Written Evidence Submitted by Safer Medicines Trust

(RFA0066)

Executive summary

- Significant advances in science and technology have provided a variety of new research methods based on the use of human cells and tissues

- Human-relevant new approach methodologies (NAMs) have the potential to transform UK biomedical science and in particular, the current drug discovery and safety testing process, where many diseases remain poorly understood and lack effective treatments

- Funding to make these approaches commercially viable and accepted into regulatory processes is often missing and this gap is currently filled by individual industry groups on an ad hoc basis

- A UK ARPA could fund the delivery of these high return, transformative technologies centrally which will benefit the whole UK science base, help improve public health and wellbeing, and enhance the profitability of industries which make vital contributions to the UK economy

Safer Medicines Trust[1] is a UK patient safety charity whose mission is to make medicines safer by facilitating the transition to *human*-focused drug development and testing. Our scientists have extensive expertise in drug discovery and development. We have hosted international conferences at the Royal Society and the House of Lords to discuss the benefits offered by a focus on *human*, rather than animal biology. We are a founder member of the Alliance for Human Relevant Science.[2] We welcome the opportunity to submit evidence to the Science and Technology Committee on the contribution that scientifically valid, human-relevant methods and technologies can make to the development of safer treatments for major diseases with unmet need.

Many of these new approach methodologies (NAMs) originate in academia and are co-developed with industry to expedite their use commercially. As we know, financial support for advancing technologies in this way typically comes from industry and is not centrally funded or co-ordinated. The development of a UK ARPA funding body could provide the link between validation of these technologies, commercial pull through and ultimately, delivery of high return, transformative technologies which will benefit the UK science base, help improve public health and wellbeing, and enhance the profitability of industries which make vital contributions to the UK economy.

1. What gaps in the current UK research and development system might be addressed by an ARPA style approach?

The UK is a world leader in scientific research. However, there are significant gaps in biomedical research which the current COVID-19 crisis has exposed. Presently, the R&D pipeline for disease treatment is not as efficient or cost effective as it should be, with 85-90% of drugs and vaccines failing to gain market approval and each taking around 10 years to develop, at an estimated cost of $2.6 billion.[3] Although the reasons for the low approval rate are multifactorial, it is accepted that the limitations of preclinical animal models play a major role. The significant advances in science and technology which have provided new research methods based on the use of human tissues and cells are increasingly being used to transform our ability to understand human disease and develop new medicines. However, sanctioning the use of these methods (and similar advanced technologies from other research fields), into both regulated testing and industry decision making processes, requires resources not currently accounted for in many R&D budgets and grants. An ARPA style funding body could address this gap with a mindset to progress transformative technologies such as NAMs, thereby delivering improved pharma (and UK science) productivity as well as improved public health and wellbeing.

Pandemics are considered to be the greatest threat to the UK's security but our current reliance on animal testing leaves us unable to respond sufficiently quickly. Immune activation is a key part of human COVID-19 disease progression but human immune systems cannot be modelled in animals. Furthermore, standard laboratory animals such as mice, are not naturally susceptible to the virus and large scale breeding and supply of genetically modified 'COVID-19' mice is under way.[4] Whether these mice develop human-like COVID-19 disease after infection with SARS-CoV2 remains to be seen, further delaying the discovery of potential treatments.

DARPA has a reputation for embracing new high risk / high return technologies, for example in 2018 it granted a further $32 million to its long term funding of the groundbreaking 'Body on a Chip' project,[5] the aim of which is to more accurately evaluate new drugs and detect possible side effects prior to clinical testing in humans. The initiative (co-funded by DARPA, the US National Institute of Health and the Food and Drug Administration) was set up to establish human-relevant medical countermeasures in response to emergencies.[6] DARPA also emphasises the need for other non-animal technologies such as AI, machine learning and new computer based approaches.

The new UK agency would benefit from a similar focus on cutting edge human-relevant technologies to maximise human health, safety and security and reduce the 'time to market' for new drugs.[7] We need to reduce our current reliance on legacy practices that have repeatedly failed to deliver an adequate return on investment or reduce the burden of disease, and instead embrace human biology-based methods which are already providing novel insights into human biology and disease. The ambition of the Life Sciences Strategy[8] to transform our healthcare system into one that identifies disease earlier, begins with modern, scientifically proven technologies delivering these insights. Examples include 3D organ models to study disease development and drug safety, stem cell models of brain development, *in silico* (computer based) models to predict drug toxicity and the use of genomics for high throughput drug screening[1] and precision medicine approaches, building on the existing UK genomics/Biobank project.[8] As discussed above, UK ARPA could serve as an independent organisation, funding the work to enable ratification of these transformational technologies (as US DARPA currently do), with the mission of bringing about scientific and societal improvements through advancing these human relevant technologies.

2. What are the implications of the new funding agency for existing funding bodies and their approach?

The remit of the ARPA-like funding agency versus other funding bodies (especially UKRI, for example) needs to be absolutely clear and understood upfront. Distinct criteria would be needed to define projects to be funded by the new agency versus those to be funded elsewhere. A pathway to commercialisation, adoption or further funding (possibly by existing bodies) of technologies benefitting from this new funding should be defined upfront and stakeholders (including "the customer" or representatives of the to-be-reformed process) engaged early on in the process of selection of projects.

The new funding agency could drive existing agencies to review and modernise their funding streams with a view to prioritising human-relevant biomedical research and safety testing. This would improve cost efficiency, R&D pipelines and most critically, human health, safety and security.

A spoke and hub model could be envisaged with ARPA-like, blue-skies funded "hub" technologies feeding into "spoke" funding bodies (or organisations/customers e.g. Pharma industry, NHS etc) where needed. UK ARPA would fill a gap (establishment of technology readiness) which is currently typically funded by industry and serves individual needs rather than the science community and / or public healthcare as a whole.

3. What should be the focus of the new research funding agency and how should it be structured?

UK ARPA should focus on high impact, transformative projects which will bring about significant shifts in current processes to address major societal or scientific challenges. These will have a relatively high element of risk associated with them but will deliver the modernisation and innovation needed to address current weaknesses in UK science processes. Pharma R&D, and specifically medicines safety, is crying out for change (as demonstrated recently by the Cumberlege report)[9] and should no longer be tied to processes clearly unfit for purpose.

4. What funding should ARPA receive, and how should it distribute this funding to maximise effectiveness?

UK ARPA should receive significant funding so that UK science can successfully progress enabling and transformative technologies. ARPA itself should identify gaps (such as those described in this submission),

with the help of expert advisers in the field, and have the autonomy to allocate money where it identifies the best people and projects to address these gaps. The Government must also agree to the strategies employed by UK ARPA and provide adequate infrastructure, support and engagement of relevant regulatory and scientific bodies to enable the delivery of projects funded by ARPA.

5. What can be learned from ARPA equivalents in other countries?

The US DARPA fund, in being linked to national security, has been protected from short term changes in government and funding commitments. As a long-term policy, typically outlasting successive governmental terms in the UK election process, UK ARPA should be insulated from short-term party-political changes and protected from significant change in remit, direction or level of funding due to a change in government. Commitment to this initiative should be upheld in all manifestos.

The customer / end policy change or reformation needs have to be defined upfront. DARPA's "customer" is the Department of Defence in the US – who would it be in the UK? We have identified the pharmaceutical industry as a primary sector which would benefit from a change in regulations enabling the use of NAMs in safety testing of medicines. Additionally, societal changes in health, wellbeing and the economy resulting from implementing these technologies in medicines development will be significant and should strongly drive pull-through of these developments.

6. What benefits might be gained from basing UK ARPA outside of the 'Golden Triangle' (London, Oxford and Cambridge)?

UK ARPA should fulfil the role of funding advanced technologies wherever in the UK they are being developed or the skills are based. Equal, or even excess weighting, should be given to institutions or people outside the 'Golden Triangle' to both address the "levelling up" of the country, as encouraged by the current government, and to allow skilled individuals to remain at (or move to) institutions outside of this triangle. UK ARPA does not need to be laboratory based and in fact would service the UK better if it had an administrative role overseeing work in regional hubs or laboratories. For example, there are plenty of regional science parks which are generally located close to academic institutions and attract a large number of technology companies and entrepreneurs to create an environment rich in knowledge-sharing, collaboration, and innovation. Indeed, four of the six locations awarded Life Sciences Opportunity Zone (LSOZ) status are outside of the Golden Triangle.[10]

References

1. https://safermedicines.org/
2. https://www.humanrelevantscience.org/
3. https://www.humanrelevantscience.org/wp-content/uploads/Accelerating-the-Growth-of-Human-Relevant-Sciences-in-the-UK_2020-final.pdf
4. http://www.informatics.jax.org/mgihome/other/coronavirus.shtml
5. https://www.kurzweilai.net/darpa-funded-body-on-a-chip-microfluidic-system-could-revolutionize-drug-evaluation
6. https://www.altex.org/index.php/altex/article/view/440/448
7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7245508/
8.https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/857348/Life_sciences_industrial_strategy_update.pdf
9. https://www.immdsreview.org.uk/Report.html
10.https://www.gov.uk/government/news/10-million-boost-to-improve-patient-care-with-new-technologies

(July 2020)