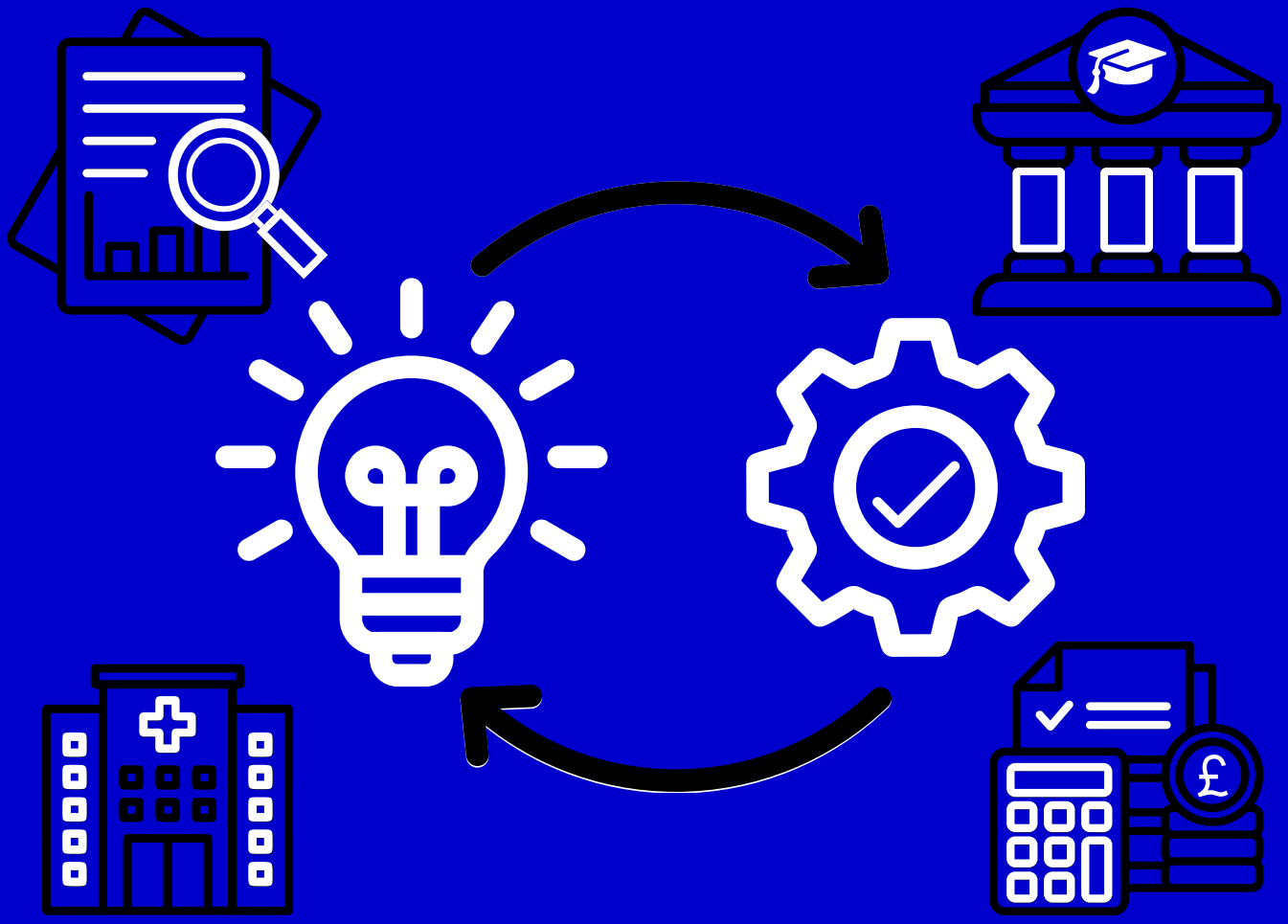
IMPERIAL

MedTechONE

FROM IDEA TO ADOPTION



MT1

COLLABORATIVE

www.imperial.ac.uk/medtechone/

FROM IDEA TO ADOPTION

The path to commercialisation is long and complex. From the synthesis of an innovative idea, through testing and iterations, through clinical trials, and through regulatory and commercialisation processes, this set of resources aims to de-mystify some of the key concepts you should be aware of.

As it was too bulky to have all of the information in a single resource, we recommend you read this document alongside the other parts of this piece on the MedTechONE Collaborative webpage.

CONTENTS

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CLINICAL RESEARCH VS MARKET RELEASE

The choice between pursuing a clinical research project vs market release depends on multiple factors:

WHAT EVIDENCE DO YOU NEED TO GO TO MARKET?

- What is required by regulatory standards?
- If aiming for the NHS, what evidence is required?
- What Risk Classification does your product come under? Higher risk devices will require more evidence.
- Reimbursement needs - You need to be able to demonstrate cost effectiveness
- What is the target market? Adoption of more novel, non-standard technologies is reliant on a solid evidence base and scientific proof of efficacy.

REGULATORY PATHWAY

- Have you achieved CE / UKCA marking?
- Do you need FDA approval?
- Do you need MHRA approval?

CLINICAL RESEARCH VS MARKET RELEASE

READINESS LEVELS: WHERE DOES YOUR INNOVATION SIT ON THE:

- **Technology Readiness Level**
- **Business Readiness Level**
- **Commercial Readiness Level**

PRODUCT MATURITY

- **What evidence of efficacy and / or value do you have?**
- **Is the product ready for market or still in development?**
- **Have you planned manufacturing?**
- **Have you completed economic assessments to price out scale up into a company, and also studies on how to price the end product?**

Ultimately you should choose clinical research first if:

- The technology is entirely novel, and there is no existing evidence base for safety and efficacy.
- The technology is high risk e.g. implantables, life-sustaining technologies etc.
- Costs – The device is expensive.
- Support is needed from Key Opinion Leaders

CLINICAL RESEARCH VS MARKET RELEASE

Alternatively, you could go straight to market release if:

- The technology is an incremental innovation, builds on existing work and evidence, and is based on well-understood existing scientific evidence.
- The technology is low risk, requires minimal intervention, and has a low invasiveness e.g. mobility aids, eyeglasses, reusable surgical instruments.
- You can demonstrate there is a very real need for real world data that cannot be measure through scientific study.

Overall, this is not a decision that would be made by a single person, and it is recommended to consult financial, legal and other experts within the field to ensure you are compliant with regulatory and safety standards across the course of your innovations journey, and to give your technology the best chance of success.

REGULATORY LEGISLATION

REGULATORY LEGISLATION

CE MARKING & OTHER REGULATIONS

CE MARKING FOR THE UK AND EU MARKET

The EU no longer recognises UK Notified Bodies, and UK Notified Bodies are no longer able to issue CE Certifications. These Bodies have become UK Approved Bodies. Refer to the IES CE Marking & UKCA Marking Guide for detailed information.

REGULATING MEDICAL DEVICES IN THE UK

The Medicines and Healthcare Products Regulatory Agency (MHRA) is responsible for the regulation of medical devices made available on the market in Great Britain. As part of this, **all medical devices must be registered with the MHRA before being placed on the market** – This includes in vitro diagnostic tools, implantable devices, and any custom-made devices, systems, or procedure packs, as well as more classical definitions for “medical devices”.

The MHRA is responsible for:

- Performing market surveillance in the UK and making decisions about the marketing and supply of medical devices in the UK.
- The designation and monitoring of UK conformity assessment bodies.
- Enforcement of legislation on medical devices in the UK.

The MHRA will only accept registrations for devices manufactured in the UK. For devices being manufactured outside of the UK, but being placed on the UK market, you must appoint an appropriately qualified Responsible Person to carry out all necessary tasks, including MHRA registration (the full responsibilities of the Responsible Person are laid out in the UK MDR 2002).

REGULATORY LEGISLATION

REGULATING MEDICAL DEVICES IN THE UK

All device manufacturers must comply with relevant product marking and conformity assessment requirements for medical devices.
Below is a short summary of the general responsibilities of the Responsible Person;

They must:

- Ensure that the declaration of conformity and technical documentation have been written, and that, where applicable, an assessment of conformity has been conducted by the manufacturer.

- Keep available a copy of the:
  - Technical documentation
  - Declaration of Conformity
  - Certificates

This includes any amendments and supplements and must be available on any request from the MHRA.

- When requested by the MHRA, provide any and all documentation required to prove the conformity of the device.

- When requested by the MHRA, and where the Responsible Person has access to the following, provide the MHRA with samples or access to the device.

- Where the Responsible Person does not have samples or access to the device, communicate any request from the MHRA to the manufacturer, and communicate to the MHRA the manufacturer's ability or willingness to provide samples or device access.

- Fully co-operate with the MHRA to eliminate and/or mitigate any risks associated with the device.

- Immediately inform the manufacturer of any complaints or incidents reported by users, clinicians, healthcare professionals or patients relating to the device.

- Where the manufacturer acts contrary to its regulated obligations under this legislation, the Responsible Person must:
  - Terminate the legal relationship with the manufacturer; and
  - Inform the MHRA, and any other relevant Approved Body, of the termination.

REGULATORY LEGISLATION

REGULATING MEDICAL DEVICES IN THE UK

N.B. Failure to register your device with the MHRA via an appropriate channel means you will not be able to lawfully place your device on the market.

Due to the UK leaving the EU, **there are some upcoming changes about the requirements for CE marks** on medical devices.

CE marked devices may be placed on the Great British / UK market to the following timelines:

- General medical devices compliant with the EU Medical Devices Directive (EU MDD) or EU Active Implantable Medical Devices Directive (AIMDD) with a valid declaration and CE marking can be placed on the market in Great Britain until the certification expiry, or 30th June 2028, whichever date is closest.
- In vitro Diagnostic Medical Devices (IVDs) compliant with the EU In Vitro Diagnostic Medical Devices Directive (EU IVDD) can be placed on the market in Great Britain until the certification expiry, or 30th June 2030, whichever date is closest.
- General medical devices including custom-made devices, compliant with the EU Medical Devices Regulation (EU MDR) and IVDs compliant with the EU In Vitro Diagnostic Medical Devices Regulation (EU IVDR) can be placed on the market in Great Britain until 30th June 2030.

It is a legal obligation to register your device with the MHRA, via an appropriate channel.

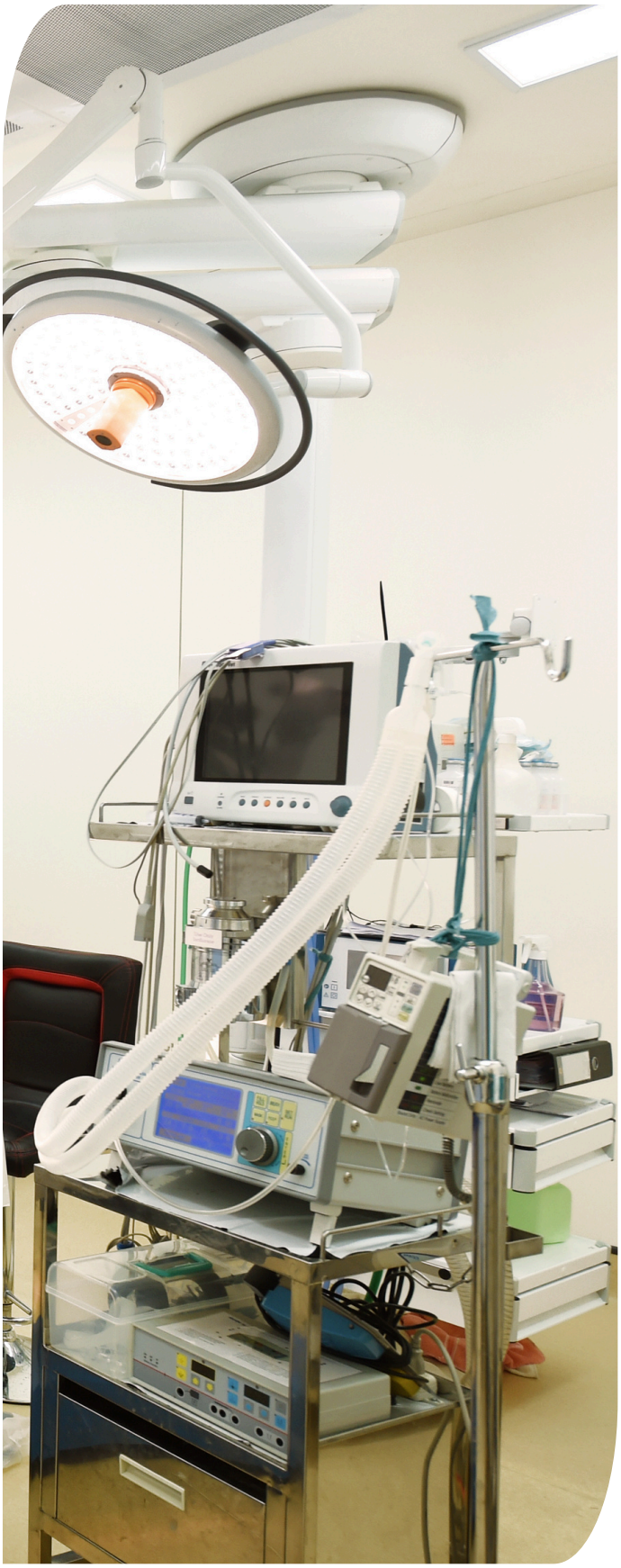
REGULATORY LEGISLATION

REGULATING MEDICAL DEVICES IN THE UK

Below is a short summary of the legislation that currently applies in Great Britain, note **that the route to market in Great Britain is informed by the below EU Directives, and may change at the end of the transition period**:

- Devices in Great Britain are regulated under the Medical Devices Regulations 2002 (SI 2002 No 618, as amended) (UK MDR 2002). This overarching legislation gave effect in UK law to the following:
  - **Directive 90/385/EEC** – Active implantable medical devices
  - **Directive 93/42/EEC** – Medical Devices
  - **Directive 98/79/EC** – In vitro diagnostic medical devices

You should consider obtaining professional expert advice and may need to check with a solicitor who specialises in this area to check which legislative framework applies to your device.



REGULATORY LEGISLATION

MHRA CLINICAL INVESTIGATIONS

CLINICAL INVESTIGATIONS UNDER THE MHRA - FOR THE APPROVAL OF NOVEL MEDICAL DEVICES

You may need to conduct a clinical assessment as part of the UKCA / CE Marking process, or equivalent. **You must inform the MHRA of the planned investigation at least 60 days prior to commencement.**

N.B. A notification is not required where the device under investigation is already approved/marked for the purpose under investigation.

The process for Clinical Investigations is as follows:

- MHRA applications are submitted automatically via IRAS.

- **Coordinated Assessment Pathway** – MHRA collaborates with the HRA to share information when assessing medical device clinical investigations. The MHRA application should be submitted first, and then the REC application submitted as soon as the MHRA approval is received.
  - When the MHRA receives the documentation, they will contact the Lead Investigator within 5 days to confirm the 60-day assessment period has commenced.
  - The assessment will involve experts assessing the medical device, and the design and safety of the planned project.
  - If you require a clarification, or if you object to any decisions, you must immediately contact the MHRA to arrange a teleconference to discuss a resolution.
  - A letter will be sent by the 60th day of the timeframe to confirm the decision as either “No Objection”, or “Objection” to the commencement of the proposed project.

REGULATORY LEGISLATION

MHRA CLINICAL INVESTIGATIONS

You will be required to pay a fee to conduct a Clinical Investigation. **N.B.** A final decision will not be received until payment has been received by the MHRA.

- For specific enquiries, email info@mhra.gov.uk
- If you require a Regulatory Advice meeting, contact the Head of Clinical Investigations at mark.grumbridge@mhra.gov.uk

Over the course of a Clinical Investigation, **you must comply with any instructions from the MHRA**, including the submission of Quarterly Summary Reports, and End of Study Reports (EoS Reports should be emailed to CI-applications@mhra.gov.uk).

AMENDMENTS

Once a Letter of No Objection is received, you must subsequently immediately notify the MHRA of any amendments or changes to the project, including:

- The device under investigation.
- Study documentation, including the clinical investigation plan.
- Investigators or investigating institutions.
- Changes requested by an ethics committee.

N.B. If you do not notify the MHRA of amendments, you may be subject to prosecution.

Amendments should be completed in IRAS.

Additionally, the MHRA requires receipt of:

- A cover letter with the MHRA Registration ID, Company/Organisation name and address, contact name and email address of the person responsible for paying the fee, and, if applicable, a PO number or equivalent.
- A table with each proposed change and the justification for each item.
- Track changes and clean copies of all amended study documents.
- Proof of payment – The website includes instructions for making payments.

REGULATORY LEGISLATION

MHRA CLINICAL INVESTIGATIONS

- A signed statement by, or on behalf of, the manufacturer that the proposed changes do not predictably increase the risk to the patient/end user/third party.
- Email the above and any relevant documentation to CI-amendments@mhra.gov.uk

EARLY TERMINATION

Sponsors must notify the MHRA of an early termination, provide justification for the termination, and submit the Final Report.

Sponsors must also notify the MHRA in the event of a temporary suspension, and the justification for it.

FEE WAIVERS FOR MHRA CLINICAL INVESTIGATIONS

- **Pilot of a medical device clinical investigation fee waiver** programme for micro and small companies: From 5th Jan – 31st Mar 2026, the MHRA is trialling a waiver programme for small companies creating novel and innovative devices in Classes I, IIa, and IIb. At the end of the pilot the MHRA plans to analyse and report on the outcomes and decide if the fee waiver will become common practice.
- **Easements for small and medium enterprises:** Available to SME companies for clinical investigations, upon receipt of a valid application the MHRA will request 50% of the fee, and the remaining 50% will be payable within 6 months of the issue date of the first invoice. This does not cover device regulatory advice meeting fees. In the event of an objection or withdrawal of the application, the remaining 50% is due immediately.

REGULATORY LEGISLATION

SPECIAL CIRCUMSTANCES

SPECIAL CIRCUMSTANCES FOR HEALTHCARE INSTITUTIONS

You <u>do not</u> need to notify the MHRA of a clinical investigation if:

- You have manufactured the medical device in-house, for your own patients only, with no intention to place the device on the market.

You may need to notify the MHRA if:

- You want to provide a medical device to another organisation, that up until now has been manufactured in-house for your patients only, including sharing the device with another organisation as part of data gathering and research exercises to support the safety and performance of a commercial product.

REGULATORY LEGISLATION

REGULATING IVDs IN GREAT BRITAIN

GUIDANCE ON THE REGULATION OF IN VITRO DIAGNOSTIC MEDICAL DEVICES IN GREAT BRITAIN

Of note, devices that are manufactured within a healthcare institution for sole use on/by their patients (in-house manufacture) are exempt from the UK MDR 2002.

Documentation: You must retain, and make fully available for inspection, the Declaration of Conformity, and any technical documentation, formal decisions, reports, and certificates from UK Approved Bodies (or equivalent), for 5 years after the manufacture of the last device.

CE Marking: CE marked medical devices will continue to be accepted on the GB market until June 2030.

UKCA Marking: Manufacturers may voluntarily use UKCA marking until June 2030. The manufacturer must not apply UKCA marking unless they have fulfilled the applicable UK MDR 2002 requirements.

Health Institutions: A body whose primary purpose is the care and/or promotion of public health (free standing labs, including those for diagnostics, do not qualify) (clinics established for purely diagnostic purposes also do not qualify) (establishments with the primary goal of "healthy lifestyles", such as gyms or spas, do not qualify).

The MHRA broadly considers a healthcare institution as a single legal entity (e.g. an NHS Trust rather than a single hospital), though there may be exceptions where two legal entities may be treated as a single healthcare institution; this is dependent on precise circumstances, including:

- Close association and common identity.
- Shared premises and facilities.

The exemption will apply when:

- A device is manufactured and used within the same health institution, on the premises of manufacture; or
- A device is manufactured and used within the same health institution, on premises in the immediate vicinity (provided the device has not been transferred to another legal entity).

REGULATORY LEGISLATION

REGULATING IVDs IN GREAT BRITAIN

The full guidance contains a comprehensive list of scenarios and when the exemption from UK MDR 2002 requirements applies.

The UK MDR 2002 may apply for joint ventures between multiple establishments, even if the device will be placed on the market by a third party.

If uncertain of whether the exemption applies, check the above guidance, or submit an application via IRAS (which will be sent to the MHRA automatically).

Check the “Further Reading & Resources” section of this document for a link to the full regulatory guidance.

LICENSE TO MANUFACTURE & LEGAL MANUFACTURER

LICENSE TO MANUFACTURE & LEGAL MANUFACTURER

The **"Legal Manufacturer"** is the business or entity that holds full regulatory responsibility for the design, manufacture, and market placement of a medical device. They are also responsible for ensuring full compliance with any applicable regulations and standards.

Core responsibilities for legal manufacturers can include:

- Design and Development of the product, including design phases, validation work, and risk management in relation to regulatory responsibilities and user needs.
- Primary manufacturing and quality control
- Regulatory compliance
- Post-market surveillance
- Labelling and Instructions for Use (IFU)

"Manufacturer" is defined as "a natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured, or fully refurbished, and markets that device under its name or trademark."

Licenses to Manufacture are issued by the Medicines & Healthcare Products Regulatory Agency (MHRA). The licensing process requires you, or your company, to demonstrate to the MHRA that your processes and product are compliant with EU Good Manufacturing Practice (GMP), and that they pass regular GMP inspections of your manufacturing sites.

You can find more information on applying for a License to Manufacture, and links to start the process, at the full guidance linked in the "Further Reading & Resources" pages of this document.

LICENSE TO MANUFACTURE & LEGAL MANUFACTURER

Items to note:

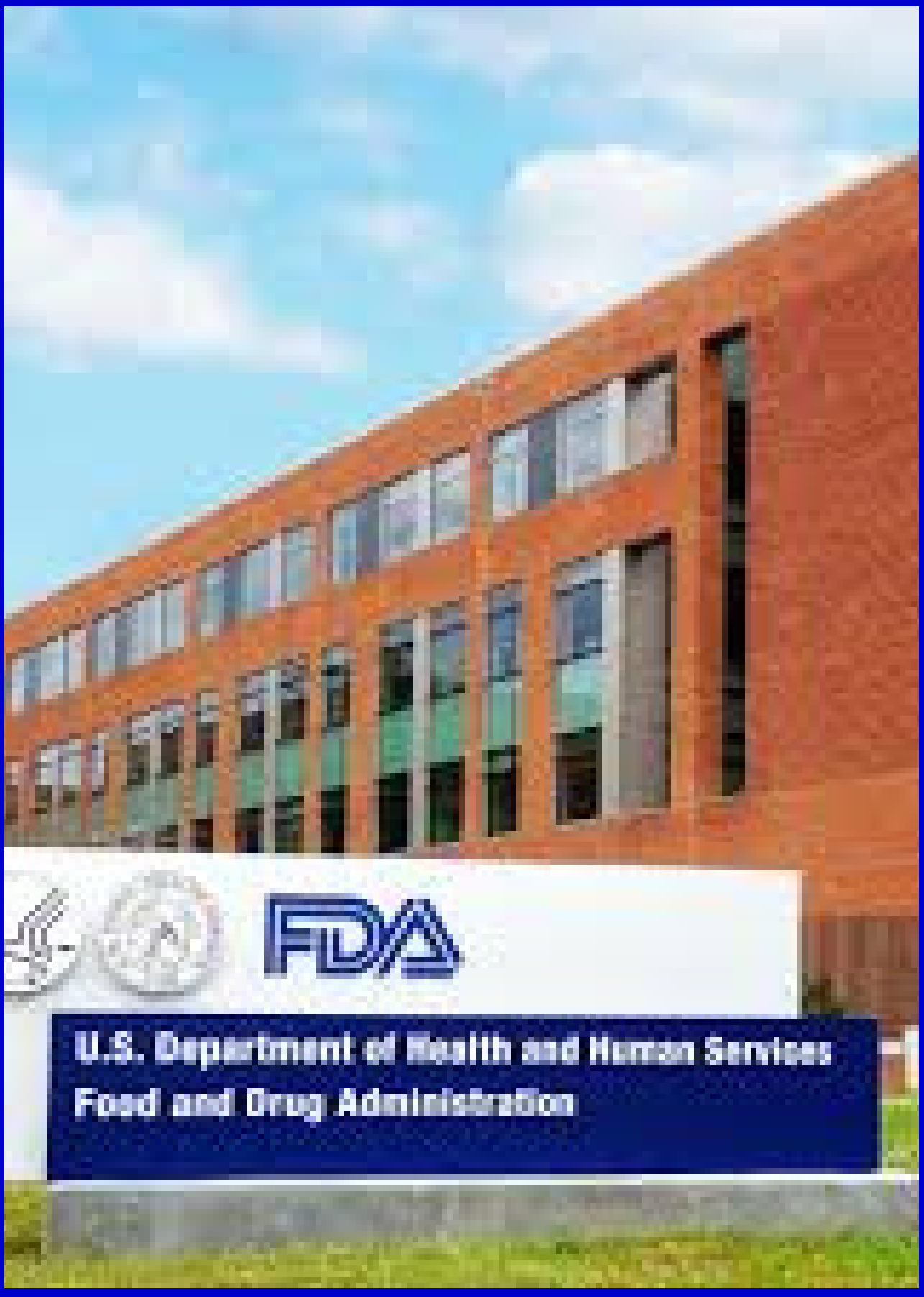
- Your application will take 90 working days to process.
- Variations to existing licenses should take 30 working days to process, extended to 90 working days if an inspection is required.
- The MHRA will check the identities of the responsible persons and named staff and will check your named company registered with Companies House.
- Inspections will require a Site Master Plan / File for every manufacturing site.

When the Inspectors are satisfied, and any identified issues have been rectified, the MHRA will complete your registration, and you will receive:

- A Licence document
- A Manufacturer's Certificate of Good Manufacturing Process (GMP) for each inspected site
- (For Wholesale Distributors) a Certificate of Good Distribution Practice (GDP) for each inspected site.

N.B. This licensing process does incur a fee from the MHRA and requires an annual fee to maintain the licence (in April of each year). You will be sent an invoice annually. The fee is directly related to the type of licence, the number of sites, and the income from any licensed wholesale businesses.

FDA REGULATIONS



FDA REGULATIONS

For access to the US market, your product and manufacturer must be approved by the FDA.

N.B. You do not need FDA approval if you only intend to market your product in the UK/EU, instead you will require UKCA/CE marking.

Medical devices are separated into:

CLASS I

Low risk, minimal harm potential, simple design

CLASS II

Moderate to high risk. Subject to special controls including performance standards and post-market surveillance, and usually 510(k) approval.

CLASS III

High risk, including implants, life-supporting equipment, life-sustaining equipment, and devices that pose a potential unreasonable risk of illnesss or injury.

FDA REGULATIONS

FDA Regulatory Controls include:

General Controls Applies to all classes, and covers registration, listing, Good Manufacturing Processes (GMP) and labelling and instructions for use.

Special Controls Specific, additional requirements for Class II devices including performance standards and specific market surveillance.

Pre-market Approval Rigorous, scientific review for Class III devices, or devices not found to be substantially equivalent to an existing Class I or II device.

510(k)

510(k) Approval A pre-market submission for Class II, and some Class III, devices designed to demonstrate they are “substantially equivalent” to an existing legally marketed device.

N.B. Most Class I and II devices are exempt from 510(k) submission. You can see a list of exempt devices here: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/315.cfm
Additionally, some devices may be required to go through multiple processes prior to approval.

For devices under clinical investigation, you can apply for an **Investigational Device Exemption (IDE)** to allow the investigational device to be used in the study to collect the safety and effectiveness data required for a Pre-market Approval application/510(k) Submission. However, clinical studies for Class III devices must be approved by the FDA and by an Institutional Review Board (IRB) prior to study commencement.

FDA REGULATIONS

The basic regulatory requirements for manufacturers of medical devices on the US market must comply with are:

- **Establishment Registration** – This applies to both domestic and foreign manufacturers, and importers, of medical devices placed on the US market. Applications are submitted digitally, and must be verified annually between 1st October and 31st December. Foreign manufacturers must also designate a US Agent to act on their behalf. This registration incurs a fee. Check the "Further Reading & Resources" section for links to more detailed information.
- **Medical Device Listing** – Manufacturers required to list their devices with the FDA include:
  - Manufacturers
  - Contract manufacturers
  - Contract sterilisers
  - Re-packagers and labellers
  - Specification developers
  - Re-processors of single-use devices
  - Re-manufacturers
  - Manufacturers of accessories and components sold directly to the end user
  - US manufacturers of export only devices

FDA REGULATIONS

Other items related to FDA Device Listing & Registration include:

- **Premarket Notification 510(k)**, unless exempt, or **Premarket Approval** – The 510(k) approval demonstrates that the device is substantially equivalent to an existing, commercially distributed device; you cannot place your device on the market without a Letter of Substantial Equivalence. Alternatively, high risk Class III devices must have Premarket Approval.

- **Investigational Device Exemption (IDE) for clinical studies** – For devices under clinical investigation, you can apply for an Investigational Device Exemption (IDE) to allow the investigational device to be used in a clinical trial. Clinical studies for Class III devices must be approved by the FDA and by an Institutional Review Board (IRB) prior to study commencement.

- **Quality Management System Regulation (QMSR)** – The QMSR covers the regulation of the methods used in, and the facilities and controls used for the design, manufacture, packaging and labelling, storage, installation, and servicing of all medical devices intended for human use. Facilities will be required to undergo inspections to ensure compliance.

- **Labelling Requirements** – This covers both physical labelling on devices as well as instructions for use and accompanying information provided with the device.

- **Medical Device Reporting (MDR)** – The mandatory reporting system for events where a medical device has, or is suspected to have, caused or contributed to a death or serious injury. Additionally, certain malfunctions or unexpected device deficiencies need to be reported.

AN INTRODUCTION TO ISO STANDARDS

INTRO TO ISO STANDARDS

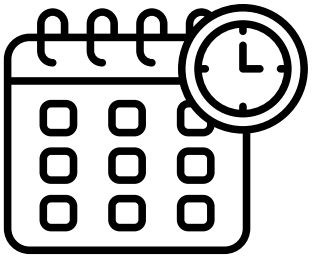
The International Organisation for Standardisation began its work in 1946, aiming to bring together global experts to create international standards for processes such as manufacturing, quality assurance, product safety, and process management. **You do not need to have an understanding of all ISO standards, but there are a few that may be applicable to your research, or to technology you are developing.** It is also possible to achieve ISO Certification, your technology can be assessed and approved / certified as being in line with the relevant ISO Standards by auditing or regulatory bodies (see in particular, ISO 13485).

It is recommended to include information on any ISOs you will be adhering to within your SOPs. Unfortunately, access to the full standards is not free, but check with your organisation who may be able to provide access to the guidance. It should also be noted that the below ISOs may be the main ISO for a family of related Standards – Make sure to check for any related sub-ISOs that could be useful for your work.

N.B. All ISO Standards are assessed for revision every five years. **It is your responsibility to monitor any changes to relevant ISOs** that may affect your product or your work.

ISO Certification demonstrates to customers, investors, and other stakeholders that your product is in line with regulated guidance.

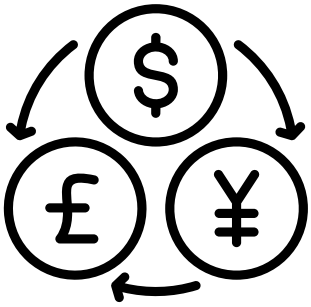
INTRO TO ISO STANDARDS



ISO 8601 – Date and Time Format

It is well established that international variations in common date and time usage can cause confusion. For example, 3rd May 2024 would be presented as 03/05/2024 in the UK, but as 05/03/2024 in the US, so anyone reading the short form date from a different country may interpret the shorthand as an entirely different date – e.g. a person from the UK reading the US form would read it as 5th March, not 3rd May.

ISO 8601 states that date and time should be represented as **YYYY/MM/DD HR:MIN:SEC:MILLISEC**. For use in research or medical settings, it is usually acceptable to not need to record milliseconds. You can use this ISO to help standardise how you record dates and times in documents such as research Case Report Forms.



ISO 4217 – Currency Codes

This standard creates three letter codes to identify currencies. The first two letters are the country code (as defined by ISO 3166), and the third letter is the currency name.

Many of the currency codes you will need to use will already be familiar:

- Great Britain's Pound Sterling – GBP
- United States' Dollar – USD
- European Union Euro – EUR
- Chinese Yuan - CNY (onshore) / CNH (offshore)

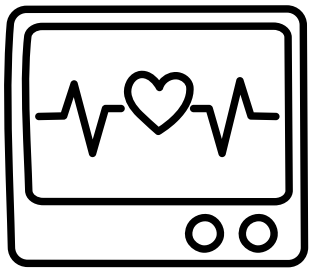
Use these codes to clearly define currency on documents such as expenses forms or purchase orders.

INTRO TO ISO STANDARDS

ISO 3166 – Country Codes

This ISO defines two-character codes for identifying countries. Many of these codes you will already be familiar with, such as GB for Great Britain, US for the United States of America, FR for France etc.

You can find a sample of the most commonly used country codes here https://www.iso.org/obp/ui/#iso:pub:PUB500001:en



ISO 13485:2016 – Medical Devices

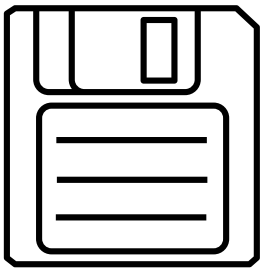
This family of codes lays out the international standards for the quality and safety of medical devices throughout their lifecycle, from development and manufacture to usage and disposal.
This ISO defines a medical device as:

"... a product, such as an instrument, machine, implant, or in vitro reagent, that is intended for use in the diagnosis, prevention and treatment of diseases or other medical conditions."

It can be particularly useful to have your technology certified to ISO 13485, as it demonstrates that your product adheres to the strict quality and that it has been audited as such. N.B. ISO does not complete certification this must be completed by an appropriately qualified third party.

N.B. Medical device manufacturers must demonstrate compliance with this ISO.

INTRO TO ISO STANDARDS



IEC 62304:2006 – Medical Device Software

This standard sets out the requirements for the life cycle of medical device softwares.

The key topics covered include:

- QMS and Risk Management in the context of software.
- Development planning, requirements analysis, and design.
- Establishing software maintenance, and how to implement modifications and changes.
- Problem and error handling.
- Relationships to other standards.

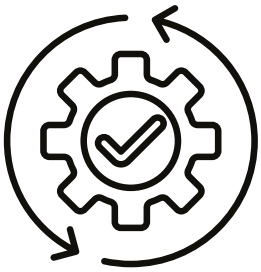
ISO 15189:2022 – Medical Laboratories

This ISO outlines the requirements for quality and competencies when using or running a medical laboratory. This Standard will most likely be the responsibility of your host organisation, e.g. Imperial College London, unless you are running your own facility. N.B. This ISO also applies to Point of Care Testing (POCT).

Topics covered include:

- Impartiality and confidentiality including record keeping and data management.
- Key staff such as the Lab Director and the structuring of teams and hierarchies of authority.
- Objectives, policies, and lab activities.
- Risk assessment and risk management.
- Personnel.
- Facilities and environmental conditions.
- Equipment, calibrations, consumables, reagents, and equipment servicing.
- Non-conformities and corrective actions.
- Governance and Quality Assurance.

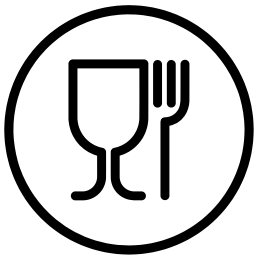
INTRO TO ISO STANDARDS



ISO 9001 – Quality Management Systems (QMS)

Establishing and deploying a good Quality Management System can improve the quality of product development, and project planning and execution, as well as demonstrating a commitment to high quality outputs. QMS focuses on the development of efficient processes, and good record keeping to support development.

For further information about how you can implement a QMS for your technology or project, contact the MedTechONE Accelerator.



ISO 22000:2018 – Food Safety Management Systems

This ISO outlines standards for food safety and processes associated with the storage and provision of food. You may find this ISO useful if you are running a project or study that involves the provision of food or food-products to participants.

It includes items such as:

- Creating food safety policies, and how to enact them.
- Understanding the needs and expectations of relevant parties.
- Defining, communicating, and monitoring the responsibilities of team members who have a role in food safety.
- Managing skills and competencies.
- Controlling or interacting with external processes, products, and services.
- What to do in emergency situations.
- Develop and test plans for product recalls or withdrawals.
- Develop product traceability.
- Hazards and risk assessments.
- Control measures and associated processes.

INTRO TO ISO STANDARDS

ISO 26000 – Social Responsibility

This ISO provides guidance to companies and organisations who want to commit to operating in a socially responsible manner. It is becoming more commonly considered that organisations with good commitments to social and environmental responsibility are rated better for overall sustainability and performance.

ISO 26000 aims to address seven core responsibilities:

- Organisation Governance
- Human Rights
- Labour Practices
- The Environment
- Fair Operating Practices
- Consumer Issues
- Community Involvement & Development

This ISO is available **for free**, but it should be noted that certification is not available for this ISO as it is only guidance and not regulation.

ISO 31000:2018 – Risk Management

The long-term success of a project, or company, can depend on how risks are assessed and managed – In short, managing the unexpected.

This ISO encompasses the principles of risk management frameworks and principles, how to identify and monitor the effectiveness of your risk management processes, and how to continually improve your processes. It also contains information on leadership and team responsibilities in the context of risk management.

INTRO TO ISO STANDARDS

OTHER USEFUL ISOs

These Standards may not directly relate to your work, but could contain useful information (such as particular Terms & Definitions defined within these Standards):

ISO 20417:2021 Medical Devices – Information to be supplied by the Manufacturer.

ISO 15223-1:2021 Medical Devices – Symbols to be used with information to be supplied by the Manufacturer: General Requirements.

ISO 15223-2:2021 Medical Devices – Symbols to be used with medical device labels, labelling, and information to be supplied: Symbol development, selection, and validation.

ISO 10933-1:2018 Biological Evaluation of Medical Devices – Principles of, and evaluation strategies and processes for medical devices. Includes details on risk assessments for biohazards relating to a medical device.

ISO 14971:2019 Application of Risk Management to Medical Devices – Outlines the definitions of terminology, processes, strategies, and principles of risk management for medical devices.

ISO 3864-1:2011 Graphical Symbols – Safety Colours and Safety Signs – Part 1

ISO 7000 Graphical Symbols for use on equipment – Registered Symbols

ISO/IEC 27017:2015 Information Technology – Security Techniques: Code of practice for information security controls.

INTRO TO ISO STANDARDS

OTHER USEFUL ISOs

ISO/IEC 27005:2022 Information security, Cybersecurity and Privacy Protection – Guidance on managing information security risks. Contains useful general information on identifying and managing risks.

ISO 14644-1:2015 Cleanrooms and associated controlled environments (Part 1 of a multi-part ISO).

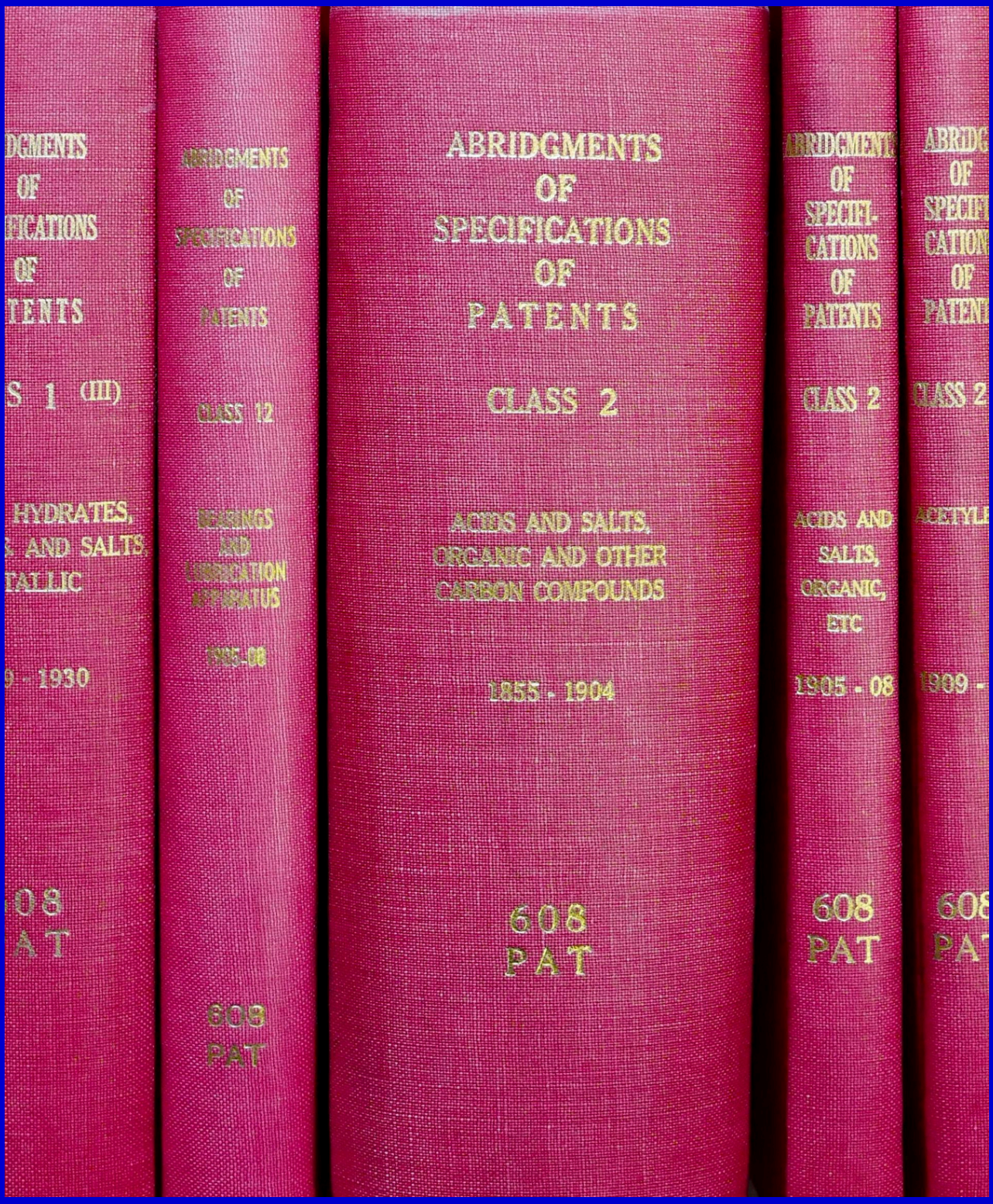
- Part 1 – Classification of air cleanliness by particle concentration.
- Part 2 – Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration.
- Part 3 – Test Methods
- Part 4 – Design, construction and start-up.
- Part 5 – Operations
- Part 7 – Separative devices (clean air hoods, glove boxes, isolators, and mini-environments).
- Part 8 – Classification of air cleanliness by chemical concentration
- Part 9 – Classification of surface cleanliness by particle concentration.
- Part 10 - Classification of surface cleanliness by chemical concentration.
-

ISO 14698 Cleanrooms and associated controlled environments – Biocontamination control.

- Part 1 – General Principles and methods
- Part 2 – Evaluation and interpretation of biocontamination data

This is a non-exhaustive list of potentially useful ISOs that it could be valuable to read up on, depending on the nature of both your technological innovation and your planned project.

THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)



THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

N.B. The following are extremely brief summaries of the above legislation. For further information, view the full legislation at the links in the Further Reading & Resources section.

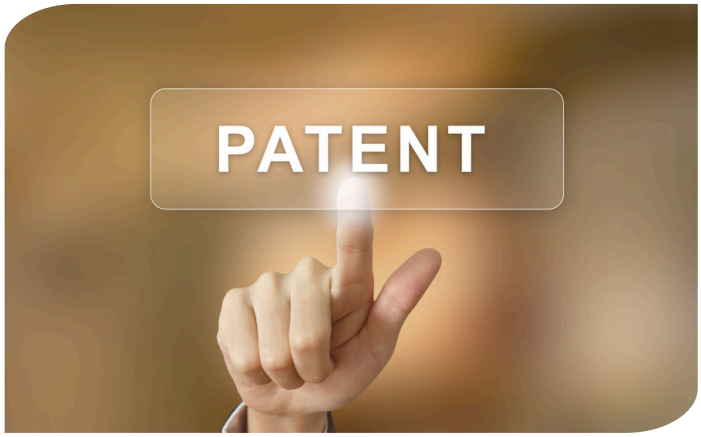
THE PATENTS ACT (1977)

Defines patentable inventions as:
"... an invention in respect of which the following conditions are satisfied...:
a) The invention is new;
b) It involves an inventive step;
c) It is capable of industrial application;
d) The grant of a patent for it is not excluded by [other] subsections...

It is hereby declared that the following are not inventions for the purposes of this Act...:
a) A discovery, scientific theory, or mathematical method;
b) A literary, dramatic, musical, or artistic work or any other aesthetic creation whatsoever;
c) A scheme, rule or method for performing a mental act, playing a game or doing business, or a program for a computer;
d) The presentation of information, "

The Act also creates an exception for patentable inventions, where **patents will not be granted for inventions where the industrial scale up or applications of the invention would contravene with public policy or morality.**

Inventions are considered novel and new when the innovation is not already covered within the state of the art (defined as the most recent developments in a given field). Additionally, it should be noted that "industrial application", is defined as an innovation that can be made or used in any relevant industry, including agriculture.



THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

THE PATENTS ACT (1977)

Important Exclusions relating to Medicine:

"**A patent shall not be granted for the invention of:**

a) A method of treatment of the human or animal body by surgery or therapy, or;

b) A method of diagnosis practised on the human or animal body.

... above does not apply to an invention consisting of a substance or composition for use in any such method."

Meaning while you could patent a specific device, for example, you cannot patent the methodology of its function i.e. you cannot patent the technique itself, e.g. laparoscopy.

The term "Priority Date", except where exclusions apply, defined as the date the patent application is filed. A key exclusion is where multiple applications have been submitted, which means the priority date will usually become the date of the first or earliest application.

Any individual can apply for a patent, or in partnership with another individual (or group), but it should be noted that the patent would be granted to:

- Primarily to the inventor/s;
- Where the inventors are not the applicant, or where the inventor has granted the rights to the invention to another party (whether due to law, legal contract, international agreement etc. or similar made prior to the invention), the patent will be granted to anyone individual or group who held full ownership of the rights to the invention (not including equitable interests) in the UK;
- These definitions also apply to the original inventor's successor/s where applicable;

And to no other person.

THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

THE PATENTS ACT (1977)

"Inventor" is defined as:
"... the actual deviser of the invention, and "joint inventor" shall be construed accordingly."

The Act also establishes that the person making the application will usually be assumed to be the person who is entitled to the patent, unless otherwise established during the application process.

The Inventor (or Joint Inventors) has a right to be mentioned in the patent application as such. It should also be noted that, where the applicant is not the Inventor/s, the application must state how the applicant has derived their right to be granted the patent. The application must always state the names (and any other identifying information) of the Inventor/s.

In the rare instance where a person has been listed as an Inventor on a patent application, but there is a dispute over that person's legitimacy as the Inventor, the person making the dispute may apply to the Comptroller for a certificate to that effect. If the certificate is granted, the Comptroller will be required to correct any unissued versions of the patent and any related documents.

In filing a patent, you must be able to prove beyond doubt who the inventor is, and if you are not the inventor filing the patent, you must be able to prove you have permission to make the filing.

THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

THE PATENTS ACT (1977)

The Patent Application must contain:

- A direct statement requesting the granting of the patent,
- The specification documents relating to the invention, and relevant claims to the invention,
- And an abstract that provides technical information (N.B. where deemed to be insufficient, the Comptroller may reframe the application or the abstract to fulfil its purpose).

It should be noted that:
"The specification of an application shall disclose the invention in a manner which is clear enough and complete enough for the invention to be performed by a person skilled in the art."

The claims should:

- Define the matter for which the applicant seeks protection,
- Be clear and concise,
- Be supported by the description and specification,
- And relate to one invention only, or a group of inventions which are intrinsically linked so as to constitute a single inventive concept.

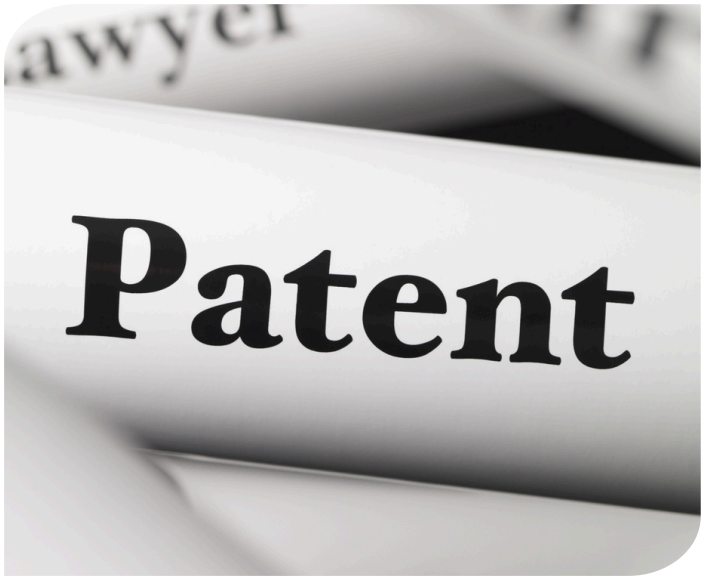
An application may be withdrawn at any point before the patent is issued.

The application will be referred for preliminary examination if:

a) The application has a date of filing (the earliest date where documents submitted to the Patent Office satisfy specific conditions i.e. the documents indicate a paten is sought, they identify the person applying with contact details and contain the appropriate description and specifications of the patent subject or make reference to a previous application containing that information).

b) The application has not been withdrawn.

c) The application fee has been paid.



THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

THE PATENTS ACT (1977)

The assessor will make a report relating to the application, and the applicant will have the opportunity to comment on the report and to make any requested amendments or provide any requested information and/or evidence.

On request, once the relevant preliminary examination and searches have been completed, the application can be referred for a substantive examination (at the request of the applicant, and after the payment of a fee).

Examinations aim to assess if the application is within the rules and requirements of the Patent Act (1977), and to determine if there are any aspects of the application which do not yet comply with the regulations. **If it is not determined that an application is compliant with the Act, after the proscribed time, it will be rejected.** There is a court appeal process, and refused applications can be reinstated, but this can be a lengthy and complex process.

If the patent is granted, the comptroller handling the application will publish a notice of the granted patent in their dedicated journal, as well as publishing the specification of the patent, the names of the applicant (and, where applicable, the inventor), and any other relevant items. The applicant will be sent a certificate as soon as is practicable.

N.B. The Patent Act (1977) is a 101-page document of the legal terms and processes around patents in the UK – **This text is a very surface level excerpt.** If you intend to file a patent, you should either familiarise yourself with the Act in full and engage with a legal advisor who specialises in patents.

THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

This Act does not significantly update or change the existing Patents legislation from the 1977 Act but rather focuses on copyright law for creative and educational materials and products. We have included here a short overview of some of the key parts of the newer Act as they relate to more general copyright law, but for information on patents you should refer primarily to the 1977 Act.

Defines "author" as "the person who creates it [the work]". "That person shall be taken to be:

- In the case of a sound recording, the producer;
- In the case of a film, the producer and principal director;'
- In the case of a broadcast, the person making the broadcast...;
- In the case of the typographical arrangement of a published edition, the publisher;"

Where there are multiple authors and the contribution of each author is not distinct from that of the other authors, this is **"joint authorship"**. Where a work is produced by collaboration of multiple authors and the works are designed to be used together e.g. a musical work and a literary work, this is **"co-authorship"**.

<u>The author of a work is the first owner of any copyright upon that work.</u>

THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

Copyright duration for literary works - Copyright naturally expires at the end of a 70-year period that commences at the end of the calendar year in which the author dies. Where there are multiple authors, this period commences at the end of the calendar year in which the last living author dies.

Where the country of origin of the work is not the UK, copyright duration is as applied by the country of origin.

If the work is computer-generated, copyright expires at the end of a period of 50-years from the end of the calendar year in which the work was created.

The owner of the copyright on a work has the exclusive rights to:

- Copy the work
- Issue copies of the work to the public
- Rent or lend the work to the public
- Perform, show or play the work to the public
- Communicate the work to the public
- Make an adaptation of the work, or do any of the above in relation to an adaptation

THE PATENTS ACT (1977) AND THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)

Infringement of copyright occurs when someone (an individual or an organisation) undertakes one of the above activities, without the approval of the author and/or without the appropriate license. Secondary infringement occurs when someone without license to use the copyright:

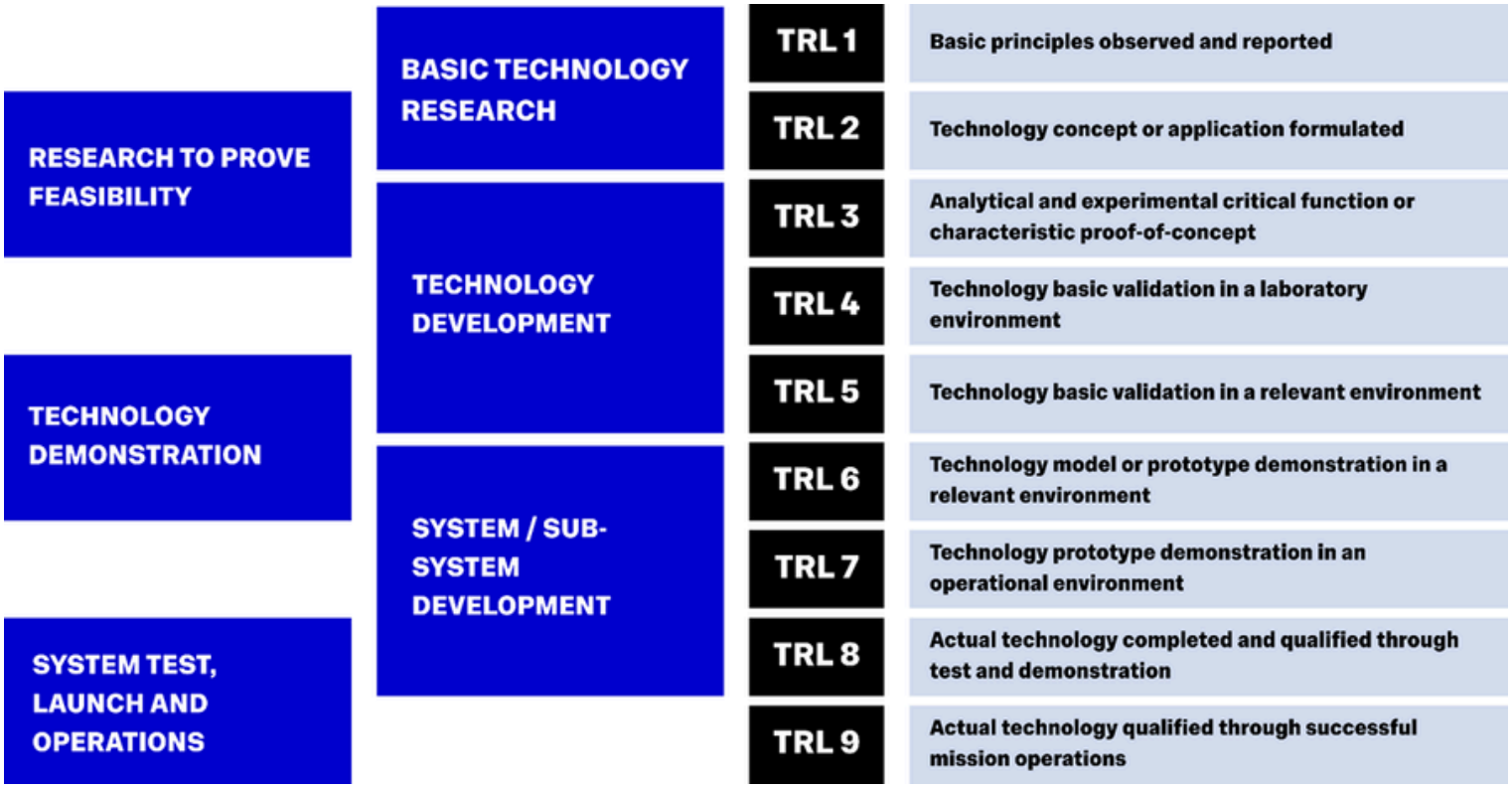
- Imports infringed work into the UK (e.g. importing pirated films)
- Possesses or deals with infringed copy, including:
  - Possessing in the course of business
  - Selling, letting, or offering/exposing for sale or hire
  - Exhibits or distributes the infringed copy to the public
  - Distributing in some other manner in such a way that it prejudicially affects the copyright owner
- Provides means to make infringing copies
- Permits the use of a premises for an infringing performance
- Provides apparatus for an infringing performance (e.g. providing speakers/amplifiers for an infringing musical performance)

TECHNOLOGY READINESS LEVELS

TECHNOLOGY READINESS LEVELS

Developed by NASA in the 1970s, Technology Readiness Level assessments allow technologies to be uniformly and consistently mapped to maturity levels, regardless of the technologies purpose or respective scientific field or basis.

TRL 1: Basic principles observed and reported
TRL 2: Technology concept or application formulated
TRL 3: Analytical and experimental critical function or characteristic proof-of-concept
TRL 4: Technology basic validation in a laboratory environment
TRL 5: Technology basic validation in a relevant environment
TRL 6: Technology model or prototype demonstration in a relevant environment
TRL 7: Technology prototype demonstration in an operational environment
TRL 8: Actual technology completed and qualified through test and demonstration
TRL 9: Actual technology qualified through successful mission operations



KTH INNOVATION READINESS LEVEL

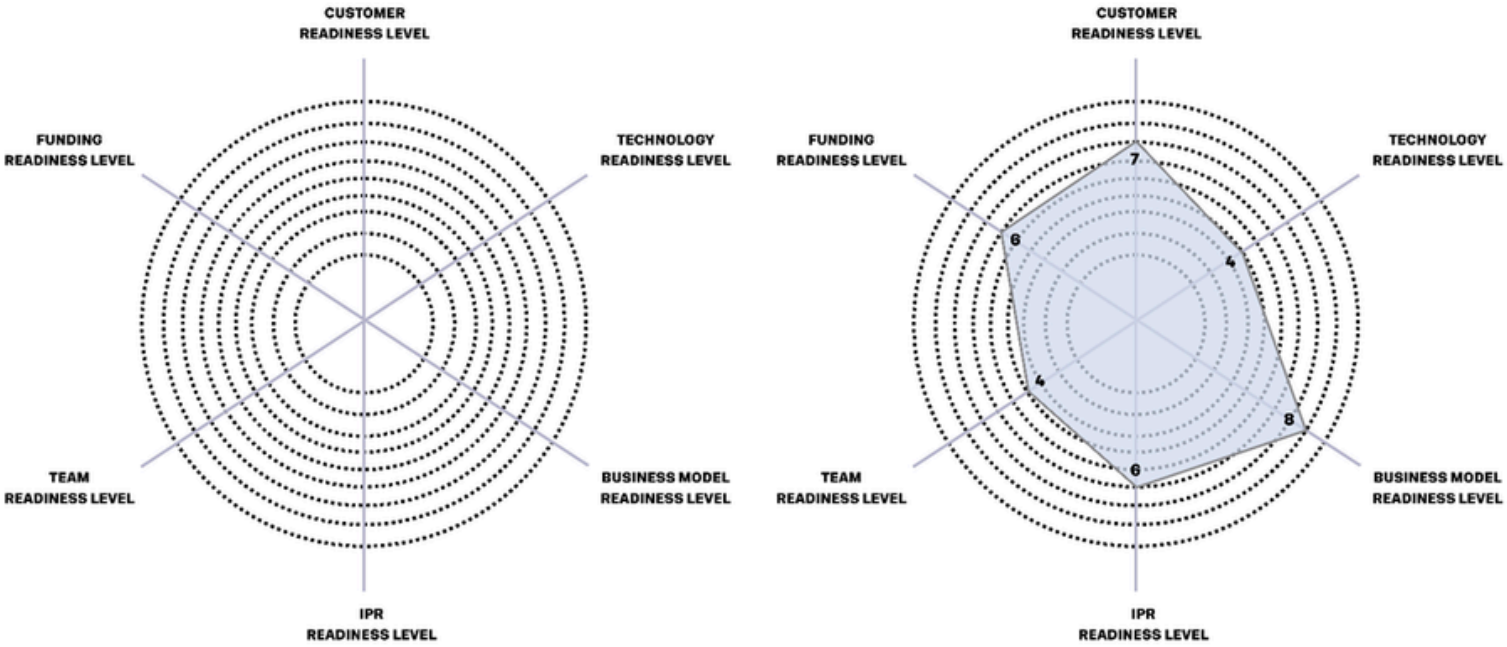
Based originally on the Technology Readiness Level devised by NASA, the KTH Innovation Readiness Level is a 6-point map of a company's, and technology's, overall readiness for market, with a focus on the early stages of developing and verifying an innovation.

The readiness levels are:

- **Funding Readiness Level –** Secure the necessary funding to take the idea to market
- **Customer Readiness Level –** Confirm customer need and interest
- **Technology Readiness Level –** Develop and test the technology, product, service, or concept
- **Business Model Readiness Level –** Establish that the concept can be financially, environmentally, and socially viable and feasible
- **Intellectual Property Rights (IPR) Readiness Level –** Clarify the legal and IP status, and secure relevant IP protection
- **Team Readiness Level –** Secure the right competencies and align the team

Each Readiness Level (RL) is a 9-point scale of criteria to meet at different stages of development and readiness. In practice, each criterion will be a group of activities and actions that need to be achieved prior to moving onto the next stage.

KTH INNOVATION READINESS LEVEL



This graphic shows an example of the KTH Readiness Level model – There is a blank version on the left, and a “completed” version on the right.

You can read more here: https://kthinnovationreadinesslevel.com/

OTHER READINESS LEVELS

COMMERCIAL READINESS LEVEL

Developed by the Australian Renewable Energy Agency (ARENA) to assess the proximity to commercial output, and commercial viability of technologies.

CRL 1: Hypothetical commercial proposition – Technology is technically feasible but lacks verifiable commercial data

CRL 2: Commercial trial, small scale – First-of-its-kind project, typically supported by equity and government funding, with limited public data

CRL 3: Commercial scale-up – Technology is scaling up with specific policy support and emerging debt financing

CRL 4: Multiple commercial applications – Technology is deployed in multiple contexts, often with subsidies, and supported by public performance data

CRL 5: Market competition – Competition drives widespread deployment, with commoditisation of components and financial products.

CRL 6: Bankable asset class – Technology is fully mature, with established standards and minimal market or technology risks influencing investment decisions

OTHER READINESS LEVELS

BUSINESS READINESS LEVEL

BRL 1: Unclear on possible business idea, potential and competition

BRL 2: First hypothesis of business concept

BRL 3: Description of sustainable business model

BRL 4: First calculation indicating economically viable business model

BRL 5: Key assumptions in sustainable business model tested

BRL 6: Full sustainable business model tested on customers

BRL 7: Viability of sustainable business model validated by initial sales

BRL 8: Sales and metrics show that sustainable business model holds

BRL 9: Sustainable business model proven to meet internal and external expectations on profit, scalability, and impact over time

MARKET ACCESS

MARKET ACCESS

KEY REQUIREMENTS SUMMARY

- **All medical devices must be MHRA registered.** This includes:
  - In vitro diagnostic devices (IVDs)
  - Custom-made devices
  - Systems or procedure packs
  - Any other, more standardly categorised medical device

- If your manufacturer is based outside of the UK, you must appoint a single UK responsible person for all of your devices who will act on your behalf to carry out specified tasks such as MHRA registration.

- **CE marked devices can be placed on the GB market up to the following dates:**
  - General medical devices compliant with EU Medical Devices Directive, or EU Active Implantable Medical Devices can be placed on the GB market up to 30th June 2028, or prior to the certificate expiry, whichever is soonest.
  - IVDs compliant with the EU IVD Medical Devices Directive can be placed on the GB market up to 30th June 2030, or prior to the certificate expiry, whichever is soonest.

- In addition to a valid CE / UKCA marking, **you may need to make the number of the approved / notified body available on the label.** Alternatively, where applicable, the name and address of the UK Responsible Person must be available on either the product label, packaging, and/or within accompanying information.

- **You must adhere to Post-Market Surveillance requirements**, including submission of vigilance reports.

MARKET ACCESS

NICE FOR MARKET ACCESS TO THE NHS

NICE can support the adoption of a pharmaceutical or technology into the NHS through their rigorous assessment and evaluation programmes.

Identifying routes into the NHS

NICE provides training and insight on how to get your innovation into the NHS, including:

- **NICE Surgery –** A 1 hour meeting with a NICE expert plus an optional written summary of the points discussed. You can access this at any point in the market access process.

- **Therapeutic Landscape Review –** An in-depth review of past NICE appraisals, trends and developments in care standards. NICE provides a virtual / in-person session with experts who can discuss the review findings, facilitate discussion, and answer questions. Designed for companies at early product development stages.

- **System Engagement Meeting –** A 2-3 hour engagement meeting facilitated and hosted by NICE. Involves relevant experts, key opinion leaders, and wider health system stakeholders and is designed to address the most pressing market access issues for your innovation. Designed for companies finishing stage 3 clinical trials, up to the start of a NICE appraisal, and is of most benefit to companies who have generated at least some clinical evidence.

- **Evidence Gap Analysis –** Supports medtech companies in refining their product's value proposition, and in identifying gaps in both planned and existing evidence. Includes a meeting with a NICE expert and a report highlighting gaps and recommended actions. You can access this at any point in the market access process.

MARKET ACCESS

NICE FOR MARKET ACCESS TO THE NHS

- **Health Economic Model Assessment –** For developers of pharmaceuticals and certain medtech innovations, this assessment is an independent, critical review and quality assessment of your existing economic model. NICE will provide a technical report that includes model optimisation and recommendations. Designed to be accessed prior to a formal NICE appraisal. You need to have completed the majority of your evidence generation and should have at least started your economic model.

The first step for any innovation is to register the product with NICE, which can be completed at one of the links available here https://www.nice.org.uk/what-nice-does/life-sciences-how-to-get-your-product-to-market - You can choose between registering a pharmaceutical or a non-pharmaceutical product.

For next steps and further advice on how to progress through the NICE infrastructure, you should consult the NICE Advice Service: https://www.nice.org.uk/what-nice-does/life-sciences-how-to-get-your-product-to-market/nice-advice-service

NICE can work with you to find the right pathway for your innovation

START UP & SPINOUT FUNDING

FUNDING A SPINOUT / STARTUP

The greatest constraint many innovations face is funding the start up phase. This is the point where your evidence generation should be completed (or at least well underway), and you have planned your market entry but now need to scale up into an actual company.

Some of the costs to consider will be:

- Staff
- Places e.g. an office location
- Manufacturing
- IP costs e.g. licensing (especially if your IP is owned by Imperial)
- Marketing
- Fees for regulatory requirements e.g. FDA submissions, MHRA submissions etc.
- Any further evidence generation and validation studies

You will likely need to acquire funding from multiple sources, but as a start, consider:

UK Research and Innovation

UKRI Biomedical Catalyst – Innovate UK's flagship grant, designed to support SMEs in developing health innovations.

- £140M total fund, aimed at supporting multiple projects across different markets, technologies, strands and themes e.g. medicines and pharmaceuticals, health technology, digital health technology etc.
- Ongoing grant with multiple opportunity rounds
- Allows projects to have additional funding partners where needed.

FUNDING A SPINOUT / STARTUP

NIHR Invention 4 Innovation (i4i) Grants – Designed for SMEs working either solo, or alongside a co-applicant with an academic or NHS partner. Created as a translational funding programme for medtech innovations aiming to address an existing or emerging health or social care need or gap, including:

- De-risking early-to-late-stage medical devices
- In vitro diagnostics
- High-impact, patient focused digital health technologies designed for the NHS

There are three i4i funding schemes:

- i4i Product Development Award: No upper funding limit, but costs must be justified. Designed to support product development.
- i4i Connect: £50,000 - £150,000 Aimed at supporting SMEs reach the next stage of their development and enables applications for further funding.
- i4i FAST (Funding At the Speed of Translation): Designed for early-stage innovators in need of a small amount of funding to answer a specific development question, or to fund a single activity e.g. small evidence generation etc.

NIHR HealthTech Funding – A list of links to relevant funding opportunities and streams occurring over the next couple of years, as well as a list of opportunities that are ongoing / do not have time limits.

FUNDING A SPINOUT / STARTUP

Medical Technology (MedTech) Funding Mandate & Support (NHS Accelerated Access Collaborative) – Part of the NHS Long Term Plan commitment to accelerate the uptake of proven and affordable health innovations.
Technologies covered by the MTFM are usually funded by Commissioners.

Technologies must meet three criteria, as well as aligning with broader NHS England Programmes (e.g. Net Zero targets):

- Are effective – Demonstrated through positive NICE Medical Technology Guidance or Diagnostic Guidance
- Are cost-saving within 3 years – NICE modelling demonstrates a net saving within 3 years of implementation, demonstrated by a published NICE resource impact template.
- Are affordable to the NHS – Budget impact must not exceed £20M nationally, within the first 3 years.
- More information at the FutureNHS Collaboration Platform.

Angel Investor Network – A social network designed to pair investors with projects and products that need funding. You can set up a profile, state how much funding you are hoping to secure, set minimum funds per investment, and network with potential investors and partners.

FUNDING A SPINOUT / STARTUP

Start Up Loans – Some lenders and venture capitalists will provide loans and seed funding to support companies in the start up phase. You should engage with an accountant or other qualified legal and financial representatives as soon as possible, both to understand your funding needs, and to protect against high-risk investing practices.

Partnering with a company – You may be able to receive some funding by partnering with an existing company or manufacturer. As this may entail contractual and IP obligations on your part, you should consult a legal professional before agreeing to a contract.

Checking funding bodies for opportunities – You can search for various funding sources such as direct NHS funding, NIHR, UKRI, or regulatory funding directly via their websites. Most funders have pages for available funding opportunities, and you can see what is available for the stage of your project or innovation.

POST-MARKET SURVEILLANCE

POST-MARKET SURVEILLANCE

"... the practice of monitoring the safety of a pharmaceutical drug or medical device after it has been released on the market and is an important part of the science of pharmacovigilance."

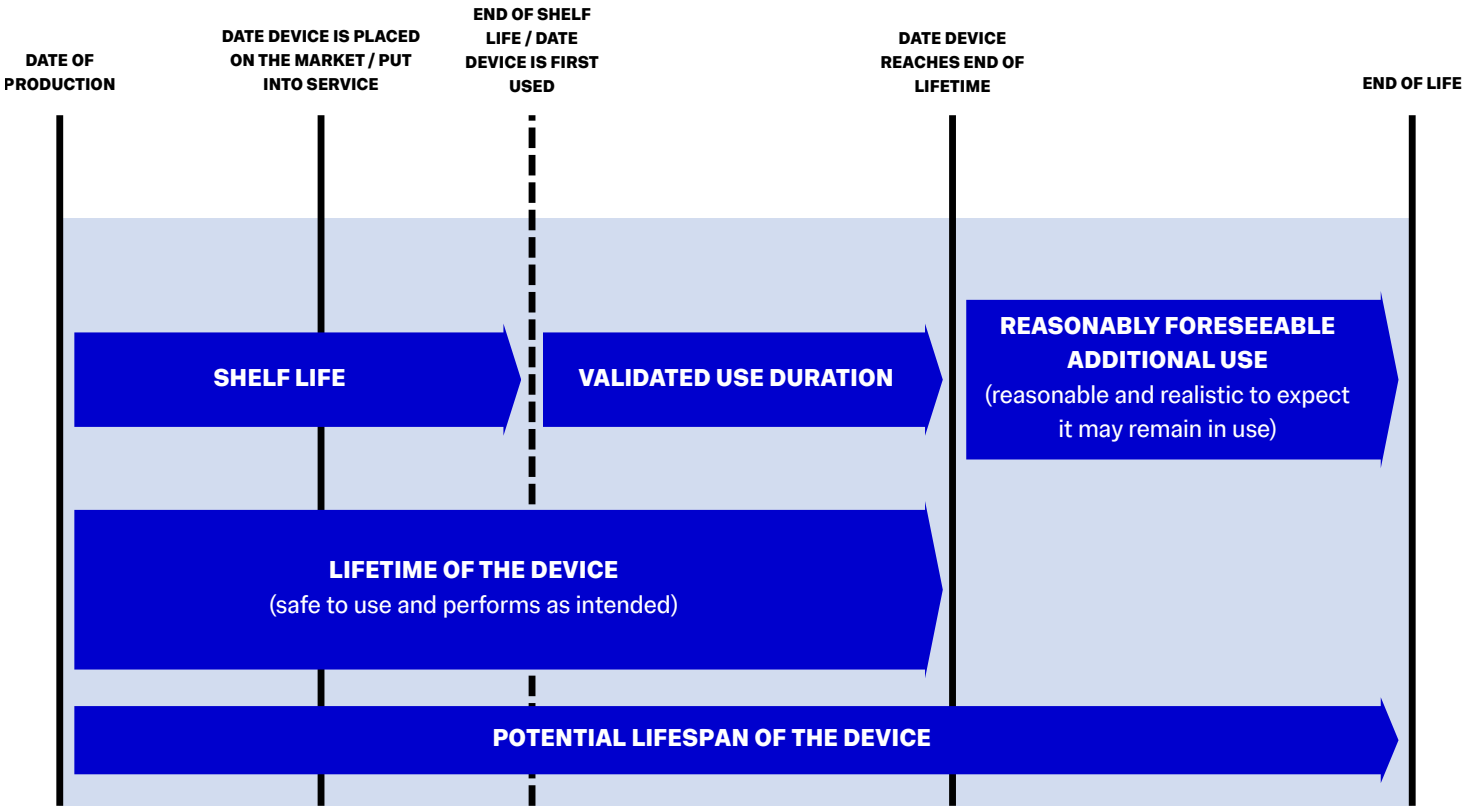
The Medical Devices (Post-market Surveillance Requirements) (Amendment)(Great Britain) Regulations 2024 amends the UK Medical Devices Regulations 2002 (MDR 2002) by adding a new Part 4A on this topic.

Devices to which the PMS Regulations do not apply:

- Devices subject to clinical investigation or performance study. This includes where the device already has a UKCA/CE mark but is being used outside of the exact conditions of that approval for the purposes of a clinical investigation. You will still need to adhere to Serious Adverse Event Reporting as per the guidance on Clinical Investigations for Medical Devices.
- Devices that have a valid Exceptional Use Authorisation in Great Britain.
- Where the device placed on the market has an authorisation issued by the Secretary of State under regulation 12(5), 26(3), or 39(2). However, you will still be required to monitor the safety and performance of the device..
- Discontinued devices, if the manufacturer no longer places any new devices of a model on the market. Different requirements apply for discontinued devices on the EU and NI markets, under "legacy devices".
- Devices manufactured in house, only for devices manufactured in house by a healthcare establishment, including custom made items, where there is no intention to place the device on the market.

LIFETIME OF A DEVICE

Defined as **"... the time of manufacture / production date to the end of the period the manufacturer has validated the device will perform as intended, sometimes referred to as the expected service life."** Which includes the device shelf life, where applicable.



POST-MARKET SURVEILLANCE

POST-MARKET SURVEILLANCE PERIOD

Defined as **"... beginning with the day on which the first device of a device model is put into service by the manufacturer or placed on the market, whichever is sooner, and ending with the end of the lifetime of the last device of that device model that is put into service by the manufacturer or placed on the market, whichever is later."**

PMS data refers to data from users and customers about a device's functioning, efficacy, any errors or malfunctions, and any other information of note.

As it is common for devices to be used beyond their lifetime, **manufacturers are encouraged to continue collecting PMS data both throughout the lifespan and after.** This can be a holistic process, and manufacturers can use their experience to decide on the natural lifespan of a device, as a starting point. Naturally this will change over time as the result of the collection of PMS data.

SERIOUS INCIDENTS & PUBLIC HEALTH THREATS

All serious incidents involving a medical device must be reported to the MHRA as part of the GB Vigilance System.

An "incident" is where any one or more of the following has occurred:

- The d**evice has malfunctioned or deteriorated** in performance when used as intended;
- A diagnostic device where **the device produces incorrect or inaccurate results** that inform clinical decisions;

POST-MARKET SURVEILLANCE

SERIOUS INCIDENTS & PUBLIC HEALTH THREATS

- **Users identify shortcomings in the device design or report difficulties using the device safely** (which can increase instances of user error), including deficiencies in provided instructions and information;
  - An inadequacy in the design of the device causing an inability on the part of the user to use the device safely and as intended by the manufacturer, including design failures in ergonomic components;
  - An inadequacy in the information supplied with the device by the manufacturer;

- The **device causes side effects** that negatively impact user/patient health, their care, or wide public health. Known possible side effects must be documented in the device's technical information but must be reported if they meet the "serious" threshold.

"Serious" incidents include those that directly, indirectly, or under different circumstances could have led to:

- Death, or;

- Serious deterioration in state of health;
  - Life-threatening illness or injury
  - Permanent impairment of a body structure or body function
  - Hospitalisation or prolongation of hospitalisation
  - Medical treatment required to prevent life-threatening illness, injury, or permanent impairment, including self-administered treatments.
  - Chronic disease
  - Foetal distress, foetal death, or congenital physical or mental impairment or other birth defect.

- A serious public health threat
  - Where the risk of death, serious illness, or serious deterioration could affect a significant population and needs urgent action to remedy.

POST-MARKET SURVEILLANCE

Other incidents may not need to be reported to the MHRA but will need to be reported in the manufacturer's post-market surveillance data, which is reported to the MHRA in accordance with the TREND Reporting Requirements.

In addition to the above definition of a "serious incident", there are three criteria that will be met when an incident needs to be reported:

1. **An incident has occurred, or an issue has been identified, including during performance testing completed by the manufacturer.** This also includes reviews of the information supplied with the device, and the event of any scientific evidence or information indicating a factor that could cause an incident.

2. **The device is suspected to be a contributor to, or the cause of, the incident,** including in incidents relating to side effects.

3. **The incident directly, or indirectly, caused, or may have caused, a death or a serious deterioration in the health of a patient**, user or other person.

The event officially becomes an incident when the second criteria applies, and becomes serious (and therefore reportable) when the third criteria applies.

VIGILANCE REPORTING REQUIREMENTS (REG 44CZ)

Who must report to the MHRA – The manufacturer, UK Responsible Person, or Authorised Representative must notify the MHRA about any incident or Field Safety Corrective Action (FSCA) that meets reporting criteria, including any periodic safety or trend reports that meet the criteria. Where the incident relates to the simultaneous or combined usage of two or more separate devices, then all related manufacturers must make the report on behalf of their involved device.

What must be reported – All serious incidents (as defined above), Field Safety Corrective Actions, and adverse trends. This is regardless of how the manufacturer became aware of the incident, and includes incidents reported to manufacturers via the MHRA as industry notifications of a public report (INPRs).

Reporting timescales – The manufacturer must notify the MHRA immediately upon being made aware of an incident. The maximum permitted timeframes are:

- **Serious Public Health threat** – No later than 2 calendar days after the manufacturer is made aware.
- **Death or unanticipated serious deterioration** – No later than 10 calendar days after the manufacturer is made aware.
- **All other serious incidents** – No later than 15 calendar days after the manufacturer is made aware.

If it is unclear whether an event is serious, or needs to be reported, the manufacturer must still make the report within the above timelines. **You must not delay reporting due to incomplete information** – You can make follow up reports with additional information later in the process.

VIGILANCE REPORTING REQUIREMENTS (REG 44CZ)

How to report to the MHRA – Reports should be submitted via the MORE Portal. The MHRA does not accept reports received through other channels.

What to include in the initial report:

- **Details of the initial reporter:**
  - **Healthcare professional** – Name, profession, contact details including email and phone number.
  - **Member of the public** – The manufacturer must verify with the person that they agree to their details being shared with the MHRA.
  - **Journal article, registry, social media etc.** – Provide details, cite sources, and provide copies of articles where possible, including any unique DOI numbers. When citing social media, ensure you adhere to data protection regulations when submitting the report.
- **Unique Device Identifier (UDI) information** – The manufacturer should be using a UDI system derived from a standardised issuing authority where possible e.g. GS1, HIBCC. This number can identify a specific device, even if other information is missing.
- **Information on other incidents related to the same device model or a variant** – "Same model" includes available devices even in different sizes, colours, naming variants, or manufacturer sites.

VIGILANCE REPORTING REQUIREMENTS (REG 44CZ)

Periodic Summary Reports – Manufacturers can submit a request to make a report via a "periodic summary report" to report multiple similar incidents with the same device / device type in a consolidated manner. This will require an overview analysis of the incident data.

Trend Reports – Part of the standard system of data recording and reporting for device manufacturers, these reports will detect when there is an increase in frequency or severity of incidents.

Vigilance Reporting must be baked into your Post-Market Surveillance procedures from the very beginning.

OVERALL TIMELINE

OVERALL TIMELINE

The natural, but rather unhelpful, answer to the question of an overall, innovation to commercialisation, timeline is: **It depends.**

As these resources show, there are many factors in bringing a medical technology to market. **Clinical research essential to the evidence base can take multiple years to complete** and may not necessarily always provide the desired results. Furthermore, **regulatory pathways can also take years to navigate**, though institutions in the UK such as NICE and the NHS are piloting programmes to improve these timelines. All of this is also dependent on achieving financial support. Then there are **the challenges of scale up** to work through, from staffing to manufacturing, all the way through to market access.

No two technologies are the same, but **studies from the UK government indicate that it takes an average of 3-7 years to get an innovation from concept to market** (on the UK market).

FURTHER READING & RESOURCES

CE MARKING AND UKCA MARKING GUIDANCE
https://www.ies.co.uk/hubfs/IES%20CE%20Marking%20&%20UKCA%20Marking%20Guide.pdf

REGULATING MEDICAL DEVICES IN THE UK
https://www.gov.uk/guidance/regulating-medical-devices-in-the-uk

THE MEDICAL DEVICES REGULATIONS (2002)
https://www.legislation.gov.uk/uksi/2002/618/contents/made

DIRECTIVE 90/385/EEC - ACTIVE IMPLANTABLE MEDICAL DEVICES
https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A01990L0385-20071011

DIRECTIVE 93/42/EEC - MEDICAL DEVICES
https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A01993L0042-20071011

DIRECTIVE 98/79/EEC - IN VITRO DIAGNOSTIC MEDICAL DEVICES
https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A01998L0079-20120111

GUIDANCE ON THE REGULATION OF IVD MEDICAL DEVICES IN GB
https://assets.publishing.service.gov.uk/media/67863a313ef063b15dca0f47/Guidance_on_the_regulation_of_IVD_medical_devices_in_GB.pdf

APPLYING FOR A MANUFACTURER OF MEDICINES LICENSE
https://www.gov.uk/guidance/apply-for-manufacturer-or-wholesaler-of-medicines-licences

FURTHER READING & RESOURCES

REQUIREMENTS FOR SITE MASTER FILES
https://www.ies.co.uk/hubfs/IES%20CE%20Marking%20&%20UKCA%20Marking%20Guide.pdf

https://health.ec.europa.eu/document/download/95af86f8-c82d-4ad0-85cb-27c7f56531b4_en

FDA MEDICAL DEVICE EXEMPTIONS
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/315.cfm

FDA DEVICE REGISTRATION AND LISTING
https://www.fda.gov/medical-devices/how-study-and-market-your-device/device-registration-and-listing

FDA GUIDANCE ON DESIGNATING A US AGENT
https://www.fda.gov/medical-devices/device-registration-and-listing/us-agents

FDA INVESTIGATIONAL DEVICE EXEMPTIONS (IDE)
https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/investigational-device-exemption-ide

FDA QUALITY MANAGEMENT SYSTEM REGISTRATION (QMSR)
https://www.fda.gov/medical-devices/postmarket-requirements-devices/quality-management-system-regulation-qmsr

FDA DEVICE LABELLING REQUIREMENTS
https://www.fda.gov/medical-devices/overview-device-regulation/device-labeling

FURTHER READING & RESOURCES

FDA MANDATORY REPORTING
https://www.fda.gov/medical-devices/postmarket-requirements-devices/mandatory-reporting-requirements-manufacturers-importers-and-device-user-facilities

ISO COUNTRY CODES LIST
https://www.iso.org/obp/ui/#iso:pub:PUB500001:en

ISO 13485:2016 MEDICAL DEVICES (PREVIEW)
https://www.iso.org/files/live/sites/isoorg/files/store/en/PUB100422_preview.pdf

IEC 62304:2006 MEDICAL DEVICE SOFTWARE (PREVIEW)
https://www.iso.org/obp/ui/en/#iso:std:iec:62304:ed-1:v1:en

ISO 15189:2022 MEDICAL LABORATORIES (PREVIEW)
https://www.iso.org/obp/ui/en/#iso:std:iso:15189:ed-4:v1:en

ISO 22000:2018 FOOD SAFETY MANAGEMENT SYSTEMS (PREVIEW)
https://www.iso.org/files/live/sites/isoorg/files/store/en/PUB100454_preview.pdf

ISO 26000 SOCIAL RESPONSIBILITY (FULL GUIDANCE)
https://www.iso.org/files/live/sites/isoorg/files/store/en/PUB100258.pdf

ISO 31000:2018 RISK MANAGEMENT (PREVIEW)
https://www.iso.org/files/live/sites/isoorg/files/store/en/PUB100464_preview.pdf

THE PATENTS ACT (1977)
https://assets.publishing.service.gov.uk/media/66fa4e32c71e42688b65ee3e/The-Patents-Act-1977-as-amended.pdf

FURTHER READING & RESOURCES

THE COPYRIGHT, DESIGNS & PATENTS ACT (1988)
https://assets.publishing.service.gov.uk/media/60180c2b8fa8f53fc62c5897/Copyright-designs-and-patents-act-1988.pdf

IMPERIAL INTELLECTUAL PROPERTY POLICY
https://www.imperial.ac.uk/media/imperial-college/research-and-innovation/research-office/public/Intellectual-Property-Policy-ROP-07-Public-Access.pdf

IMPERIAL RESEARCH PUBLICATIONS OPEN ACCESS POLICY
https://www.imperial.ac.uk/research-and-innovation/support-for-staff/scholarly-communication/open-access/oa-policy/

IMPERIAL GUIDELINES FOR PROPER SCIENTIFIC CONDUCT IN RESEARCH POLICY
https://www.imperial.ac.uk/research-and-innovation/research-office/research-policies/imperial-research-codes-of-practice/

IMPERIAL FINANCIAL REGULATIONS POLICY (RELATED TO IMPERIAL BRAND IDENTITY AND USAGE)
https://www.imperial.ac.uk/media-access/internal/?folder=administration-and-support-services/finance/internal&filename=Imperial-Financial-Regulations-Final-February-2024.pdf

MARKET ACCESS IN GREAT BRITAIN
https://www.gov.uk/guidance/regulating-medical-devices-in-the-uk

NICE FOR MARKET ACCESS TO THE NHS
https://www.nice.org.uk/what-nice-does/life-sciences-how-to-get-your-product-to-market
https://www.nice.org.uk/what-nice-does/life-sciences-how-to-get-your-product-to-market/nice-advice-service/nice-advice-working-on-your-objectives#routes

FURTHER READING & RESOURCES

POST-MARKET SURVEILLANCE - EXCEPTIONAL USE AUTHORISATION
https://www.gov.uk/guidance/exceptional-use-authorisation

IMPERIAL

MedTechONE

CONTACTS

https://www.imperial.ac.uk/medtechone/

mt1-info@imperial.ac.uk

LinkedIn@MedTechONE