GLOBAL CLINICAL SUPPLIES GROUP

Supplying Clinical Trial Sites Within Great Britain, 2022 and Onwards

As the regulatory landscape continues to adjust in the post-Brexit world, a nuance to importation of clinical supplies to sites based in Great Britain (GB) came into force at the start of 2022. Sponsors need to ensure they have appropriate controls within their supply chain to avoid falling foul of this change in requirements. In this short article we detail what those changes are and measures needed to maintain regulatory compliance.

The UK Medicines and Healthcare Agency published their guidance on Supply Chain Oversight, in which they state:

"If you are the Sponsor of a UK clinical trial using IMPs imported into Great Britain from countries on an 'approved country for import' list (initially, all EU and EEA countries) you will require a UK Manufacturing and Import Authorisation (MIA (IMP)) holder to put in place an assurance system to check these IMPs have been certified by a Qualified Person (QP) in a listed country, before release to the trial."[1]

The transition period for implementing the new arrangements ran from 01st January 2021 for one year, therefore as of now, import of clinical trial material from an approved country must follow this guidance.

NOTE: The guidance does not require that IMPs imported to GB from an approved country be subject to a second QP certification. Instead the importer has to have a system in place which verifies that the IMP has been suitably QP certified within the approved country.

When the UK was working through its transition out of the European Union, many sponsors acted to move their batch certification site to an EU location to maintain uninterrupted batch certification for ongoing trials. In the immediate aftermath of Brexit, the UK announced that it would continue to accept EU QP certification. That position has not changed, but the requirements issued by the MHRA add an additional nuance to maintaining GB supply.

Here is a step-by-step guide to ensuring your trial remains in compliance:

SCENARIO: If your IMP is QP certified within an approved country and you wish to supply GB clinical trial sites:

- Identify a UK facility that has been licenced by the MHRA to act in the role of Supply Chain Oversight
- Initiate an amendment to an existing UK CTA or initiate a new UK CTA that identifies the site acting as Supply Chain Oversight
- Provide copies of UK CTA approvals and UK ethics approvals including details of authorised GB clinical trial sites to the body providing Supply Chain Oversight
- Ensure Quality Agreements are in place between Sponsor, Contract acceptor and other parties as applicable, which outlines roles and responsibilities within the Supply Chain Oversight arrangements
- Provide evidence that the certifying site in the listed country is appropriately licensed and holds a current GMP certificate for the IMP dosage form(s) and associated activities

The sponsor should determine the shipping strategy into GB, two options are available:

1. Direct from EU Hub to the clinical site – in which case the facility providing Supply Chain oversight would need to determine that:
   a. They hold evidence of QP certification of the batch being imported
   b. There had been no shipping excursions prior to approving the supplies for use
2. From EU Hub to UK Hub – in which case the facility providing Supply Chain oversight would need to determine:
   a. That they hold evidence of QP certification of the batch being imported
   b. That there had been no shipping excursions prior to approving the supplies for use.
   c. Orders for GB sites would then be picked and shipped from approved stock in the UK Hub

Option 1 may be preferable if there are only a small number of GB clinical sites, whereas Option 2 would be the choice to manage a greater number of GB sites.

In both cases the Sponsor remains responsible for the Regulatory release under the two step release process required for IMPs.

IMPs coming to GB from Northern Ireland do not require this additional oversight when:

- QP certified IMPs are supplied from the EU/EEA for use at Northern Ireland clinical trial sites and are then onward supplied to GB
- IMPs are QP certified by a Northern Ireland MIA(IMP) holder

IMPs coming directly to Great Britain from third countries that are not on the approved country for import list will continue to require import and QP certification in the UK by the MIA(IMP) holder as per the existing requirements.[2]

The MHRA guidance also covers trials involving the supply of Auxiliary medicinal products, arrangements must be in place for import into the UK and subsequent supply to GB trial sites.

a. EU/EEA commercial medicinal products used as Auxiliary medicinal products – these must be imported into the UK via a WDA(H) licence holder with suitable checks conducted prior to distribution from the WDA(H) holder to GB trial sites.

b. RoW (e.g. USA or MRA region) commercial medicinal products used as Auxiliary medicinal products – these must be imported into the UK following MHRA Guidance Note 14 "The supply of unlicensed medicinal products ("specials")"; import of this supply is via a UK Manufacturers Specials (MS) licence holder.

Maintaining compliance with the new rules within the UK could well be dictated by managing your supply chain complexity. For example:

If a sponsor has their own QPs within the EU and a suitably licenced and authorised site within the UK then ongoing compliance may simply involve amendments to the existing Quality Management System to facilitate Supply Chain Oversight.

However, should a sponsor be reliant on CMOs to act as their QP, they would be well advised to select a CMO who has QPs within the EU and a suitably licenced and authorised site within the UK, thus removing the difficulty of having different facilities needing to put in place additional QP agreements.

These changes bring an additional level of complexity to conducting Clinical Trials within the EU/EEA/UK region. Coupled with the introduction of the clinical trial regulation, new GMP legislation for IMPS across the EU/EEA and a recently announced UK consultation on proposals for legislative changes for clinical trials, it remains a challenge to ensure compliance with each region's requirements.

Additional Information can be found here:

1. https://www.gov.uk/government/publications/importing-investigational-medicinal-products-into-great-britain-from-approved-countries/importing-investigational-medicinal-products-imp-from-countries-on-a-list-to-great-britain
2. https://www.gov.uk/government/publications/importing-investigational-medicinal-products-into-great-britain-from-approved-countries/list-of-approved-countries-for-clinical-trials-and-investigational-medicinal-products
3. https://www.gov.uk/government/publications/importing-investigational-medicinal-products-into-great-britain-from-approved-countries/authorisations-and-procedures-required-for-importing-investigational-medicinal-products-to-great-britain-from-approved-countries