JRO Brexit Position Statement: UCL Clinical Trials Portfolio UPDATE

The UK has left the EU, and the transition period after Brexit comes to an end on 01 January 2021, there is still the potential for a no deal. The immediate consequence of this action is that the UK's current participation in the European regulatory network for clinical trials would end and the Medicines and Healthcare products Regulatory Agency (MHRA) will be the UK's standalone medicines and medical devices regulator taking responsibility for the UK processes that currently function through the UK system.

The Government have advised that the UK's current regulatory framework, as per the 2004 Regulations, will remain in force after a no deal (but will be modified using powers under the EU Withdrawal Act (EUWA) to make sure they still work in the UK after exit).

In the event of no deal, following the UK's withdrawal from the EU, the UK will be treated as a "third country" for the purposes of the Clinical Trials Directive 2001/20/EC (the "Clinical Trials Directive"). Under the Clinical Trials Directive, the University as a non-EU sponsor of an EU clinical trial will have to appoint a legal representative that is established in the EEA before the withdrawal date.

There is more information on the European Commission website:

https://ec.europa.eu/info/sites/info/files/brexit_files/info_site/clinical-trials_en.pdf

The new EU Clinical Trials Regulation (CTR) 536/2014 will not be in force in the EU at the time that the UK exits the EU and so will not be incorporated into UK law on exit day. In the event of no-deal, the Government have confirmed they will re-align with the parts of the EU's CTR legislation that are within the UK's control. The logistics of this realignment will not be clear until post Brexit.

This position statement sets out the changes executed to ensure UCL remains compliant with all applicable clinical trial regulations and can continue recruiting at the time of a no deal.

Investigational Medicinal Products

UCL has responded to the Department of Health and Social Care (DHSC) requests for information on IMP supplies. Each CTU and the JRO Clinical Trials Team (JCTT) has considered the supply chains for supplies (including Investigational Medicinal Products, devices/in-vitro diagnostics devices, advanced therapy medicinal products, radioisotopes and other clinical consumables) to ensure appropriate arrangements are in place to assure supplies in the event of any possible border delay. Each CTU and the JCTT have also confirmed that arrangements are in place to guarantee adequate levels of IMP at site.

EU legal Representative Status.

UCL has established a wholly owned subsidiary in Ireland, UCL Research Limited, to act as its legal representative for the EU clinical trials sponsored by UCL. The impact of this change is:

1. Sponsorship of the relevant clinical trial will remain with UCL.
2. "UCL Research Ltd" will need to become the legal representative in the EU for each trial, thereby enabling the trials to continue in the EU in event of a no-deal Brexit.
3. UCL's senior officer with ultimate responsibility for the trials will continue to be the UCL Provo and President, not the Director of UCL Research Ltd. This may change in future if UK or EU legislation affecting the responsibilities of the legal representative changes.
4. For affected trials, a substantial amendment will need to be submitted to reflect that each trial will have a legal representative in the EU. This an administrative process with a small charge attached. Some EU competent authorities are waiving, or at least reducing this fee.

The UCL legal entity has been established since late February/Early March 2019 and correspondence was forwarded to each UCL Clinical Trials Unit at this time advising them of the above. A representation agreement is in place between UCL and UCL Research Limited that sets out the relationship between the two entities. All trials with sites within the EU must ensure that a substantial amendment is made to reflect that UCL Research Limited will be the EU legal representative for EU clinical trials for which UCL is the sponsor. This amendment should take place before the UK leaves the EU in the event of a no-deal Brexit.

For these trials as the sponsor remains UCL, the default contact details for JRO or CTU on behalf of UCL remain and the addition of the legal representative contact details will be added to the Clinical Trials Application (CTA). Therefore, it is anticipated that the majority of paperwork from the Competent Authorities will be directed to the default contact. There may be some information (hardcopy of letters) which may be sent to the EU legal Representative office in Ireland. In these circumstances, the information will be forwarded to the JRO on the *JRO.sponsorship* email address (scanned copy) and will be disseminated to the relevant CTU. This process will be documented between the JRO and the UCL Legal Representative.

<u>Continuity of UCL Insurance for trials</u>

The UCL Brokers have established a new legal entity of the Gallagher group in the EEA that is authorised to conduct intermediation activities under the EU Insurance Distribution Directive (these will be written out of Lloyds Brussels). The insurance will cover UCL Research Limited and the activities that it will carry out. There are no extra processes for insurance that need to be taken by researchers for trials that have EU sites. For existing trials with local EU policies in place, these can continue as they are. If there are any new developments, these will be disseminated to relevant parties by the JRO.

GDPR

The DPO have provided templates for the standard contractual clauses; these are from the European Website. The contracts teams alongside the CTUs have been working to ensure that Standard Contractual Clauses are implemented to ensure free flow of data. On an individual trial level, all teams should confirm that the data will continue to flow to the data controller:

1. Data Protection Impact Assessments (DPIA) are updated by consulting with the DPO to manage any risks identified with restricted transfers of personal data outside of the EEA.
2. Privacy Notices are no longer valid. Standard Contractual Clauses (SCC) are implemented as appropriate to ensure the free flow of data into UCL.
3. Protocols and Data Sharing Templates are up to date.
4. Check where data is stored – In the event that data stored in the EEA, the supplier organisation must be contacted – including cloud service providers – to seek assurances from them that they will continue to provide data services.

The HRA have provided a General Summary of arrangements to be considered for GDPR. However, it is advised that any arrangements be discussed with UCL DPO for affected trials:

Data from the UK to EEA	Remains as normal due to the Statutory Instrument being in place.
Data from the EEA to the UK	Where there is a (UK) Data Controller (DC) to (EEA) DC an SCC is required. Where it is a UK (DC) to (EEA) Data Processor (DP) – there is no solution and the UK ICO is awaiting the outcome of Brexit discussions on how to proceed. Where there is UK (DP) to (EEA) DC an SCC is required Requires Standard Contractual Clauses and Legally Binding Enforceable Instrument in place, for trial where the data controller is in the EEA but not where the data processor is in the EEA.
Data from UK to USA	Implement a SCC, LBEI or Derogation. Privacy shield is no longer valid.
Data from USA to UK	Remains unchanged
Data from UK to Rest of World	Remains unchanged
Data from Rest of World to UK	Remains unchanged
Date from the Rest of the World to UK	Remains unchanged

MHRA submissions gateway

The Medicines and Healthcare Products Regulatory Agency (MHRA) have established a submissions gateway to ensure that if the United Kingdom (UK) does leave the European Union (EU) with no deal, companies can continue to submit regulatory and notification information to the UK. Currently the only areas enabled on the MHRA Submissions home page are the User Maintenance and Pharmacovigilance Gateway Management. UCL is registered to use the gateway and is in discussion with the regulator on setting up the CTUs as individual entities under the sponsor.

The MHRA have provided updated information on 01/09/20 on the processes for the registration and publication of a clinical trials. Existing and established international registers such as ISRCTN registry (UK), or ClinicalTrials.gov (USA) should be used. For trials involving both UK and EU sites a record in the EU Clinical Trials Register will exist (other than adult Phase 1 studies). The time frame for publishing the summary of results is within 6 months of the end of trial for paediatric clinical trials or within one year of the end of trial for non-paediatric clinical trials for the EU clinical Trials register. For trials on other registries, results should be published as stipulated by the registry.

https://www.gov.uk/guidance/guidance-on-substantial-amendments-to-a-clinical-trial-from-1-january2021--2

Northern Ireland Protocol

The UK requirements will differ between Great Britain (GB, consisting of England, Scotland and Wales) and Northern Ireland due to the Northern Ireland Protocol. The proposal for Northern Ireland will need to be agreed but the current position is that Northern Ireland will remain in compliance with EU legislation and comply with EU requirements with respect to medicinal products and medical devices.

The Northern Ireland Protocol for category 1 good Importation requirements has been extended for 1 year:

https://www.gov.uk/government/news/irelandnorthern-ireland-specialised-committee-05-november2020

Government Freight Capacity Solutions

The Department strongly recommends that suppliers of medicines and medical products review their supply routes and, where necessary, put in place robust plans to re-route supply away from the disrupted short straits routes (Dover, Calais, Dunkirk, Folkestone and Coquelles) into the UK, especially during the first three months following Jan 1st 2021 when the most significant disruption is anticipated.

The **Government secured freight capacity** is designed to support supplier rerouting plans through securing 'roll-on, roll-off' freight capacity on which medicines and medical products will be prioritised. For the latest information on the procurement of Government freight capacity, please see here.

The Department's **Express Freight Service** is a logistics service, designed to support the uninterrupted supply of medicines and medical products. Access to this service will be granted by DHSC via the National Supply Disruption Response centre where a supplier's own contingency measures fail. There is a charge for this service.

If you require urgent use of the service for your IMP or supplies for your trial please discuss with the JRO..

https://www.gov.uk/government/publications/critical-goods-for-government-secured-freightcapacity/critical-goods-for-government-secured-freight-capacity-a-list-of-category-1-goods