Medicines & Healthcare products Regulatory Agency

Accompanying Guidance for MHRA flow chart for clinical investigations in Great Britain under UK MDR (2002)

November 2025

Note	
SCOPE	This guidance document and the flow chart it accompanies apply to general medical devices and active implantable medical devices only. Where the device in question is an in vitro diagnostic (IVD) device being used in a clinical study, separate guidance applies. In determining whether your device is a medical device, active implantable or IVD, please consider MHRA's borderlines guidance resources: https://www.gov.uk/guidance/borderline-products-how-to-tell-if-your-product-is-a-medical-device This document applies to studies conducted in Great Britain only, under UK Medical Device Regulations 2002 (SI 2002, No 618, as amended). All references to 'UK MDR' refer to this regulation. For studies with sites in Northern Ireland, or conducted in whole or in part in Northern Ireland, please see MHRA's guidance on clinical investigations in Northern Ireland: https://www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device#northern-ireland
[1]	**Pre-clinical or bench testing** 1. Studies not involving humans are likely to be considered pre-clinical or bench testing and will not fall within the remit of UK MDR. For example: Retrospective clinical studies and non-interventional software/AI studies – these provide performance data of a medical device using existing data with no safety implications for participants. Could support conformity assessment of a device but may not fit the

	definition of CI if they are not performed on humans (e.g. software tested using existing patient data, with no patient interaction in the study, and not informing patient management decisions in study). **Studies of this nature do not require notification to MHRA Clinical Investigations team. Please see note [6].** *However, once retrospective data is used to inform patient management then 'Yes' should be selected for the 'study involving human participants' decision step, and studies should continue through the flow chart.* *Examples here include studies of AI devices trained on compiled retrospective data, which will then influence the triaging, processing or care pathway of present or future patients.*
[2]	**Post-Market studies (including PMCF)** UK MDR 2002 Regulations 16 & 29 exempt studies of medical devices and active implantables that are validly UKCA or CE marked and used within their marked indication. As such, for studies of this category which are occurring in Great Britain, no clinical investigation application to MHRA is required (note: some post-market studies in Northern Ireland *do* require notification to MHRA – please see MHRA's Northern Ireland Clinical Investigations Guidance - https://www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device#northern-ireland). <u>Post Market Clinical Follow Up (PMCF) studies</u> Part II of the UK MDR 2002, Annexes VIII and X (medical devices) and Part III, Annexes 6 and 7 (active implantable devices) (as modified by Schedule 2A to the UK MDR 2002) require manufacturers to actively update their clinical evaluation with data obtained from post-market surveillance. When a CE/UKCA-marked device is further assessed, for safety or performance within the intended purpose, this may be done as part of the manufacturer's post market clinical follow-up (PMCF) activities. **Studies of this nature do not require notification to MHRA Clinical Investigations – see note [6]. However, please note, the device must be used as per the exact conditions of the CE/UKCA mark.** Where a CE/UKCA-marked device is being used outside of its intended purpose, the study must **not** be considered a post-market study for that device.

[3]	**Medical Purpose** Under the UK MDR Regulation 2 definition of a medical device, a medical purpose is considered as any of the following: i) diagnosis, prevention, monitoring, treatment or alleviation of disease, ii) diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap, iii) investigation, replacement or modification of the anatomy or of a physiological process, or iv) control of conception; For the purposes of clinical investigations, there are borderlines that must be drawn with respect to some aspects of purposes (i)-(iv), above. These are discussed below. Where a device is being used for one or more medical purposes, 'Yes' should be selected for this decision step. Note: a medical purpose does not take into consideration (and may be established regardless of) whether the device outputs are subsequently used as part of a participant's clinical pathway. Generally, a device will be being used for a medical purpose where its mechanism of action in practice achieves said purpose, regardless of the aims or objectives of the study. For example: • Comparator studies, where participant data is input into/measured on the device and the outputs are compared against standard of care (e.g. clinician decision making, state-of-the-art UKCA/CE marked devices in a diagnostic context, etc.) but the outputs are not acted on in any way. In these instances, the device is still considered to have a medical purpose at this decision step. Research purposes In certain instances, where it is unclear whether a device is achieving a medical purpose, the context of the study should inform this determination. It is MHRA's general opinion that a device being used on humans for research purposes could be a research tool, rather than a device being used for a medical purpose. This is particularly relevant when determining whether investigation of a physiological process should be considered a medical or research purpose.

	Investigation of a physiological process Examples of research studies here may include using a device which aims to produce a better understanding about a particular aspect of the human body. Further, the investigation of a physiological process will only be a medical purpose where it is intended for a medical use. For an applied comparison: • a study using a device to examine participants' heart rate for the purpose of identifying a pathological abnormality (e.g. an arrythmia) is clearly both seeking to diagnose a medical condition and investigating a physiological process with the intention of a medical use. • by contrast, a sports study using the same device, examining participants' heart rates to identify optimum heart rate for exercising or heart rate trends in different demographics, would not be considered either diagnosis of a medical condition or investigation of a physiological process with the intention of a medical use. Multiple purposes Where a device achieves multiple purposes in a study, some of which are considered medical purposes and some of which are considered research purposes, the medical purposes take precedence and 'Yes' should be selected at this decision step. Claims Where a device is being used for a research purpose, no explicit or implicit claims to a medical purpose should be made by the study documentation. For example, the study information should not imply that a participant's disease diagnosis will be updated, or that their disease state will be improved, by participation in the study. Studies explicitly or implicitly making these claims are studies of devices being used for a medical purpose, per the paragraphs above. **Where the device is being used for a medical purpose in the study, 'Yes' should be selected at this decision step.** Software Please note, there are cases where standalone software, including apps, which appear to have a medical purpose are considered not to fit the definition of a medical device, and are therefore NOT required

	to be CE or UKCA marked as a medical device and regulated by the MHRA.
	
	In general, the following are unlikely to be considered a medical device:
	
	• Monitors fitness/health/wellbeing – the monitoring of general fitness, general health and general wellbeing is not usually considered to be a medical purpose
	• Software is unlikely to be a device if:
	  ○ The software only reproduces a paper document in digital format - it is down to the health care professional to make the decisions based on the data displayed. (However, contrast with where the software provides some form of summarisation, which may be a medical device)
	  ○ the software only follows the path of a procedure/treatment - there are no decisions - may provide information.
	  ○ It offers only lifestyle treatment choices or referral to seek professional advice (e.g. see your GP).
	
	On the other hand, software is most likely to be a device if:
	
	• It is linked to a specific medicine/device (is likely to be an accessory).
	• It is intended to influence the actual treatment - dose, size of implant, time or type of treatment, etc.
	• It results in a diagnosis or prognosis - provides future risk of disease.
	
	This list is indicative only. Please refer to MHRA's available software guidance, which contains resources to help you determine if your software or app is a medical device with a medical purpose.
	
	Non-exhaustive list of guidance provided here:
	
	• MHRA Software flowchart: https://www.gov.uk/government/publications/medical-devices-software-applications-apps
	
	• Digital mental health technology: qualification and classification: https://www.gov.uk/government/publications/digital-mental-health-technology-qualification-and-classification

[4]	**Research Tools / Non-medical Purpose Studies** Please review note [3] above for clarification between medical and non-medical purpose and research tools.

	Annex I of *ISO 14155:2020 Clinical investigation of medical devices on human subjects – Good clinical practice* has further useful information on clinical development stages. If you reach this outcome, please review note [6] for further guidance. MHRA recommend that manufacturers contact the MHRA Clinical Investigations team if guidance is needed on whether the regulations will apply before undertaking a study of this nature. - When contacting MHRA for assistance in this manner, please provide your current view on whether the study requires notification to MHRA, and your reasoning for arriving at this view, linked to the principles of MHRA's flow chart and guidance. - Contact details are found at the end of this document.
[5]	**In-house manufacture of medical devices in Great Britain** (also known as Health Institution Exemption) This section of the document will be updated in due course.
[6]	**Notification to MHRA Clinical Investigations not required** If you reach this outcome, a notification and application to MHRA Clinical Investigations under UK MDR Regulation 16 / 29 is not required for your study **at this point in time**. However, MHRA strongly supports the use of local governance technical reviews for studies that do not require notification to MHRA. Further, all studies intending to use the data collected in their study for conformity assessment of the medical device are required to notify MHRA under UK MDR Regulation 16 / 29, and should see note [7]. It is MHRA's view that data collected under exempted studies will not be usable for conformity assessment. If, subsequent to commencing a study without notification in line with this guidance, a sponsor chooses to make changes / amendments / modifications to the device or study, the device and study should be reconsidered within the context of this flow chart and guidance. Modifications to studies which alter the pathway within this flow chart or guidance may subsequently result in the study falling within the remit of Regulation 16 or 29 and requiring notification to MHRA. Please also be aware that while *UK MDR 2002* Regulation 16 / 29 may not apply to your study, other regulations pertaining to facilities or patient care will continue to apply. Study sponsors and investigators

	must consider where their legal responsibility lies with respect to the use of the device in the planned study.
[7]	**Clinical Investigation** **If you reach this decision step, your device / study is a clinical investigation and requiring notification to MHRA Clinical Investigations.** This requirement will apply to medical devices that are not UKCA/CE marked, or devices to be used for a medical purpose other than their UKCA-CE marking (off-label devices), and to which an exemption does not apply. • Applications are submitted electronically using the Integrated Research Application System (IRAS) • A list of the required documents can be found in MHRA's *Clinical investigations of medical devices – compiling a submission to MHRA*. • Guidance on MHRA's review process can be found in *Clinical investigations of medical devices – guidance for manufacturers*. For links to the above reference documents, as well as further guidance on clinical investigations, please visit MHRA's main guidance page for clinical investigations: https://www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device
	Please note: this is general guidance only. If you need further assistance in determining the correct regulatory route, please provide an annotated copy of the flow chart showing and explaining your decision pathway to info@mhra.gov.uk with the title '[Company Name] – Is a Clinical Investigation required?'. When contacting MHRA, please provide details of: - Who has manufactured the device - Who is conducting the proposed study - What the intended purpose of the device is - What the intended purpose of the proposed study is - Whether any medical application is foreseen for the device - Please provide a copy of the study protocol where possible

	Once received, the MHRA Clinical Investigations team will reply to you to confirm. *Please note this guidance is a living document and is regularly updated as further information becomes available.*

Version	Published	Changes
V1.0	August 2025	New explanatory document published alongside version 2 of GB flow chart.
V3.0	November 2025	• Removed row 4 of previous flow chart – Expanded definition of a 'clinical investigation' to include studies outside those investigating safety and performance, in alignment with current UK MDR. Under previous version, when exiting the flow chart, UK MDR Regulation 10 would have required devices used in these studies to be UKCA/CE marked in order to be conducted. With latest version, these studies may now be conducted as clinical investigations under UK MDR Regulation 16 / 29. • Moved some sections of Note [4] to Note [3] in line with feedback. • Expanded discussions of a 'medical purpose' vs a 'research purpose', with examples provided. • Skipped version 2 of document to align version numbers with flow chart versions