



WHO GUIDANCE ON THE ETHICAL CONDUCT OF CONTROLLED HUMAN INFECTION STUDIES



**World Health
Organization**

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PREFACE

Alleviating the impact of infectious diseases on human health remains a key global health priority. In controlled human infection studies (CHIS), healthy volunteers are intentionally exposed to pathogens in a controlled environment, in order to promote understanding of the pathogenesis, transmission, prevention and treatment of infectious diseases in humans. Such studies may be conducted to gain insights into how pathogens infect human hosts and cause disease, to better understand immune responses to infection, or to evaluate the efficacy of vaccines and drugs designed to prevent and treat infectious diseases. CHIS have a long history and have made important contributions to the treatment and prevention of many infectious diseases of global health importance.

Although recognition of the potential value of CHIS is leading to such studies increasingly being conducted in a wider range of contexts, they remain a relatively unfamiliar research method. This guidance has been developed in response to requests to the World Health Organization (WHO) for guidance on ethical questions associated with CHIS, especially in the context of growing interest in conducting CHIS in endemic settings.

The concept of conducting research in which healthy volunteers are intentionally exposed to pathogens which can cause infection, and in some cases disease, can appear ethically counter-intuitive – particularly when natural infections with such pathogens can lead to severe adverse outcomes, including death. This was clearly evidenced during 2020, when CHIS received unprecedented public and social media attention following proposals to conduct CHIS to accelerate COVID-19 vaccine development pathways. Recent debates about the ethical acceptability of COVID-19 CHIS illustrate the diversity of stakeholder views: social acceptance of CHIS is influenced by a complex global landscape in which there are different levels of confidence in health-related research. This underlines the importance of carefully considering the consultative and trust-building approaches needed to inform CHIS research proposals. Consultation and engagement activities with the public, regulators and ethics review boards have been recognized as particularly important when CHIS involve factors such as novel models of infection, populations in which such research may be

unfamiliar, higher levels of risk and/or burdens, risks to third parties, and/or outbreaks of novel pathogens, among others. Engagement and associated social science research have played an important role in settings where CHIS are unfamiliar and can play a key role in the development and conduct of research programmes seeking to address local health priorities and incorporating CHIS.

This guidance aims to inform well-considered and contextualized decisions about the ethical acceptability of proposed CHIS, including priorities for engagement and social science research to support deliberation and practice, and requirements for oversight and governance. In addressing ethical issues that should be considered during the planning, design, conduct and governance of CHIS, this guidance takes the position that CHIS are not, in themselves, an exceptional and morally distinct form of research, but instead fall within the continuum of health-related research conducted with human participants. As such, this guidance should be read in conjunction with relevant national and international ethics guidance and regulations for health-related research in humans.

When applying this guidance, stakeholders involved in CHIS are encouraged to develop approaches that take into account their own local social, cultural, and political contexts. WHO is committed to providing countries with regulatory considerations in support of these efforts.

In addition to the guidance itself, included in the annexes are essential information on consent (Annex 1), a checklist for ethics committees (Annex 2) and eight case studies (Annexes 4 to 11), all designed to further assist with the implementation of this guidance.

Furthermore, during the development of this guidance, discussions began around the possibility of conducting CHIS in the context of COVID-19. As such, and building on the expertise and knowledge gained from this work, WHO formed a working group to produce guidance on the key criteria for the ethical acceptability of COVID-19 human challenge studies, which can be found in Annex 3. Lastly, Annexes 12 and 13 contain scoping reviews of engagement studies and social science studies on CHIS.

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Susan Bull (consultant, University of Oxford, United Kingdom of Great Britain and Northern Ireland) was the rapporteur to the project and the lead writer of this document. Euzebiusz Jamrozik (Monash University, Australia) wrote six of the case studies. Dorcas Kamuya, Primus Che Chi, Vicki Marsh and Esther Awuor (Kenyan Medical Research Institute (KEMRI)-Wellcome Trust Research Programme, Kenya) wrote the literature reviews in Annexes 12 and 13.

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Roma Chilengi (Centre for Infectious Disease Research in Zambia, Zambia), Thomas C. Darton (University of Sheffield, United Kingdom), Claudia Emerson (McMasters University, Canada), Euzebiusz (Zeb) Jamrozik (Monash University, Australia), Ibrahim Khalil (Consultant, WHO), Michael Selgelid (Monash University, Australia), Seema K Shah (Lurie Children's Hospital, United States of America).

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Roma Chilengi (Centre for Infectious Disease Research in Zambia, Zambia), Mohamed Ahmed A El Sheikh (University of Khartoum, Sudan), Claudia Emerson (McMasters University, Canada), Euzebiusz (Zeb) Jamrozik (Monash University, Australia), Dorcas Kamuya (KEMRI-Wellcome Trust Research Programme, Kenya), Gagandeep Kang (Christian Medical College, Vellore, India), Ruth Karron (Johns Hopkins University, The United States), Joseph Mfutso-Bengo (University of Malawi, Malawi), Ricardo Palacios Gomez (Instituto Butantan, Brazil), Punnee Pitisuttithum (Mahidol University, Thailand), Annette Rid (National Institutes of Health, The United States), Meta Roestenberg (Leiden University, The Netherlands), Michael Selgelid (Monash University, Australia), Seema K Shah (Lurie Children's Hospital, The United States), Vina Vaswani (Yenepoya Medical College, India).

Observers:

Cecilia Chui (Wellcome Trust, United Kingdom), Devan Duenas (Seattle Children's Research Institute, The United States), Helena Wilcox (Wellcome Trust, United Kingdom).

Members of the COVID-19 Challenge Studies Ethics Working Group:

Susan Bull (University of Oxford, United Kingdom), Claudia Emerson (McMasters University,

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