Developing Healthcare Products

If you are involved in healthcare technology or translational research (i.e. in the development or repurposing of a ‘product’ for the diagnosis, prevention, monitoring or treatment of a health condition), then these pages will help you understand the relevant regulation. You can learn more about previously funded translational research in MRC’s translational case studies.

The precise regulatory path and evidence to demonstrate that a product is safe and effective is specific to the product, commercial intent and where you plan to market or trial your product. For the UK, the best place to get bespoke regulatory advice is from the MHRA Innovation Office. You may also have access to local expertise (e.g. Research Sponsor office, Translation or Technology Transfer office).

EU Exit has changed the UK regulatory environment for healthcare products, you can find details in the MHRA EU Exit guidance and the HRA guidance for health and social care researchers at the end of transition period. More change is coming, so look out for consultations on new draft regulations (e.g. MHRA Medical Devices consultation open until 25th Nov 2021).

The following resources help answer some questions that we are often asked:

- **Is my study research?** Helps you understand if NHS research policies apply.
- **Do I need NHS Research Ethics Committee review?** To know whether you need NHS Research Ethics Committee review, if not, University REC review may still be required.
- **Integrated Research Application System** - to apply for NHS and regulatory approvals.
- **Available health data is listed on HDRUK Innovation Gateway;** our Health Data Access Toolkit shows how to access it; and we guide on data law.
- **UKCRC Tissue Directory** for available clinical samples, and we guide on human tissue law.

If there is other guidance that you’ve found helpful which we haven’t signposted in this section, please let us know: rsc@mrc.ukri.org

Medical Devices & In Vitro Diagnostics

The definition of a medical device is very broad and encompasses products ranging from plasters to pacemakers. Standalone software and apps are also medical devices if they have a medical purpose.

In vitro diagnostics are devices that diagnose disease or certain conditions and include companion diagnostics (the identification of biomarkers to inform treatment options supporting precision medicine strategies).

Clinical Trials of Medicinal Products & Advanced Therapies

UK Clinical Trials Regulations apply to trials that test the safety or efficacy of medicinal products, including medicines, vaccines, and advanced therapies such as gene or cell
therapies. This page covers some basics and links to new regulatory and approvals guidance for these trials. A comprehensive guide to the UK Clinical Trials Regulations is in the Clinical Trials Toolkit. For studies that explore mechanism of action, see our Experimental Medicine Toolkit.

Facilities and initiatives that can help with translation

A list of national and local facilities or initiatives that can help you develop your healthcare product.

Influencing new regulations

Find out what we are doing in the MRC Regulatory Support Centre to influence new regulations, and about the role that regulatory science can play.
Medical Devices & In Vitro Diagnostics

Know the basics

- Knowing whether your product is a medical device isn’t always easy, it depends on legal definitions which differ within the UK, and between Great Britain and the EU.
- In order to place a medical device or in vitro diagnostic on the market, it needs a mark to show that it conforms to relevant regulatory requirements (mark of conformity), this is a CE mark, CE NI mark, or UKCA mark, depending on the regulations and market.
- What manufacturers need to do to obtain a mark of conformity depends on the device risk class. For low-risk devices and diagnostics, manufacturers can self-assess; high risk ones need conformity assessment by an independent body, a Notified Body or a UK Approved Body.
- As an academic researcher you are unlikely to manufacture the device or diagnostic and will not therefore apply for a mark of conformity yourself. However, academic research will need to conform to relevant regulations in order to accelerate translation and commercialise. This is likely to include having an appropriate quality management system in place. Work with your University Translation office and/or commercial partner to determine what this means for you.
- There are exemptions for in-house manufacture, also known as the health institute exemption in new EU regulations.
- A clinical study that trials a device in/on a person, is called a Clinical Investigation.
- A study that validates an in vitro diagnostic for medical use is a Performance Evaluation.
- The MHRA regulates devices and in vitro diagnostics in the UK; they must be notified of Clinical Investigations and Performance Evaluations; and they oversee UK Approved Bodies.

UK Medical Device Regulation

MHRA’s overview of medical device regulation in the UK, outlines the differing requirements for Great Britain and Northern Ireland (where the new EU Medical Devices Regulation applies).

If you are in a position to market your device before 30 June 2023, you may wish to comply with EU Medical Devices Regulation (EU MDR) or EU in vitro Diagnostic Regulation (EU IVDR) in order to gain a CE mark and access both the UK and EU markets. EU Notified bodies and CE marking will continue to be recognised by the MHRA up to this date.

All Medical devices and IVDs which are to be placed on the UK market need to be registered with the MHRA. The manufacturer is responsible for registration.

Requirements for marketing in Great Britain (Scotland, England, Wales)

The Medical Devices Regulations 2002 apply to manufacturers of medical devices, active implantable devices and in vitro diagnostics; and to academics who intend to commercialise.
The following will help you determine if your product is a medical device in Great Britain:

- **Overview of MHRA legal compliance guidance** for definitions of: Medical Device, Active Implantable Medical Device and In vitro Diagnostic Medical Device.
- **Classifying your medical device**, helps you apply the classification rules in practice.
- **Borderlines with medical devices and other products in Great Britain** for guidance on whether or not your product is a medical device.
- **Borderline between medical devices and medicinal products in Great Britain** for guidance on whether your product is a medical device or a medicinal product.
- **Medical devices: software applications (apps)**, helps determine if your software/app is a medical device or an in vitro diagnostic, and which class.

**Legal compliance guidance for Great Britain**

MHRA have detailed guidance on how to comply with the legal requirements for the Great Britain market and around Conformity assessment and UKCA marking and specific guidance for In vitro diagnostics.

MHRA **summary of requirements for Class 1 medical devices**.

MHRA guidance on exemptions for in-house manufacture: for medical devices and for in vitro diagnostics (section 2.7 and appendix).

**Requirements for Northern Ireland and EU**

Northern Ireland and the EU implemented the new EU Medical Devices Regulation in May 2021 and the new EU In Vitro Diagnostic Regulation will apply from 26 May 2022. The following resources provide help with compliance:

- **MHRA guidance for Northern Ireland implementation of EU MDR and EU IVDR** and their interactive guide.
- **MHRA guidance on health institute exemption under EU MDR and EU IVDR**.
- **Oxford Global Guidance** to help you determine whether your medical device is within scope of EU MDR or EU IVDR, and its class.
- The EU Commission has a series of factsheets to help navigate EU MDR and EU IVDR.

Two publications regarding **Companion diagnostics** under the new IVDR.

- **Companion Diagnostics: requirements under the new IVDR**
- **Implementing the EU in vitro diagnostic regulation – a European regulatory perspective on companion diagnostics**
Clinical Investigations of Medical Devices - UK

MHRA Clinical investigations of medical devices - guidance for investigators. gives an overview for investigators involved in the clinical investigation of unmarked medical devices.

MHRA’s Clinical investigations of medical devices - guidance for manufacturers has more detail on UK requirements, outlines when you need to do a clinical investigation, addresses special circumstances and things to consider when planning a clinical investigation.

The MHRA needs to be notified of the intention to run a clinical investigation for a medical device. This must be done at least 60 days in advance. An overview of the process can be found in notify the MHRA about a clinical investigation for a medical device.

See also MHRA guidance on in-house exemptions for notification of clinical investigations.

Clinical Investigations of medical devices - compiling a submission to MHRA details how to make an application in IRAS. Including specific guidance on the requirements for software (i.e. standalone software or software incorporated into a medical device).

Guidance on demonstrating the biological safety of a medical device can be found in Clinical investigations of medical devices - biological safety assessment.

Clinical investigations of medical devices - statistical considerations offers guidance on the design for clinical investigations, for example considerations for sample size and the study population.

Performance Evaluation of an in vitro diagnostic - UK

Performance Evaluations can be done by comparing the in vitro diagnostic under investigation with an established method/device with regards to sensitivity, specificity and ability to meet clinical needs. Instruments, apparatus, appliances, materials or other articles which are intended to be used for research purposes without any medical objective are not regarded as devices for performance evaluation. For more on performance evaluations, see section 2.5 of MHRA IVD Guidance.

 Companion diagnostics - Trials which determine the clinical performance of an assay (biomarker validation) are performance evaluation studies.

All IVD performance evaluation studies need to be registered with MHRA.

Other sources of guidance and scientific publications

The Health Research Authority (HRA) has various e-learning modules, one of which covers medical devices.

The NIHR offers advice for medical technologies and in vitro diagnostic tests.

Guidance from the British Standards Institution

The British Standards Institution (BSI) is a UK Approved Body/EU Notified Body for medical devices. You can read more about UKCA marking in BSI’s gaining market access in the UK. You can also learn about CE marking in BSI’s CE marking for medical devices.
BSI’s medical devices on demand webinars may also be of interest. Those around performance evaluation of devices under EU Medical Devices Regulation (EU MDR) and EU in vitro Diagnostic Regulation (EU IVDR) and UKCA and post Brexit changes under “Market access requirements”.

Software and AI

Medical devices: software applications (apps), MHRA guidance to help determine if your software/app is a medical device or an in vitro diagnostic, and which class.

Learn about MHRA’s software and AI as a medical device change programme.

Standalone medical device software: The evolving regulatory framework by McCarthy and Lawford 2015, introduces the regulatory framework in the US and EU and includes six examples of standalone software classed as a medical device.

If you are working on AI for healthcare then the NHS AI Lab provides guidance on AI development, case studies and challenges faced by others and how they overcame them.

These publications highlight the importance of diversity of the data used to develop AI algorithms to avoid any bias, an Opinion piece in the American Scientific and Geographic Distribution of US Cohorts Used to Train Deep Learning Algorithms by Kaushal et al (Sep 2020).

For help with health data discovery and access, see HDR UK’s Innovation Gateway and our Health Data Access Toolkit.
Clinical Trials of Medicines & Advanced Therapies

Clinical Trials Regulation - Know the basics

- Trials within scope of the Clinical Trials Regulations are called Clinical Trials of Investigational Medicinal Products (CTIMPs), or MHRA tend to just say Clinical Trials.
- UK Clinical Trials Regulations apply to trials that test the safety or efficacy of medicinal products, including medicines, vaccines, gene and cell therapies, etc. If you are planning an Experimental medicine study, exploring mechanism of action, the regulations may not apply. Our Experimental Medicine Toolkit has more on these (see also the next point).
- It isn’t always easy to determine if your trial is within scope of the UK Clinical Trial Regulations. See MHRA guidance When a Clinical Trial Authorisation is needed.
- It is a legal requirement to have a sponsor for a CTIMP. In academic trials this is generally the employer of the chief investigator (it’s unlikely to be the funder). Sponsors have legal obligations and corporate systems in place to manage these.
- Your trial must get approval from the relevant department in the sponsoring organisation. In Universities this is usually the University Sponsor’s office, Research Office or Research Governance department. In the NHS, it is usually the NHS R&D office.
- Other approvals include the Clinical Trial Authorisation from the MHRA and NHS Research Ethics Committee (REC) approval. In England and Wales HRA Approval includes NHS REC review and global governance checks. NHS trial sites also need to do local capacity and capability assessment. All applications should be made in IRAS.
- It is a legal requirement to work to the principles of Good Clinical Practice (GCP). If you are conducting a trial with commercial partners and the data will be used to support a marketing authorisation, you are likely to meet the more prescriptive demands of ICH GCP.
- You must register your CTIMP and publish your results.

Clinical Trials Toolkit for guidance on the legal requirements for CTIMPs.

UK clinical trials regulation

Overview of MHRA requirements for UK clinical trials. Certain aspects are highlighted below.

MHRA scientific advice for medicines, including clinical trial advice.

Is it a CTIMP?

MHRA guidance: When is a Clinical Trial Authorisation needed?

MHRA guide to what is a medicinal product.

Borderline products: how to tell if your product is a medicine.

Where it is unclear whether a product is a medical device or a medicine see Borderline between medical devices and medicinal products in Great Britain.
MHRA and HRA approvals for Clinical Trials

Guidance on MHRA and HRA approvals can be found here:

- MHRA guidance on clinical trial applications in the UK.
- HRA guidance on HRA approval (for trials led from England or Wales).
- Guidance for Trials led from Scotland
- Guidance for trials led from Northern Ireland

The Combined Review Service brings together a single CTIMP application for both Clinical Trial Authorisation and Research Ethics Committee opinion. Open now, combined review will be the only way to apply for these approvals from Jan 2022.

The MHRA has published common problems with clinical trial applications and guidance on how to avoid them Common issues identified during clinical trial applications.

Your clinical trial sponsor is responsible for submitting your clinical trial application to the MHRA. (Clinical trial sponsors must register to make submissions to the MHRA).

Amendments and reporting

If you make changes to your trial after approval, an ‘amendment’, then the MHRA (and others) may need to know about this. For further guidance on amendments please see:

- HRA Amending an approval
- MHRA guidance on substantial amendments to a clinical trial

Change of Principal Investigator (PI) or the addition of an NHS site (or HSC site in Northern Ireland) are no longer substantial amendments: Key changes to UK amendment process.

Your clinical trial sponsor is responsible for submitting substantial amendments to the MHRA.

There are various reporting requirements for clinical trials (e.g. safety reports, progress reports, end of trial notifications, etc). For further guidance, please see HRA managing your approval.

Your clinical trial sponsor is responsible for submitting end of trial notifications and Developmental Safety Update Reports (DSURs) to the MHRA.

If you are a clinical trial sponsor MHRA Guidance for Sponsors on submitting Clinical Trial safety reports is useful, this includes information on the transition between reporting to EU and UK systems.

Importing and Exporting

If you need to import or export clinical trial supplies for your trial, you should contact your clinical trial sponsor.

If you are a clinical trial sponsor you may find the following resources useful:

- MHRA guidance list for import and export (is the headline page with full list of guidance)
• Importing IMP to Great Britain from approved countries
• Supplying IMP to Northern Ireland

Trials with sites in the EU

For clinical trials in the EU, your clinical trial sponsor will need to make submissions on the Clinical Trials Information System which will go live on 31 January 2022. (The EMA is providing training for the new system).

Additional information specific to Advanced Therapies

MHRA provide guidance on Advanced therapy medicinal products regulation and licensing, including how to get Regulatory advice for Regenerative Medicines.

Please also see Human Tissue Authority human application pages for those developing cell and tissue-based therapies. HTA regulates those undertaking procurement, testing, processing, storage, distribution, import and export of tissues and cells for human application.

If using human embryos, please see guidance from HFEA on research.

Information around advanced therapies in the EU can be found on the EMA website. A good overview of the EU (also US and Japan) regulatory framework can be found in the following resources:

• Taking Advanced Therapy Medicinal Products (ATMPs) to Market, by Daniel Rabbie 2018
Facilities and initiatives that can help with translation

National Initiatives

This is not a comprehensive list of national resources, please let us know of others that you are aware of: rsc@mrc.ukri.org

MRC Translation research for funding opportunities

MHRA Innovation Office for regulatory advice

NIHR Experimental Medicine Infrastructure enables researchers to develop clinical applications from scientific breakthroughs, and translate these discoveries into new treatments for patients.

NIHR Medical Technology, device and diagnostic support

NIHR can provide collaborations, services and support for your research

NHS Accelerated Access Collaborative

NHS AI Lab

Multi-agency advice service for AI – in development

Cell and Gene Therapy Catapult

Digital Catapult

Examples of local initiatives and facilities

Here are a couple of examples of how universities are accelerating translation, if you would like to showcase any others, please let us know: rsc@mrc.ukri.org

Therapeutic Innovations Networks are hosted by the UCL Translational Office. They aim to bring together multidisciplinary researchers and industry experts to tackle common obstacles and mobilise around strategic opportunities to accelerate translation. Networks include Biologics, Cell & Gene Therapies, Devices & Diagnostics, Regenerative Medicines, Repurposing and Small Molecules.

The University of Edinburgh Healthcare Technology Accelerator Facility (HTAF), is an initiative to expedite the development and commercialisation of healthcare technology. HTAF remove the barriers that frequently prevent the development and translation of new healthcare technology, by providing facilities and services such as biological validation labs, specialist manufacture, regulatory experts, experienced project managers, access to industry collaborators, etc.
Influencing new regulations

Following EU Exit, there is an opportunity for UK to regulate healthcare product development differently. The Medicines and Medical Devices Act 2021 paves the way for this. The detail of this regulation will be in secondary legislation, which the MHRA is currently planning for.

MRC Regulatory Support Centre activities

In the MRC Regulatory Support Centre, we help ensure that the academic voice is heard by those drafting new regulations. We do this in the following ways:

- **Membership of MHRA-led working groups**
- **Convening academic groups.** Establishing stakeholder groups with representation from investigators, Clinical Trial Units and university sponsors to provide written comments and discuss proposals with key staff at MHRA.
- **Hosting events** for the academic community in collaboration with regulators, to facilitate wider discussion and input. E.g. hearing from the academic devices community what works and doesn’t work in current legislation. Furthering the discussion with a small working group to see how RSC can add value to facilitate academic device development.
- **Responding to public consultations**, convening input from the MRC-funded translational research community.

If you are interested in learning more or want to get involved, please email rsc@mrc.ukri.org

Regulatory Science

In the recent past new technologies have accelerated advances in fields such as use of AI in medicine, personalised healthcare and drug discovery. New technologies in healthcare (and some existing ones) are not always well catered for by current regulation, and different approaches and regulatory standards may be required to ensure that these products are safe and effective, and that they work as intended. Regulatory science determines how best to do this, it is multidisciplinary by nature, bringing together experts in ethics, regulation, policy-making, quality management, medicine, economics, research and biotechnology, etc.

**Birmingham Health Partners Centre for Regulatory Science and Innovation (CRSI)**

This centre was established in 2020 to support the development and delivery of novel therapeutics and medical devices in the UK, through advanced regulatory standards and tools. A truly multidisciplinary initiative, CRSI brings together experts in medicinal science, health policy and management, clinical trial design, medical law and patient-reported outcomes research, from across Birmingham Health Partners member organisations.

**Newcastle University Centre for Regulatory Science**

The Newcastle Regulatory Science Centre aims to deepen understanding of safety, effectiveness and value of medicines and devices using interdisciplinary scientific knowledge. The team works in development and translation of pharmaceutical, medical devices and health
products. They carry out empirical work on safety, efficacy, quality and cost effectiveness, that they link to regulatory systems for health technology assessment, approvals and market access, clinical guidelines for medicines, vaccines devices and other new therapies.