Lord Dowding Fund for Humane Research – Written evidence (COV0034)

About LDF

1. The Lord Dowding Fund for Humane Research (LDF) supports and funds advanced methods of scientific and medical research and training, which replace the use of animals or lead to the adoption of non-animal research methodologies. LDF present evidence to the Science and Technology Committee to demonstrate why it is vital to prioritise the growth of new approach methodologies (NAMs) in the UK in order to speed up and increase the success rate of vaccine and drug development.

The situation

2. While there has been an unprecedented surge in collaboration and funding of research and testing to find vaccines and treatments for COVID-19, the current requirement of regulatory bodies for data from animal models may be responsible for causing significant delays in responding to the current pandemic. This has been acknowledged by national and international agencies: the World Health Organization-China Joint Mission has advised that the "ideal animal model for studying routes of virus transmission, pathogenesis, antiviral therapy, vaccine and immune responses has yet to be found",[1] and the US National Institute of Allergy and Infectious Diseases report that "replicating human disease, particularly its more severe manifestations, in an animal model may be challenging."[2] In a move to accelerate the process, the International Coalition of Medicines Regulatory Authorities (ICMRA) has advised that the usual animal disease models to test the effectiveness (efficacy) of potential vaccines for the virus are not required before proceeding to human clinical trials.[3] Despite this, such tests are still taking place, and in some cases in parallel with clinical trials.[4]

The problem

3. In the UK animal models are being used for vaccine testing, including in rodents,[5,6] ferrets and primates,[7] and for therapeutic antibody production.[8] Outside of the UK animal models are also being used for drug testing[9] and to study how different species are affected by the disease,[10] how the disease transmits[11] and ventilator testing.[12]

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4. Significant funding and precious time are being spent on animal studies, with known species differences affecting the translation of research data to humans. Mice are one of the most commonly used species in drug and vaccine research.[13] In addition to major differences between human and mouse respiratory systems,[14,15,16] species differences specific to research for SARS-COV-2 include that mice do not naturally have the same receptor gene (ACE2) the virus uses to infect human cells.[17] Researchers are now attempting to use "humanized" mice to ensure they contract the virus.[18] While other species, including non-human primates, do not experience the disease in the same way as humans, some only showing a mild illness.[19,20]

5. Furthermore, vaccine research and development typically takes 15-20 years,[21] with animal research, currently, a major part of the process and more than 90% of drugs which prove promising in animal trials fail in humans, either due to lack of effectiveness or safety concerns.[22] Such fundamental species differences risk impeding the production of vaccines and treatments to help prevent and reduce the symptoms of COVID-19 in humans.

The solution

6. While time, resources and efforts are being put into attempting to find the "ideal"[23] animal model, advanced non-animal scientific methods, which relate directly to the disease in humans, are being progressed. Agencies across the world are beginning to prioritise the growth of new approach methodologies (NAMs) in biomedical research and testing.[24,25,26,27,28,29,30,31] NAMs are defined as

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"new scientific approaches that focus on human biological processes to investigate disease and potential treatments, using human cells, tissues, organs and existing data".[32] NAMs have been identified as disruptive technologies,[33] which have the potential to revolutionise disease research and drug development, bringing safer and more effective treatments to the market at a lower cost, and, as vitally important to speeding up the development of vaccines, more quickly than compared to traditional animal methods.[34,35,36,37]

7. Such advanced research techniques currently being used to investigate vaccines and drugs for COVID-19 include: artificial intelligence models to predict which drugs could be used to prevent or treat COVID-19;[38,39,40] human organ-on-a-chip technology for emulating human lung infection,[41] and in vitro 3D human airway cell models for evaluating drugs.[42] In addition, NAMs are also being deployed to investigate the virus and the disease it causes, including: mathematical modelling to study how the virus transmits and replicates;[43] patient lung fluid cultures to study the virus genome;[44] patient biopsy samples to investigate how

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the virus damages the body;[45] and organoids to investigate how the disease infects human tissue.[46] Such sophisticated research methods have the potential to deliver safer, more effective vaccines and treatments to the market more quickly[47] but require more funding and support to accelerate their progress for research into COVID-19 and future pandemics.

8. Following the report from Innovate UK and others, LDF co-authored a white paper as part of the Alliance for Human Relevant Science, alongside NAM experts and businesses which further outlined actions required by the UK to capitalise on the health and economic benefits of NAMs, including:
   - supportive infrastructure to enable strategic coordination of the development and uptake of NAMs, and to provide access to resources and communication networks
   - strategic funding to incentivise full engagement with NAMs, particularly those with market potential that might attract business investment
   - improved education on the benefits of NAMs, alongside skills training for new and established scientists
   - multidisciplinary collaboration and forging of new partnerships between basic and applied researchers, industry and end-users
   - engagement with regulators to promote the adoption of data generated from NAMs into regulatory guidelines. [48]

9. In this regard, LDF calls on the Science and Technology Committee to prioritise the growth of NAMs in the UK in order to speed up and increase the success rate of vaccine development.

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