Communication to sponsors of clinical trials and clinical investigations in preparedness for the end of the transition period.

Target audience: Sponsors of commercial and non-commercial clinical trials and clinical investigations involving patients being conducted in the UK including industry, universities, NHS Trusts and charities; entities running clinical trials and clinical investigations on behalf of sponsors e.g. Clinical Research Organisations (CROs) and Clinical Trial Units (CTUs); trade associations e.g. AMRC, ABPI, BIA, BIVDA, ABPHI; research charities including CRUK and BHF; University Hospital Association, R&D Directors' Group and Medical Schools Council.

Introduction

The transition period is due to end at 11pm on the 31 December 2020, at which point the UK will cease to be part of the EU Single Market and Customs Union. This will mean from 1 January 2021 there will be changes in how the UK trades with the EU, with new border and customs procedures.

The Department of Health and Social Care's (DHSC) objective is to make sure no clinical trial or clinical investigation should be disrupted due to this change, to ensure all patients taking part in clinical trials and clinical investigations continue to have access to medicines and medical products. The DHSC is doing everything appropriate to prepare for the end of the transition period on the 31 December 2020 by using a multi-layered approach with all our partners to ensure the supply of medicines and medical products remains uninterrupted. You can find more detail on the department's plan here and an update here.

DHSC has communicated widely with industry (individually and via trade associations), the NHS and charities (via Association of Medical Research Charities), and Universities, and has emphasised that **organisations running clinical trials and clinical investigations in the UK should consider their supply chains for supplies (including Investigational Medicinal Products, devices/in-vitro diagnostics devices, advanced therapy medicinal products, bio samples, radioisotopes and other clinical consumables)** to ensure appropriate arrangements are in place to assure supplies in the event of any possible border delays.

Sponsors are formally responsible for the delivery and safety of patients on their clinical trials and/or clinical investigations.

Sponsors are asked to:

- continue to mobilise their own plans for operational **trader readiness**;
- Have **put in place contingency arrangements** and have systems in place for monitoring stock positions and supply chain performance that allow for developing issues to be identified at the earliest opportunity
- have in place effective procedures for monitoring and managing demand to detect and challenge excessive ordering, and control stock despatches and;
- have put in place the necessary governance structures and approvals processes to allow for rapid response and collaboration with the **National Supply Disruption Response (NSDR)** on supply disruption incidents;

- ensure that customer service functions are adequately resourced and equipped where appropriate to manage an increase in enquiries, in the event that supply disruption events do start to impact care providers and patients;
- ensure processes are in place for the rapid reporting of all supply disruption incidents (including potential incidents) through the NSDR (described in detail below) – the sooner the NSDR is informed of an incident or potential incident, the sooner it can take action to ensure providers and patients receive the products they need on time.

Should sponsors, or other organisations running clinical trials and clinical investigations, become aware of any issues regarding supply, key contacts have been established, and are discussed in further detail in this document.

Summary of Key Contacts:

- **Queries or early intelligence on potential issues/concerns– DHSC Clinical Trials Disruption Response Group: ctcontingencyplanning@dhsc.gov.uk**

- **Immediate notification of a supply disruption where support is needed to resolve - DHSC National Supply Disruption Response (NSDR):**
  - **Freephone number in the UK: 0800 915 9964**
  - **Direct line: 0044 (0) 191 283 6543**

- **General queries to the MHRA:**
  - **info@mhra.gov.uk**
  - **Telephone (weekdays 9:00-17:00): 020 3080 600**
  - **https://www.gov.uk/guidance/contact-mhra**
- **Queries to MHRA on UK and Pan European clinical trials of medicines:**
  - **Telephone (weekdays 8:30-16:30): 020 3080 6456**
  - **clintrialhelpline@mhra.gov.uk**
- **Queries to MHRA on UK and Pan European clinical investigations of medical devices:**
  - **devices.regulatory@mhra.gov.uk**

Trial sites should contact the Chief Investigator using established processes to resolve the issue.

This document provides information and links to published guidance addressing the following areas:

1. **Clinical Trials and Clinical Investigations Supplies**
2. **Shipping Routes between the EU and the UK**
3. **Trial sites storing additional stock of clinical trial supplies**
4. **National Supply Disruption Response (NSDR)**
5. **Data**
6. **Customs Procedures at ports, including airports**
7. **Importing and Exporting tissues and cells, including biosamples**
8. **Guidance on submitting MHRA clinical trials submissions**
9. **Import Licences for Investigational Medicinal Products**
10. **Further guidance and other areas of interest**

1. Clinical Trials and Clinical Investigations Supplies

Established processes and systems should already exist for responding to serious supply disruption events for clinical trial/investigation supplies and these systems should continue to be used; for example, **trial sites should seek to resolve the issue through the chief investigator of the clinical trial or investigation, or through the organisation running the clinical trial/investigation e.g. CRO or CTU**.

As part of our contingency planning, DHSC has conducted a comprehensive analysis of all live and in set-up clinical trials and clinical investigations funded and/or supported by the NIHR in England and trials and clinical investigations within Northern Ireland, Scotland and Wales. These trials are sponsored and funded by a range of industry, public and charity organisations. This analysis informed our understanding of which clinical trials and clinical investigations are dependent on supplies coming from or via the EU27/EEA and assisted with gaining assurance from sponsors on the state of the preparedness and contingency planning for any possible disruptions to clinical trials and clinical investigations supplies.

While DHSC is working very closely across government (including the devolved administrations) and with NHS England to limit any impact on clinical trials and clinical investigations, early intelligence of any potential or developing issues would help DHSC consider any action at the earliest opportunity, ideally before the disruption has occurred.

The Clinical Trials Disruption Response Group in DHSC would welcome sponsors, or other entities running clinical trials and clinical investigations supplies, getting in contact as soon as they are aware of an issue with supply by emailing ctcontingencyplanning@dhsc.gov.uk.

2. Shipping Routes between the EU and the UK

The **Government has Secured Freight Capacity** from freight operators which will be sold at market rates to suppliers of medicines and medical goods, including supplies for clinical trials and clinical investigations. Access to the freight capacity will be via tickets; there will be no ‘turn up and go’ access.

DHSC has procured an **Express Freight Service** to provide access to an end-to-end solution able to deliver small consignments on a 24-hour bases and a two to four day pallet delivery service. This is designed to be used only if suppliers’ own contingency measures encounter difficulties or there is an urgent need for specific medicines and medical products, clinical trial or investigation supplies.

Suppliers will need to register online to be eligible for access to the Government-secured freight capacity, regardless of whether they registered last time. However, if you registered for the Express Freight Service in the lead up to October 2019, this code is still valid, so you do not need to register again but should check and confirm that the current details we have for your company are up to date.

Suppliers should register at
https://ship.mixmove.io/customForm/DHSCSupplierRegistration

Suppliers can check and confirm details at
https://ship.mixmove.io/customForm/DHSCSupplierRegistration/login

3. Trial sites storing additional stock of clinical trial supplies

It is the responsibility of clinical trial and clinical investigation sponsors to ensure continued supplies for their clinical trial/investigation. Sponsors should not ask study sites to hold additional clinical supplies or stock where this is managed/supplied through the routine NHS supply chain. Any clinical trial/investigation supplies which are provided via the routine NHS supply chain should be managed as for all other medical supplies. Providers should not stockpile or hold additional stock.

For specific clinical trial and clinical investigation supplies which are provided by trial sponsors, in exceptional circumstances, a case could be made for holding short-term additional stock locally, calculated by patient need, recruitment rates/numbers and the anticipated extended time between placing an order and receiving the clinical trial product. This would need to be agreed locally and would depend on availability/capacity of adequate appropriate storage space and storage requirements e.g. temperature controlled. However, sites should not be expected to hold stock for whole trial periods (unless very short) or for other sites in the study. Where holding additional trial stock may impact on stock supplied via the routine NHS supply chain (i.e. open label studies) then the default should be referral to the central process.

4. National Supply Disruption Response (NSDR)

Each clinical trial and clinical investigation should have established processes and systems in place for responding to serious supply disruption events for clinical trial/investigation supplies and these systems should continue to be used; for example, trial sites should seek to resolve the issue through the chief investigator of the clinical trial or investigation.

While DHSC has every confidence that the measures put in place by sponsors and the Department will provide continued access to clinical trial and clinical investigation supplies, it is important that DHSC is prepared to respond to supply disruption incidents should they occur.

How does the NSDR work?

- The NSDR includes a call centre to record supplies disruption concerns from any source, and route them to specific case management teams to lead the resolution. There are separate case management teams for each product category, including a clinical trial case management team.
- The NSDR unit will coordinate suppliers/sponsors, the health services and social care and central Government to resolve incidents, minimising impact on care provision and patients; It will offer logistics trouble-shooting to

suppliers/sponsors whose consignments are stuck in border disruption which includes getting the supplies onto the Department of Health and Social Care Express Freight Service;

If a sponsor experiences disruption to any part of its normal supply routes, with no immediate resolution available, they should report it to the NSDR unit on

- **Freephone number in the UK: 0800 915 9964**
- **Direct line from abroad: 0044 (0) 191 283 6543**

5. Data

At the end of the transition period, the UK will become a 'third country' for data protection purposes. The UK is currently seeking an adequacy decision from the EU. The EU's adequacy assessment of the UK is underway and making steady progress. The UK is in a strong position to secure adequacy decisions, and the European Commission has committed to conclude the process by December 2020. If secured by the end of the transition period, this will allow for the free flow of personal data from the EU/EEA to the UK to continue uninterrupted.

However, it is reasonable that contingency plans are in place should an agreement not be reached. As part of these preparations, DHSC has circulated End of Transition Period Data Preparedness Guidance for health and social care organisations. This guidance sets out what sponsors need to do now to prepare for any eventuality at the end of the transition period.

This guidance was distributed via email to all sponsors on 29 October 2020. To request a copy of this guidance contact: queries@hra.nhs.net

The 4 critical steps for your organisation to take before the end of the transition period are:

- **Data transfers:** identifying your personal data flows from the EU/EEA and putting in place alternative transfer mechanisms such as Standard Contractual Clauses to allow these flows to continue. Pseudonymised data does fall under the remit of personal data in GDPR, therefore sponsors will require a legal mechanism to allow continued flow from the EU to the UK at the end of the transition period. The UK has, through regulations, recognised EU/EEA member states as adequate. As a result, personal data can flow freely from the UK to the EU/EEA.
- **Data storage:** identifying where your data is stored by EEA based processors, for example with cloud storage providers based in the EU, and engaging with them to gain written assurances that data will continue to flow back to the UK.
- **Data audit:** conducting an audit of all your personal datasets, ensuring information is up to date and relevant meta-data is held, including geographical origin of the data and the legal basis for transfer.
- **Data protection:** ensuring you are compliant with UK GDPR.

It is the responsibility of individual organisations to assess their level of risk and take the necessary actions. However, the guidance will help ensure your data can continue to flow legally and uninterrupted from the EU/EEA to the UK.

If the EU has not deemed the UK to be adequate by the end of the transition period, you will need to have put in place alternative transfer mechanisms for your personal data to continue to flow legally and uninterrupted from the EU/EEA to the UK.

6. Customs Procedures at ports, including airports

From the 1 January 2021 the process for importing and exporting goods between GB and the EU will change. To help prepare for these changes please follow the below links:

- Exporting - https://www.gov.uk/prepare-to-export-from-great-britain-from-january-2021
- Importing - https://www.gov.uk/prepare-to-import-to-great-britain-from-january-2021

From 1 January 2021 you will need an Economic Operator Registration Identification (EORI) number if you move goods between Great Britain and EU countries in the same way you currently need one to move goods between the UK and 'the rest of the world'.

In the case of goods moving between GB and the EU:

- When exporting from GB to the EU, a UK EORI number (starting with GB) must be used by the business making the export declaration and an EU EORI number must be used by the business making the import declaration.
- When exporting from the EU to GB, an EU EORI number must be used by the business making the export declaration and a UK EORI number (starting with GB) must be used by the business making the import declaration.

In many cases, the business making the export declaration will be the business sending the goods and the business making the import declaration will be the one receiving the goods, but this is not always the case. Those businesses will need to use the principles above to determine which EORI number to use.

It is possible for the same business to be responsible for both the export and import declarations in which case, it will need both a UK EORI number (starting with GB) and an EU EORI number.

Further information on getting an EORI number- https://www.gov.uk/eori

Customs procedure code information can be found at:

Imports: https://www.gov.uk/government/publications/uk-trade-tariff-customs-procedure-codes/imports-aphabetical-index-of-customs-procedure-codes

Exports: https://www.gov.uk/government/publications/uk-trade-tariff-customs-procedure-codes/exports-aphabetical-index-of-customs-procedure-codes

For further guidance to learn move about trading with the EU from 1 January 2021, including upcoming webinars:

www.gov.uk/guidance/help-and-support-if-your-business-trades-with-the-eu

Useful links

Border Operating Model
https://www.gov.uk/government/publications/the-border-operating-model

Exporting/Importing Goods between GB and the EU
https://www.gov.uk/government/publications/how-to-import-and-export-goods-between-great-britain-and-the-eu-from-1-january-2021

Moving goods into, out of or through Northern Ireland
https://www.gov.uk/government/collections/moving-goods-into-out-of-or-through-northern-ireland-from-1-january-2021

https://www.gov.uk/guidance/trading-and-moving-goods-in-and-out-of-northern-ireland-from-1-january-2021

Customs Declarations
https://www.gov.uk/guidance/customs-declarations-for-goods-brought-into-the-eu

To sign up for HMRC alerts
https://www.gov.uk/help/update-email-notifications

UK Global Tariff applicable from 1 January 2021:
https://www.gov.uk/guidance/uk-tariffs-from-1-january-2021.

7. Importing and Exporting tissues and cells, including biosamples

Importing and Exporting tissues and cells for human application (including starting material for ATMPs):

The Human Tissue (Quality and Safety for Human Application) Regulations 2007 transpose the EU Tissues and Cells Directive (EUTCD) in UK law.

Under these Regulations, the Human Tissues Authority (HTA) regulates establishments that undertake the procurement, testing, processing, storage, distribution, import and export of tissues and cells for human use. This includes any steps involved in the handling of tissues and cells prior to them being manufactured into medicines.

From 1 January 2021, the UK will become a third country for the purposes of the EU Tissues and Cells Directive. The UK will also consider EU Member States to be third countries.

Transport of tissues and cells from and to EU Member States will need to be covered by an appropriate import or export licence from the Human Tissue Authority (HTA). More information is available on

- the HTA website: https://www.hta.gov.uk/uk-transition-guidance and
- GOV.UK: https://www.gov.uk/guidance/quality-and-safety-of-human-organs-tissues-and-cells-from-1-january-2021

This licensing requirement applies to the export and import of all tissues and cells intended for use in human application, including those that will be used in the manufacture of an advanced therapy medicinal product (ATMP) where the tissues and cells are referred to as starting materials.

Further information is available on the HTA website at: https://www.hta.gov.uk/faqs-hta-licensing-requirements-human-tissues-and-cells-used-clinical-trials-and-medicines-0

Importing and exporting biosamples for analysis:

Biosamples may be obtained for analysis purposes to provide data for a clinical trial. These types of samples are considered relevant material under the Human Tissue Act 2004. For the purposes of the Act, import and export is considered as into and out of England, Wales or Northern Ireland. This definition will be unchanged following the end of the transition period. Where import and export are taking place, these are not licensable activities under the Act. However, the storage of the material once it is imported may be licensable if this is for a scheduled purpose, such as research within the scope of the Act.

Biosamples are included in the DHSC Express Freight Service discussed above.

8. Guidance on submitting MHRA clinical trials submissions, Developmental Safety Update Reports (DSURs)

The MHRA has published guidance on how to make submissions from 1 January 2021. The guidance provides information to both commercial and non-commercial clinical trials applicants on:

- How to register to use MHRA Submissions
- How to enable other users in your organisation to submit via MHRA Submissions
- How to submit Clinical Trials Submissions via MHRA Submission
- How to submit Developmental Safety Update Reports (DSURs) via the new system

If a sponsor has any questions regarding registration for MHRA Submissions; please email submissions@mhra.gov.uk

9. Import Licences for Investigational Medicinal Products

If you are the sponsor of a clinical trial running in Great Britain using IMPs imported 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.

This assurance system must be overseen by a QP who may be based in the UK or EEA, however IMPs that have been QP certified in a listed country will not require recertification in the UK. The IMP supply chain from a country on the approved country list will allow direct supply to clinical investigator sites. There will be a one-year transition period following the date to implement this guidance.

Additional information on the importation of Investigational Medicinal Products (IMP) from EEA to Great Britain is available.

https://www.gov.uk/government/publications/importing-investigational-medicinal-products-into-great-britain-from-approved-countries-from-1-january-2021/importing-investigational-medicinal-products-imp-from-countries-on-a-list-to-great-britain

Investigational medicinal products may be supplied from the EEA to clinical trial sites in Northern Ireland without the need for a UK MIA(IMP) to oversee the supply chain. Further guidance on supply of IMPs to Northern Ireland will be provided in due course.

General queries to the MHRA

If a sponsor has any other queries concerning MHRA's remit on clinical trials of medicines or clinical investigations of medical devices, they should contact the MHRA's;

- Clinical Trials Unit on:
  - Telephone (weekdays 8:30-16:30): 020 3080 6456
  - clintrialhelpline@mhra.gov.uk
- Clinical Investigations Unit at:
  - devices.regulatory@mhra.gov.uk

10. Further guidance and other areas of interest

Please follow the below link to the MHRA transition guidance page.

https://www.gov.uk/government/collections/mhra-post-transition-period-information

UK and Pan European trials

From 1 January 2021 the UK will 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/EEA countries. The MHRA offers to discuss any issues with organisations directly via their helpline below:

- **MHRA Clinical Trials Helpline: 020 3080 6456.**

The EU's current position is that where trials are pan EU, sponsors or legal representatives must be based in the EU. There is more information on the European Commission website.
https://ec.europa.eu/info/sites/info/files/notice_to_stakeholders_brexit_clinical_trials_final.pdf

EU Transition Trader and Industry Forum
A new online forum has been designed to help businesses and traders find answers to questions regarding the transition period.
The forum can be accessed here: https://transition-forum.service.cabinetoffice.gov.uk/forums/
You will need to register on the forum to ask a question.

Using personal data in your business or other organisation from 1 January 2021
What action you need to take regarding data protection and data flows with the EU/EEA after the end of the transition period.
https://www.gov.uk/guidance/using-personal-data-in-your-business-or-other-organisation-after-the-transition-period