Guidance on substantial amendments to a clinical trial if the UK leaves the EU with no deal

This guidance covers significant amendments to a clinical trial including changes to the trial sponsor/legal representative, Investigational medicinal product (IMP) certification and importation and amendments to the Research Ethics Committee (REC).

Published 3 April 2019
Last updated 7 August 2019 — see all updates

From:

Medicines and Healthcare products Regulatory Agency

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Note that any arrangements solely for sites outside the UK that do not affect the approved UK trial do not need to be notified as substantial amendments in the UK.

Changes to the trial sponsor/ legal representative

The UK would require the sponsor or legal representative of a clinical trial to be in the UK or country on an approved country list which would initially include EU/European Economic Area (EEA) countries.

A change in sponsor or legal representative for an UK trial is a substantial amendment requiring submission to both MHRA and the Research Ethics Committee (REC).

Action to take if there is a no deal Brexit

Where the sponsor is from the rest of the world and the legal representative is established in the UK and there are sites elsewhere in the EU/EEA, the sponsor will need to assign an EU/EEA legal representative for these sites.

No amendment is required where the sponsor or legal representative for an ongoing trial is established in the EU/EEA as the UK will continue to accept this.

No amendment will need to be submitted in the UK if the sponsor retains the UK legal representative for the UK study. Similarly, no amendment will need to be submitted in the UK if a sponsor remains in the UK and a legal representative is added to cover EU/EEA sites.

Investigational medicinal product (IMP) certification and importation

As is the case today, a substantial amendment will be required to be submitted to MHRA to change (add/replace) any IMP manufacturing, importation or certification site relevant for supply of IMP to an ongoing UKtrial.

If the sponsor chooses to retain an existing UK IMP release site for the ongoing UK trial but includes an additional EU/EEA site for trials in the EU/EEA only, then no substantial amendment to MHRA will be required.

As described in the further guidance note on the regulation of medicines, medical devices and clinical trials if there's no Brexit deal, the IMP supply chain from a country on the approved country list which

would initially include EU/EEA countries, will allow direct supply to clinical investigator sites.

Action to take if there is a no deal Brexit

After a transition period of 1 year from the date the UK leaves the EU, this direct supply must be supervised by a Manufacturing and Import Authorisation for Investigational Medicinal Products (MIA(IMP)) holder who will be required to put in place an assurance system to check these IMPshave been Qualified Person (QP) certified in the EU or EEA. This assurance system must be overseen by a QP.

The holder is required to be included for importation to an ongoing UK trial, a substantial amendment should be submitted to the MHRA to include the details of the MIA(IMP) holder performing the 'supply chain oversight' role within 1 year of the UK leaving the EU.

This means that for up to 1 year after the UK leaves the EU, IMPs may be supplied direct from the EEA MIA(IMP) holder to the UK trial site without the UK MIA (IMP).

Amendments relevant to the Research Ethics Committee (REC)

The Health Research Authority (HRA) has produced guidance on when amendments are required to be submitted for REC review.
This guidance will apply from exit day in line with the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019.