The future of clinical trials and their regulation in a post-Brexit UK: Maximising the potential of early stage clinical research

Overview

On 30th April 2021, representatives from government, parliament, the scientific community, patient groups and industry met for a roundtable discussion on the future of clinical trials and their regulation in a post-Brexit UK. In particular, they discussed the opportunity to make best use of the UK's capabilities in early-phase clinical research. The event was chaired by Rt Hon Lord Patel KT, and hosted by Silence Therapeutics and the Foundation for Science and Technology (FST). Participants in the discussion included representatives from the Department for Health and Social Care (DHSC), the Office for Life Sciences (OLS), the Medicines and Healthcare Products Regulatory Agency (MHRA), Oxford University, the Faculty of Pharmaceutical Medicine of the Royal College of Physicians and Cancer Research UK.

This roundtable followed a similar meeting held last year which explored how the United Kingdom (UK) can maintain and increase its global influence after departing from the European Union (EU) and the Government taking on new responsibilities for its own independent regulatory system. Since then, the Government has published a Vision, 'Saving and improving lives: the future of UK clinical research delivery', which seeks to embed clinical research in the NHS, deliver patient-centred research, ensure a streamlined, efficient and innovative research environment, capitalise on data and digital tools and promote a sustainable and supported research workforce. These aims are intended to showcase the UK's life sciences capabilities and cement its position as a global leader for the conducting and regulation of clinical trials, which was exemplified by the accelerated development of the COVID-19 vaccine, and can be built upon by leveraging the success of this, particularly by learning the benefits of a risk-based and contextual approach.

The Government and devolved nations have subsequently set out the actions they will take to deliver the Vision and make the UK a world leader in clinical research in its 2021/22 Implementation Plan, which is backed by over £64m in funding. This Plan will be delivered by the Government's Recovery, Resilience and Growth Programme (RRG) with oversight and support from DHSC, OLS, MHRA, the Health Research Authority (HRA), as well as representatives from industry, medical research charities and academia. This write up brings together the key topics of discussion from the roundtable meeting to demonstrate how this Implementation Plan can create a more attractive environment for early phase research in the UK.

The challenges facing early stage research in the UK

The UK continues to be a European leader in early-phase research, but as of 2018 its early clinical research activity remains behind China and the USA. China and the USA started 526 and 234 Phase 1 trials respectively in 2018, in comparison to 95 in the UK.[1] To utilise better the strengths of the UK's life sciences ecosystem and catch up with global competition, the Government should address the following challenges:

- The UK's departure from the EU means that the UK must set itself apart as a competitive and attractive place to conduct early-phase research, but the regulatory

[1] https://www.abpi.org.uk/media/8307/11275_abpi_clinical-trials-report-2020_aw-v1-high.pdf

requirements currently placed on biotech and pharmaceutical companies may have a hindering effect on its ability to compete with its European counterparts.

- The regulatory burden placed on biotech and pharmaceutical companies by preclinical requirements, such as repeated dose toxicity and animal testing, is considerable and does not take into consideration the technological advances offered by modern precision medicines. Although accelerated mechanisms exist for dialogue with regulators, resource constraints create delay.
- The high costs associated with early-phase research are also detrimental to the ability of biotech and pharmaceutical companies to attract inward investment, as the risk-reward profile may not be attractive to investors. Without proper funding, early-phase research is stifled and companies miss out on the opportunity to develop, trial and deliver innovative treatments to patients.

Key insights and recommendations to the Government

The roundtable discussion highlighted some key areas on which the RRG could focus when delivering the implementation plan to improve the facilitation of clinical research across the UK. These have been developed into a set of recommendations, which are as follows:

- **Early-phase clinical trials are an integral part of delivering new and innovative treatments to patients. Therefore, the Government's roadmaps should address the challenges currently facing early-phase research so that the UK can continue to be an attractive destination to conduct this crucial step in drug development.**
    - While delivering on the Plan, there is an opportunity to identify the specific challenges facing early-phase research and address them in order to accelerate the pace at which innovative drugs, cell and nucleic acid therapies can reach patients.
    - The transition from preclinical to first-in-human trials is a crucial transition in the development of new drugs and therapies, but current regulations mean that companies must undergo extensive animal testing requirements that are used to predict toxicity in humans and may have limited clinical relevance in relation to the product in question. This is particularly the case for some precision medicines and genetic therapies, where human-specific drug targets are not present in the rodents or primates typically used for these tests.
    - In cases where candidate drugs target genes or molecules that are only present in humans, it would be more effective to prioritise recruiting patients for Phase 1 trials who have a strong genetic link to the disease in question. Identifying the most suitable patients will help assess efficacy and maximise the chance of success, meaning drugs and therapies can progress quickly from early- to late-phase trials and be delivered at pace to the patients more likely to benefit from them.
    - To support this, as part of its commitment to capitalise on digital tools to support recruitment, set up and monitoring, the Government should make best use of tools such as the UK Biobank, which can use its extensive records of genetic and health information to help identify potential disease-related targets.

- **The Vision for clinical research must be backed up by long-term funding beyond 2021/22, to ensure that the health and life sciences ecosystem in the UK is best set up to deliver innovative treatments to patients at pace, across the UK and beyond.**
    - While the COVID-19 pandemic has highlighted the key strengths of the UK's NHS and life sciences capabilities, it has also meant that vital funding for research and development has been reallocated to help navigate the UK out of the crisis. Consequently, the Association of Medical Research Charities

(AMRC) has projected a shortfall in non-COVID research spending of between £252 million and £368 million in 2020-21,[2] which has had consequences for patients suffering from diseases that are reliant on the progression of clinical trials to find new and innovative treatments.
    - Further, private investment in the research sector has been stifled while clinical trials for potentially life-saving treatments have been, understandably, placed on hold as resources have been redistributed across COVID-focussed research such as the RECOVERY trial.
    - Currently, the Vision is only supported by the funding agreement set out in this one-year Plan, which creates uncertainty as to the scale and deliverability of the Vision over the longer term. To improve confidence among the research community, it should be backed up by long-term, significant funding commitments that can have a real impact over a longer period of time. This will be essential to helping the community recover its losses from the past year and ensure that patients have access to potentially life-saving medicines. In addition, it is needed to secure and protect the future of a sector which plays an integral role in defending the UK and global population from public health threats such as COVID-19.
    - The Spending Review, expected in Autumn 2021, is a key opportunity for the Government to deliver a multi-year settlement for Departmental budgets. It must recognise the importance of this Vision and to fund properly its commitment to raising ambitions for clinical research post-pandemic.

- **The Implementation Plan sets out a commitment for the MHRA to review clinical trials regulation, in order to reduce bureaucracy and improve efficiency so that the UK can be an attractive destination to conduct research. This review should have a primary focus on the benefits that a risk-based approach for fast tracking potentially life-saving treatments could have for patients across the UK and beyond, applying key learnings from the COVID pandemic with regards to drug development.**
    - Following its departure from the EU, the UK has an opportunity to redesign its approach to conducting and regulating clinical trials and should emulate its approach to progressing the COVID-19 vaccine when doing this.
    - To meet the urgency of the pandemic and accelerate the development of the COVID-19 vaccine, companies and the regulator adopted a risk-based approach which allowed for proportional regulatory requirements while upholding high patient safety standards. This allowed for what is usually a multi-year process to be condensed down to a matter of months.
    - To speed up the vaccine's development, researchers drew on experience and information generated by products developed using the same technology platform, showcasing the opportunity to use previous experience to support the use of a new drug in a clinical trial.
    - To expedite trials, some firms were able to run Phase 1 and Phase 2 trials simultaneously to measure safety, immune responses and dose efficacy in parallel. Doing so enabled timelines to be shortened significantly.
    - Further, the Government modified legislation which granted the Medicines and Healthcare Products Regulatory Agency (MHRA) the ability to give temporary authorisation to a COVID-19 vaccine without needing to seek approval from the European Medicines Agency. This decision allowed for the first vaccine to be approved for use by December 2020, only 9 months after the UK went into lockdown.
    - Digital tools have played a central role in monitoring large-scale COVID-19 trials and rolling out the vaccine across the country, showcasing what can be

[2] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32397-7/fulltext

achieved when we harness our digital capabilities. By implementing a more flexible approach to using digital tools in drug development, trials can be made more effective and potentially at a lower cost to smaller companies. Furthermore, integrating digital platforms under NHSx and NHS digital has the potential to connect patients to research.
    - These decisions have had a transformative effect on the UK's response to COVID-19. When delivering on its commitment to review regulation, the Government and MHRA should keep at front of mind the importance of taking a pragmatic approach to drug development and approvals, and give key stakeholders the ability to make risk-based judgements to meet the needs of patients across the UK and beyond.

- **The implementation of the Vision provides a great opportunity to address the huge unmet need in the area of rare disease. In order to ensure that patients are receiving the most innovative treatments at pace, the actions to implement the Vision both in Phase 1 and beyond should seek to address the challenges facing clinical trials in this area.**
    - Research and drug development in rare disease remains largely neglected, despite estimates that 3.5 million people in the UK are affected.[3] Many of these people will also be unable to access the appropriate treatment for their condition.
    - The number of patients with a specific rare disease in an individual country, like the UK, is likely to be low by definition, but in order for clinical trials to gather sufficient efficacy data, they require larger numbers of patients to take part. In light of the UK's departure from the EU, there is growing concern for the increasing complexity to conduct multi-nation clinical trials and the possibility that the UK could be excluded from Europe-wide trials.
    - Further, there remains uncertainty about whether there will be an issue of compatibility now that the UK and EU can design clinical trials differently. Maintaining alignment with the EU in this area will be crucial to ensuring that rare disease patients in the UK and EU can access innovative treatments being developed elsewhere.
    - The Plan in its current form stresses the need for compatible and consistent ways of working across the four nations. It is equally important that we have consistency with our EU counterparts, so that the UK can continue to attract patients globally to tackle medicines for rare disease and address the huge unmet need in this area. This clarity should provide an incentive for more companies to focus on early-phase research into new emerging treatments, which should help to secure the UK's place as a European leader in early-phase trial activity.

- **To secure the long-term sustainability of the UK's health and life sciences ecosystem, and build on the Plan's commitments to expand research capacity in the NHS, the Government should ensure that the UK is protecting its pipeline of healthcare practitioners trained in trial delivery so that the NHS can continue to work alongside the life sciences sector to deliver potentially-life saving treatments.**
    - The Plan details commitments to free up NHS capacity for clinical research and empower NHS staff to conduct research, which is a positive step towards addressing the current constraints on resources which dampen the UK's competitiveness. To build on this, the Government should work with the NHS to ensure that it is set up properly to accelerate visa applications

[3] https://www.raredisease.org.uk/uk-strategy-for-rare-diseases-2/#:~:text=In%20the%20UK%20it%20is,some%20point%20in%20their%20lives.

and agreements for international researchers, so that the UK can continue to have access to a talented pool of clinicians in the post-Brexit environment.

- To encourage a pipeline of clinicians who are interested in clinical research, undergraduate students should be given the necessary training in early-phase research and medicines development, so that they are empowered to participate once they are qualified. To facilitate this, the Government should work with key partners such as the Faculty of Pharmaceutical Medicine, the Royal Colleges of Physicians and Health Education England to develop appropriate training modules.
- This training should not be limited to the NHS, but also encouraged in the commercial sector where a large portion of first-in-human trials are carried out. By delivering training across the workforce spectrum, we can ensure that high standards of safety, quality and governance are upheld across the life sciences ecosystem and build a workforce fit for the future.