**Title:** Ethical approval for research on Operation TRENTON and beyond - a rapid, unified approach

**Word Count:** 980

As demonstrated by the collection of scientific papers published in *BMJ Military Health*1-5 and elsewhere6 regarding Operation TRENTON and preceding operations, the Defence Medical Services are established world leaders in the field of military medical research7. Many aspiring researchers have been guided on their journey by articles in this journal, covering aspects ranging from Higher Degrees in the firm base8 through to cutting-edge deployed research9.

Hand in hand with the clinical and technical aspects of research is a solid framework in which military projects designated as research (as opposed to service evaluation or audit) require ethical scrutiny and approval by the Ministry of Defence Research Ethics Committee (MODREC). This committee is the successor to previous military ethical approval systems which emerged as a result of a crisis of ethics in the mid-20th Century10 11. This process is formalised in a directive designed to be clear about the stages of obtaining ethical approval for research conducted on military personnel, or which utilises other military assets12, with the procedure clearly laid out and regularly updated by MODREC13. Although acknowledged as an essential part of modern research, the time required to obtain ethical approval is frequently underestimated14 and the process has often been perceived by military researchers as ‘an additional hoop’ to jump through15. It has previously been considered inflexible and frustrating16, particularly when operational opportunities and constraints have demanded rapid responses. One paper17 suggested that applications can take up to 6-12 months to be processed and another stated that ethical approval was not received in time for the deployed researcher to begin the project before returning from theatre18. Such timelines, which have not been unique to the military ethical approval system, may discourage research in either the civilian or military sphere.

These delays in gaining ethical approval have decreased over the last decade following the introduction of a coordinated national response to research and ethics committee (REC) applications in the UK19. This system enabled the sharing of requests and information between different geographical RECs, to reduce the backlog of requests and the time taken to process them. Recent operational needs and a rejuvenation of MODREC have demonstrated that the system can respond when speed and flexibility are required for military project approval. Such operations have included Operation GRITROCK, where the speed of research required to counter a threatening global pandemic needed support from the military research ethics community, with difficult ethical decisions required about the research and implementation of unlicensed and untested therapies20.

Similar speed and flexibility were available to our group for deployed research on Operation TRENTON. Because of the relatively short warning off period for the deployed physicians, the conception of research projects did not begin until the initial training period shortly before deployment. Review of the first serosurveillance project was completed in 64 days from receipt of application, via dstl Scientific Advisory Committee (SAC) approval, MODREC review and approval of subsequent protocol amendments. This required considerable reciprocal inputs from the research team and the ethics committee; the end product was a robust protocol which benefited from the abundance of experience on the MODREC panel and willingness to engage from all sides. This rapid approval was essential as blood samples were required from volunteers already on standby for deployment; without the approval in place this time-critical step could not have occurred, and the entire project prevented from proceeding.

A second project6 was conceived while waiting for deployment and was prioritised by MODREC to ensure approval before departure. This project required confirmation that ethical approval was required (6 days), SAC approval (fast tracked by the dstl SAC chair, 5 days) and MODREC examination, amendment and approval (25 days). Once the project was commenced, it was established that significant improvements to the quality of data could be made by utilising samples already in theatre. Amendments to this protocol (focussing particularly on informed consent of research on samples taken for clinical reasons) were made whilst in theatre, prioritised by a sub-committee, and reviewed, re-amended and approved within 3-5 days. MODREC suggestions regarding storage of samples and the ethical requirements for consent for this were incorporated, so that samples were recovered to the UK and will be used for further research on military diarrhoea - a critical output for the DMS research effort.

In an unhappy coincidence, the earlier statement regarding untested therapy in a global pandemic on Operation GRITROCK rings as true now as it did then, with the same challenges to both researchers and ethics committees, civilian or military. The COVID-19 crisis has required new ways of working across all aspects of operations and research21, which have benefitted from accelerated but robust ethical review processes22. In the military system the flexibility and speed of the system required and demonstrated by our projects on TRENTON continues today, as exemplified by the following projects.

During the current pandemic a randomised controlled trial of the influence of vitamin D on seroconversion to SARS CoV-2 was conceived, the "RAID-CoV-2 study" ("REducing Asymptomatic SARS-CoV-2 Seroconversion with Vitamin D (COVID-19)). Following a full review cycle, written approval was received in mid-August 2020, 38 days after first submission to MODREC and via the Army SAC. Sadly this study was not funded. However, two months later MODREC provided written approval within 7 days of submission and a full remote “out of committee” review of a major amendment to an existing study, to allow assessment of the influence of vitamin D status on seroconversion to SARS-CoV-2 (the "IMPACT-COVID-19" study). As this study involves an assessment of Force Health Protection measures in reducing transmission seroconversion to COVID-19, it did have support at 1\* level as an "urgent operational requirement".

The increased efficiency and timeliness of SAC and MODREC processes are very welcome. However, the timelines illustrated are only achievable if researchers remain agile and responsive to committee requests for further information or amendment. Quality research continues to be undertaken at pace, and military researchers and ethical scrutiny committees, working in partnership, continue to be at the forefront of this.

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peer review, and the Version of Record can be accessed online at <http://dx.doi.org/10.1136/bmjmilitary-2021-001814>

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