Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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ascending dose study and a volunteer infection study with M5717.[8] The study design was similar to previous first-in-human volunteer infection studies:[9] in the single ascending dose part of the study, single doses of up to 2100 mg were tested in healthy adult volunteers, and in the volunteer infection study, participants were infected with *Plasmodium falciparum*-infected red blood cells and treated with 150, 400, or 800 mg M5717. A total of 88 volunteers were enrolled: 66 in the single ascending dose study and 22 in the volunteer infection study. M5717 was well tolerated up to 1250 mg; at doses of 1800 and 2100 mg, transient oral hypoesthesia (in three participants) and blurred vision (in four participants) were observed, and further dosing was suspended after dosing of the two sentinel participants in the 2100 mg cohort.

In the volunteer infection study, parasite clearance was biphasic, showing an initial plateau with slow parasite clearance lasting for approximately 35–55 h, followed by a steep decline of blood-stage parasitaemia. Recrudescence occurred in three (50%) of six participants dosed with 150 mg and two (25%) of eight dosed with 400 mg. No recrudescence was observed in participants who received a single dose of 800 mg. Parasites of the five cases of recrudescence were genetically analysed, and mutations were detected in four cases that are associated with resistance to M5717 (in two participants dosed with 150 mg and two dosed with 400 mg).

These results are encouraging for further development of M5717, yet important questions remain. What is the role of a drug for which resistance can be induced after a single dose? Partner drug selection for the development of a combination treatment must carefully assess this risk and evaluate early in the development of the combination whether it will be possible to prevent the emergence of resistance. As the initial parasite clearance of M5717 is slow, the partner drug should also exhibit a rapid elimination to ensure fast symptomatic and parasitological relief and avoid M5717-treated parasites replicating and acquiring mutations that could lead to the emergence of resistance. To ensure that the selection of a suitable partner molecule to M5717 follows a data-driven process, Merck KGaA has joined a platform with other organisations that have antimalarial drug candidates in translational development, which is hosted by MMV. This platform allows sharing of information and data, the conduct of in-vitro and in-vivo combination experiments, and the identification of the most appropriate drug combinations for further investment. The first combinations emerging from this platform are expected to enter clinical studies in 2022.

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An urgent need: vaccines for neglected tropical diseases

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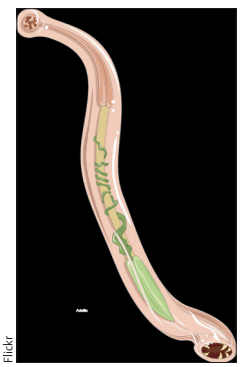
Recent experience with the development of COVID-19 vaccines might, hopefully, herald a new era for the rapid development and approval of vaccines to confront the still high global burden of disease created by other infectious agents, especially in low-income regions. An example has been set for governments, the pharmaceutical industry, and regulators, that things can be done quickly. Why not build on that experience for other vaccine needs, including the introduction of new technologies, such as the use of synthetic mRNA strands, to speed up the development and manufacture of vaccine products?



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The control of neglected tropical diseases (NTDs) without vaccines remains a challenge. These infections affect many millions of people and are endemic in low-resource settings in Africa, Asia, and South America. In 2010, it was estimated that NTDs collectively caused 26 million disability-adjusted life-years lost worldwide, with helminths the greatest contributors to this burden, at roughly 40% of the total.[1] Among the major helminth infections, the soil-transmitted helminths (STHs) *Ancylsotoma duodenale, Necator americanus*, *Ascaris lumbricoides*, and *Trichuris trichuria*, caused 50% of the total disease burden. Today, more than half of the world's population live in places endemic for STH infections,[2] and although global control efforts of mass drug administration and improvements in clean water supply, sanitation, and hygiene have greatly reduced the burden of infection, the new WHO roadmap for 2021–30 for the control of NTDs documents the many challenges in making further progress over the next decade.[3]

The inability of the human host to generate protective immunity to reinfection by helminths means that parasite control can only be achieved by the repeated treatment of individuals. The frequency of administration required varies by helminth infection and depends on parasite life expectancy in the human host and the magnitude of the basic reproductive number, R_0, which measures transmission intensity. For STH infection, biannual or annual treatment is required.[4] Considerable progress has been achieved in regions of endemic infection over the past two decades in lowering the prevalence of infection, and concomitantly reducing morbidity. However, pockets of infection remain because treatment coverage does not approach the high levels required to stop transmission (R<1), and in many populations, persistent non-adherence to drug treatment creates reservoirs of infection that maintain community-wide transmission.[5] If treatment ceases, infection bounces back to pre-mass drug administration levels. As infection levels fall, maintaining interest in STH control is challenging in the face of other health priorities, especially when resources are scarce. Sustaining interest in NTD control applies not just to ministries of health, but also to the major pharmaceutical companies who, after the London Declaration,[6] generously donate drugs for helminth infection control in low-income and middle-income countries. The neverending requirement for mass drug administration in the absence of transmission interruption makes clear the urgent need for other interventions.

Vaccines for helminth infections have been produced in the veterinary field for the lung worm *Dictyocaulus viviparus* in cattle, the nematode *Haemonchus contortus* in sheep, and the tapeworm *Echinococcus granulosus* in sheep.[7] In the case of human helminth infections, encouraging progress has recently been made for schistosome vaccines with a candidate entering early-stage trials.[8]

In *The Lancet Infectious Diseases*, Paul Chapman and colleagues[9] assessed the effects of a live attenuated human hookworm vaccine—an interesting step forward. The study involved a trial (part one to assess dosing and part two a randomised, placebo-controlled challenge study) with volunteers being inoculated with a live ultraviolet C light-attenuated *N americanus* larvae vaccine. Numbers were low in the randomised trial, with five participants in the placebo group and ten in the vaccine group, but no serious adverse events were recorded after vaccination or when the participants were challenged with live hookworm larvae. Clear humoral and cellular immunological markers of exposure to parasite antigens were recorded, but this is also true with people in endemic areas of infection who are repeatedly reinfected. Of greater interest, however, was the observation that larval output in faeces in the vaccinated group was significantly lower than in the placebo group. The vaccine did not fully protect against infection, but it did reduce transmission-stage output. Partially efficacious vaccines that both lower worm burden and reduce transmission would be of great value to augment mass drug administration, provided the duration of the effect is long term (ie, many years).[10]

Larger studies are required, as are plans to assess the duration of the protective effect, to move to phase 3 studies in areas with natural exposure to infection, and to assess the issues surrounding the manufacture of a vaccine that is based on live attenuated nematode larvae. Research in the field of NTD vaccine development is sparse, but perhaps the recent excitement of the rapid development of SARS-CoV-2 vaccines can act as a stimulant to remedy this situation.

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The value of open-source clinical science in pandemic response: lessons from ISARIC

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The International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) is a global federation of clinical research networks that work collaboratively to prevent illness and deaths from infectious disease outbreaks. In 2014, we proposed that effective and timely research during outbreaks of emerging infections would benefit from pre-prepared research tools, global collaboration, and research-ready clinical networks.[1] After applying this research model to several outbreaks, and particularly the COVID-19 pandemic, we can now explore what has been achieved to date.

ISARIC launched the Clinical Characterisation Protocol (CCP), in collaboration with WHO in 2012.[1] A key aim was to avoid delays in initiating research, such as those seen during the 2009–10 influenza A H1N1pdm09 pandemic and other outbreaks.[2] The CCP and associated case report forms (CRFs) were the first steps towards global, harmonised clinical datasets to create frameworks for characterising current and potential future emerging infectious diseases. These adaptable research tools were developed and shared early in the COVID-19 pandemic by ISARIC[3] to prepare the health community for outbreak research.

After receiving approvals from the WHO Ethics Committee in 2013 (RPC571 and RPC572, 25/04/2013), the CCP was implemented in various settings (appendix p 2). This broad uptake of the CCP, and the development of tools to support its implementation for various diseases and contexts, meant that ISARIC partners were primed for a rapid response when COVID-19 emerged and spread in 2020. Working with WHO, ISARIC used early reports from Wuhan, China, to inform the adaptation of the CRF. On Jan 24, 2020, when less than 1000 COVID-19 cases had been reported globally, the ISARIC-WHO COVID-19 CRF was launched and made available globally.[3] ISARIC provided a data management platform, using REDCap, to collect and store data for institutions that lacked available resources or necessary infrastructure. Rapid access to the CRFs enabled collection of critical data for early characterisation of the disease in hospitalised patients, first in Wuhan,[4] and then globally.[5–8] Institutions that chose to use the CRF and database simultaneously, collected data for local analyses and also contributed data for aggregated international analyses. As the COVID-19 pandemic progressed and an increasing number of institutions contributed data, the research benefits of a large, aggregated dataset also increased. To disseminate this knowledge, ISARIC and international collaborators issued the first online report analysing risk factors, symptoms, treatments, and outcomes of patients with COVID-19 in March, 2020.[9]

As of July, 2021, 1651 sites in 57 countries have contributed data from 516 689 individuals with COVID-19 (appendix p 1),[10] including 272 759 individuals

See **Online** for appendix