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Client Alert

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UK—legislative changes for clinical trials on the horizon

Life Sciences analysis: Julia Gillert, of counsel, Tanvi Shah, senior associate, and Jaspreet Takhar, senior associate, at Baker McKenzie discuss the proposed amendments to the legislative process for the conduct of clinical trials involving medicinal products in the UK.

In brief

The Medicines & Healthcare products Regulatory Agency (MHRA) launched a consultation in early 2022 as part of its post-Brexit efforts to develop a world-class and flexible regulatory environment for clinical trials (see: LNB News 18/01/2022 90). The consultation closed in March 2022, but continues to offer insights into what the future holds for the UK regime for clinical trials.

It deals with improving the speed and efficiency of approvals of medicinal products, supporting innovation, enhancing transparency, encouraging greater risk proportionality, and promoting patient and public involvement in clinical trials. The proposals will result in updates to the current UK legislation governing clinical trials, the Medicines for Human Use (Clinical Trials) Regulations 2004, SI 2004/1031 (as amended), which transposed Directive 2001/20/EC (the EU Clinical Trials Directive) into UK law. Having exited the EU, the UK is not subject to the EU's long-awaited Regulation (EU) 536/2014 (the EU Clinical Trials Regulation), which entered into application across the EU on 31 January 2022, and which updates the EU Clinical Trials Directive, modernising and creating a more robust regime across the EU Member States.

The UK government also intends to update the UK's requirements for compliance with the principles of Good Clinical Practice (GCP) in order to ensure that they are flexible and can be applied to a broad range of clinical trials, particularly from an international interoperability point of view.

In parallel, the UK also made a surprise proposal on 26 January 2022 for a new World Health Organization (WHO) resolution on clinical trials focusing on improving the capability of clinical trials, strengthening international collaboration and improving standards. This results from the coronavirus (COVID-19) pandemic, which according to the government's Chief Medical Adviser, Chris Whitty, has exposed weaknesses in the clinical trials ecosystem, such as the failure to generate robust clinical evidence to inform decision-making and practice change.

In this issue

In more detail

The proposals

The MHRA proposals outlined below aim to strike a balance between removing current obstacles to sponsors carrying out clinical trials while ensuring the continued protection of clinical trial participants.

Patient involvement in trial design

- placing patients and the public at the forefront of the design, management, conduct and dissemination of trials will improve the quality of research and its direct relevance to trial participants
- the idea is to impose a legal requirement on sponsors to work with patients and the public (e.g. carers with experience of the relevant condition) or, if this is not appropriate, to justify why not in their application to an ethics committee

Research transparency

- increasing transparency in relation to why clinical trials are being carried out and their findings, but also sharing information on participants, health professionals, funders, etc. The idea behind this is that clinical trials results should be publicly available for the benefit of all
- in line with international standards, it is proposed to impose a requirement for the registration of trials with a WHO-compliant public register and for the publishing of results within 12 months of the end of the trial
- the obligation to publish results would be subject to an exception where a deferral is agreed with the Research Ethics Committee
- another legal requirement will be to share trial findings with participants, within 12 months of the end of the trial

GCP

- GCP is a set of internationally recognised requirements based on ethical and scientific principles in relation to the designing, conducting and reporting of clinical trials involving individuals. UK legislation on clinical trials currently stipulates that GCP must be followed and that the MHRA is responsible for inspecting sponsors' compliance with these requirements
- the proposal is to maintain those principles and set them all out into national legislation. However, sponsors in the UK will still be able to adopt the International Council for Harmonisation GCP instead when producing data for Marketing Authorisation applications
- the proposal would also update the UK GCP principles in order to ensure more flexibility as well as their suitability to a broad range of trials. In summary, the GCP changes proposed are:
    - as part of the broader focus towards risk proportionality, including in the legislation a requirement that regulators must adopt a proportionate approach throughout the clinical trial life cycle
    - future-proofing the applicability of GCP to electronic systems used in relation to clinical trials, by introducing clear wording in legislation in relation to the design and control of those systems that may have an impact on safety and results of clinical trials
    - the repository of information kept by sponsors, referred to as the ‘Trial Master File’, must be proportionate and directly accessible to MHRA inspectors. It also needs to be retained for a minimum of 25 years
    - making it clear that participants should not be liable for any treatment costs in relation to clinical trials (i.e. scans, consultations, medicine, etc.)

Combined approvals

- current legislation stipulates that trial regulatory approvals are separate from the ethics opinion. This means that the sponsor usually seeks regulatory approval from the MHRA and the Chief Investigator of the clinical trial applies to the Research Ethics Committee for the ethics opinion
- the proposal is to amend the legislation in order to enable sponsors to make combined applications to the MHRA (for regulatory approvals) and the Research Ethics Committee (for the ethics opinion) through the ‘Integrated Research Application System
- there will also be a single process for appeals in relation to the joint decision
- the proposal also includes specific timeframes in relation to the joint review and decision on the clinical trial application. In summary, the regulatory and ethics review of the application must be completed (i.e. approval or request for further information) within 30 days from the date of acknowledgment of a valid application
- in relation to multi-national trials, the proposal is to allow a generous time period (60 days with extensions if required) for sponsors to respond to requests for further information, which would facilitate the harmonisation of international protocols

Low-intervention trials

- introducing into legislation a notification system for low-intervention trials (e.g. studies relating to a product's dosages), replacing the need for formal approval
- this would allow sponsors to notify the MHRA about clinical trials where the risks are similar to that of standard medical care (i.e. they involve marketed products either used in accordance with the marketing authorisation or supported by published evidence and/or guidance and/or established medical practice)
- this means that the trial can be approved without the need to go through regulatory review, which will speed up the approvals process. However, the ethics review will still be required

Reactions from the industry

As a whole the reaction from industry to the proposals has been positive. For example:

- the Association of British HealthTech Industries is considering how medical device legislation can be aligned with these legislative changes
- the Health Research Authority (HRA) expressed that the proposals will make the UK the best place to research and develop safe and innovative medicines. Indeed, it is an opportunity to update current regulation by introducing a more proportionate and flexible regulatory regime, which promotes clinical trials and is in the best interests of patients
- the BioIndustry Association (BIA) wrote that this will ensure that the UK retains and continues to grow its reputation as a world-leading base for life sciences, in line with Life Sciences Vision. BIA is working with the Regulatory Affairs Advisory Committee on a consolidated BIA response to the consultation

What does this mean for the future?

Divergence and similarities with EU Clinical Trials Regulation

- the UK is seeking to implement risk-based processes (e.g. the relaxation of the approval process for low-intervention trials) and quicker timelines for approvals of clinical trials, with a view to gaining a competitive advantage and encouraging trials in the UK
- similar changes are underway in EU legislation. For example, the EU Clinical Trials Regulation which entered into application on 31 January 2022 aims to reduce paperwork and duplicate trials between Member States • the UK proposal and the EU Clinical Trials Regulation both include a requirement to publish clinical trial results within 12 months. The only difference in this regard is that in the EU this is limited to results of drug trials, while the UK intends to extend the publicity requirements to all types of clinical trials
- since January 2021, the UK no longer has access to the EU clinical trial database (EudraCT). This means that where a UK trial was registered in the EU Register prior to 31 December 2020, the results can be posted in EudraCT. For any clinical trials from 1 January 2021, the results should be posted in the public register where the study is registered and the MHRA notified
- from 2022 onwards, the HRA will publish results of UK-based clinical trials of investigational medicinal products on the ISRCTN registry, which is recognised by the WHO
- the MHRA intends to facilitate harmonisation of international protocols and to enable sponsors to make changes to how trials are conducted in the UK in order to align with requests from regulators in other countries, for example by giving sponsors sufficient time to respond in a co-ordinated way to requests for information

Still no reference to Decentralised Clinical Trials

We are seeing a new model for clinical trials evolving where, instead of treating patients from and at a central clinical trial site, patients receive their treatment at home, and clinical trial investigators monitor those patients remotely. Even if fully decentralised clinical trials are not being implemented on a larger scale yet, many clinical trials are at least operating on a hybrid basis, where some elements of the trial are decentralised.

The EU Clinical Trials Regulation does not expressly refer to this new model, and nor do the UK proposals. This is an omission which we hope can be rectified. In the absence of legislative proposals, we await guidance from EU regulators and the MHRA on implementing both hybrid and fully decentralised trials in the UK and across the EU.

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