levels of other PFAS chemicals (PFOA, PFBS, PFPeS, PFHpS, PFDS, PFBA, PFPeA, PFHxA, PFHpA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeDA, 4:2 FTS, 6:2 FTS, 8:2 FTS, 10:2 FTS, FOSA 10, MeFOSA, EtFOSA, MeFOSE, EtFOSE, MeFOSAA, EtFOSAA) in each group from post-test to 3 month follow-up

5. Significant differences in lipid profile (total cholesterol, LDL, HDL and triglycerides) between groups.

6. Significant differences in thyroid function tests (TSH, T4, T3) between groups.

7. Significant differences in liver function tests (bilirubin, ALT, AST, GGT and albumin) between groups.

8. Significant differences in renal function tests (Electrolytes, urea, creatine) between groups.

Eligibility criteria:

Inclusion Criteria	**Exclusion criteria**
Current or former MFB staff or contractors, with 10 or more years of previous occupational exposure to PFAS or with known elevated PFAS levels (PFOS ≥ 5ng/mL).	Medical contraindication to blood donation.
PFOS levels ≥ 5ng/mL	Other severe acute or chronic medical or psychiatric condition, or laboratory abnormality that may increase the risk associated with study participation or may interfere with the interpretation of study results, and in the judgment of the investigator would make the participant inappropriate for entry into this study.
Eligible to donate blood.	Planned travel or extended leave (e.g. >6 weeks) that would prevent access to blood donation facilities.
Not donated blood in the past 3 months prior to randomization.	
Signed and dated informed consent document indicating that the participant has been informed of all pertinent aspects of the study prior to enrolment.	
Willingness and ability to comply with scheduled visits, laboratory tests and other study procedures.	

Statistics:

We would consider a 25% reduction in serum PFAS levels to be significant after 12 months of plasma or whole blood donation. Based on the serum levels of PFHxS, PFOS, and PFOA found in 149 Australian firefighters in Rotander et al. (2015), and a correlation between the assessments at baseline and 12 months (post-test) of r = .6, this corresponds to a standardised effect size of mean difference dz > .31. We would require each group to have 94 participants to have 90% power to detect a 25% reduction in PFAS levels.

In order to test whether plasma donation reduces serum PFAS levels at a faster rate than whole blood donation, we would require each group to have 105 participants at pre-test for 90% power to detect a conventional small effect size (partial eta-squared of .01) difference between the groups from pre-test to post-test.

To further compare the efficacy of plasma donation and whole blood donation to the observation only group (control), a sample of 105 participants per group would provide 80% power to detect the same small effect size (and 90% power to detect partial n squared = .013) after correction for multiple testing.

We have planned our analyses based on intention-to-treat and will use multiple imputation to handle missing data. Our power analyses are conservative to account for the possibility of inflated Type II error and indicate a required total sample size of 315 participants (105 per group).

Status:

The trial is currently underway. The 3-month recruitment period has been completed and 333 participants were screened. After all eligibility requirements were assessed, 285 participants were randomized. This resulted in 95 participants in each arm-blood donation, plasma donation, and observation. Follow-up continues, with the final data collection expected to be completed by 1st March 2021. Results shall be published as soon as possible thereafter.

Principal Investigator and Trial Contact:

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Reference:

1. Rotander, A., Toms, L-M.L., Aylward, L., Kay, M., Mueller, J.F. (2015). Elevated levels of PFOS and PFHxS in MFB staffs exposed to aqueous film forming foam (AFFF). Environment International, 82, 28-34.

Yours sincerely,

[redacted]

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