Health Research Council of New Zealand
Te Kaunihera Rangahau Hauora o Aotearoa

4 November 2021

Maxwell
Email: fyi-request-17126-8e7b8fd9@requests.fyi.org.nz

Tēnā koe Maxwell

Official Information Act request

The Health Research Council of New Zealand (HRC) received your email request for official information on 11 October 2021. You requested the following information under the Official Information Act 1982 (OIA):

> *In your "Update on COVID-19 clinical trials" dated 17 February 2021 you state:*
>
> *"...all three clinical trials planned to include hydroxychloroquine in their evaluation of potential treatments for COVID-19, however given the rapidly emerging evidence on potential COVID-19 treatments from other international trials, all three trials have adapted significantly and have removed hydroxychloroquine as a candidate for treatment or prevention."*
>
> *Source:*
> *https://apc01.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.hrc.govt.nz%2Fnews-events%2Fupdate-new-zealands-rapid-response-covid-19-clinical-trials&data=04%7C01%7Cllon%40hrc.govt.nz%7Cf42979e3b5d142d9a09c08d98c4ebd2d%7Cd8599fa25a0d4d6b8698ccfae7f9b041%7C0%7C0%7C637695092074450518%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C1000&sdata=lrVp8SQ3WkKkRuPDjJzfRtx8KOgxt70lpNKf%2BcHx2nU%3D&reserved=0*
>
> *Can you please provide all the evidence from international trials and related documentation held or received by HRCNZ and/or related agencies that went into this hydroxychloroquine removal decision?*

The HRC funded the three clinical trials (as indicated in your request) that initially included hydroxychloroquine as a potential COVID-19 treatment in their proposals. However, based on the evidence indicated below, all three trials removed hydroxychloroquine as a potential COVID-19 treatment from their proposals.

The reasons provided to the HRC for making the decision to remove hydroxychloroquine as a potential COVID-19 treatment from their proposals are:

- **Clinical trial of COVID-19 treatments for the critically ill (REMAP-CAP COVID)**

  Principal Investigator Dr Colin McArthur
  Contact email: colinx@xxxx.xxvt.nz

  https://www.hrc.govt.nz/resources/research-repository/clinical-trial-covid-19-treatments-critically-ill

  Recruitment for the hydroxychloroquine-containing arms of the antiviral domain of REMAP-CAP COVID was paused in New Zealand pending publication of hydroxychloroquine data from the RECOVERY trial (refer https://www.recoverytrial.net/). Enrolment into the hydroxychloroquine and combination therapy arms was subsequently halted internationally based on external data from other clinical trials (for example, refer RECOVERY trial https://www.recoverytrial.net/).

  Please note the following:
  - Although it did not form part of the decision to stop randomisation to hydroxychloroquine at the time, when the futility trigger was met for the remaining intervention (lopinavir/ritonavir) in the antiviral domain, the results for the full domain were analysed and published, which demonstrated harm for the use of hydroxychloroquine in the trial's critically ill population. This is strong evidence that the decision to stop was correct. Refer https://link.springer.com/article/10.1007%2Fs00134-021-06448-5

- **Australasian COVID-19 Trial (ASCOT)**

  Principal Investigator Dr Susan Morpeth
  Contact email: susan.morpeth@middlemore.co.nz

  https://www.hrc.govt.nz/resources/research-repository/australasian-covid-19-trial-ascot

  The initial ASCOT study protocol was designed as a factorial randomised clinical trial of hydroxychloroquine and lopinavir-ritonavir in the treatment of COVID-19. Both of these agents were withdrawn due to external data from other clinical trials. For example, refer to the SOLIDARITY trial (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments) and the RECOVERY trial (https://www.recoverytrial.net/).

  Please note the following:
  - Equipoise was lost for most clinical trials of hydroxychloroquine once the RECOVERY trial reported no benefit with a trend toward harm. Subsequent publications (and unpublished studies) of hydroxychloroquine / chloroquine as summarised in this meta-analysis (https://www.nature.com/articles/s41467-021-22446-z) confirmed the mortality hazard. RECOVERY and the WHO-led SOLIDARITY trial provided the greatest number of patients leading to this conclusion.

  - ASCOT in New Zealand opened under a revised study protocol to align with its partnering Australian sites. Subsequently, the ASCOT protocol was amended to

transform it into ASCOT ADAPT, a platform trial with antiviral, antibody and anticoagulation domains.

- **Clinical trial of hydroxychloroquine prophylaxis in frontline healthcare workers**

  Principal Investigator Professor Richard Beasley
  Contact email: richard.beasley@mrinz.ac.nz

  https://www.hrc.govt.nz/resources/research-repository/clinical-trial-hydroxychloroquine-prophylaxis-frontline-healthcare

  The clinical trial of the efficacy of a prophylactic weekly hydroxychloroquine regimen for frontline healthcare workers at high risk from SARS-CoV-2 infection was stopped before recruitment began due to the elimination of community transmission in New Zealand (2020), and concerns regarding the lack of efficacy and risks with hydroxychloroquine treatment in COVID-19. For example, refer to the SOLIDARITY trial (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments) and the RECOVERY trial (https://www.recoverytrial.net/).

Please see above the contact details (email addresses) of the principal investigators of these three research studies, who have all agreed to answer any additional queries that you may have in this regard.

If you are not satisfied with our response, you have the right to seek an investigation and review by the Ombudsman of this decision. Information about how to make a complaint is available at www.ombudsman.parliament.nz or freephone 0800 802 602.

Ngā mihi

Signed by: Sunny Collings
Date & Time: 08 Nov, 2021 10:04:31 NZDT

Professor Sunny Collings
Tāhuhu Rangapū | Chief Executive