Medicines & Healthcare products Regulatory Agency

Accompanying Guidance for MHRA Flow Chart of Clinical Investigations in Northern Ireland

December 2024

Note	
[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 EU MDR medical device regulations. Example: Retrospective clinical studies and non-interventional software studies – provide performance data of a medical device using existing data with no safety implications for participants. Could support conformity assessment but may not fit definition of CI if 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) 2. Devices that are not patient contacting or do not deliver a placebo or energy to the patient in the study, or influence the patient to take actions which would be considered treatments, even if clinical safety & performance data is not the purpose of the use (i.e. usability), are likely to be considered pre-clinical or bench testing and will not fall within the remit of EU MDR medical device regulation. Example: Acceptability studies of apps that are testing usability of the device only, and are not collecting clinical safety or performance data, provided the treatment / clinical decision support provided by the app is not put into practice. **Studies of this nature do not require application to MHRA Devices.**
[2]	**Is the device being used for a medical purpose in the study?** As Per Regulation (EU) 2017/745 ('EU MDR') Article 2(1), ***medical purposes*** are the following: - diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease

	- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability, - investigation, replacement or modification of the anatomy or of a physiological or pathological process or state, - providing information by means of *in vitro* examination of specimens derived from the human body, including organ, blood and tissue donations - for the control or support of conception - intended specifically for the cleaning, disinfection or sterilisation of medical devices or Annex XVI devices note: this includes active devices and software
[3]	**What is a 'health institution'?** A 'health institution' is defined in Article 2(36) as meaning: an organisation the primary purpose of which is the care or treatment of patients or the promotion of public health; MDCG 2023-1 notes that according to recitals 29 and 30 of the IVDR and MDR, health institutions include hospitals as well as institutions, such as laboratories and public health institutes that support the health care system and/or address patient needs, but which do not treat or care for patients directly. **What is NOT a 'health institution'** As described in MDCG 2023-1, the concept of health institution does not cover establishments primarily claiming to pursue health interests or healthy lifestyles, such as gyms, spas, wellness and fitness centres. The recognition as a health institution can also depend on national legislation and could thus differ between Member States. Currently, the UK has no national provisions elaborating on what is or is not a health institution in Northern Ireland. Always check this document and latest guidance when determining whether an application is needed for NI clinical investigations. **Not to be UKCA / CE marked (in-house manufactured devices)** Under EU MDR Article 5(5), the notification requirements for clinical investigations will not apply to devices which are manufactured and used only within health institutions in Northern Ireland, provided the following conditions are met: (a) the devices are not transferred to another legal entity, (b) manufacture and use of the devices occur under appropriate quality management systems, (c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the

	appropriate level of performance by an equivalent device available on the market, (d) the health institution provides information upon request on the use of such devices to its competent authority, which shall include a justification of their manufacturing, modification and use; (e) the health institution draws up a declaration which it shall make publicly available, including: i. the name and address of the manufacturing health institution; ii. the details necessary to identify the devices; iii. a declaration that the devices meet the general safety and performance requirements set out in Annex I to this Regulation and, where applicable, information on which requirements are not fully met with a reasoned justification therefor, (f) the health institution draws up documentation that makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and that is sufficiently detailed to enable the competent authority to ascertain that the general safety and performance requirements set out in Annex I to this Regulation are met; (g) the health institution takes all necessary measures to ensure that all devices are manufactured in accordance with the documentation referred to in point (f), and (h) the health institution reviews experience gained from clinical use of the devices and takes all necessary corrective actions. **However, please be aware**: EU MDR Article 5(2) requires that "A device shall meet the general safety and performance requirements [GSPRs] set out in Annex I which apply to it, taking into account its intended purpose." Article 5(5) specifies that the need to meet relevant GSPRs still applies to devices/studies which are exempt from clinical investigation application requirements under the health institution exemption. **If your device meets the definition of an in-house manufactured device (EU MDR Article 5(5)), and it meets the required GSPRs (EU MDR Article 5(2)), then no application to MHRA Devices is required.** **If you do not meet <u>both</u> articles, then you do not meet the requirements for in-house exemption.**
[4]	**Not to be UKCA / CE marked (custom-made devices)** A 'custom-made device' is defined in EU MDR Article 2(3) as meaning: *any device specifically made in accordance with a written prescription of any person authorised by national law by virtue of that person's professional qualifications which gives, under that person's responsibility, specific design characteristics, and is intended for the sole use of a particular patient exclusively to meet their individual conditions and needs.*

	However, mass-produced devices which need to be adapted to meet the specific requirements of any professional user and devices which are mass-produced by means of industrial manufacturing processes in accordance with the written prescriptions of any authorised person shall not be considered to be custom-made devices; MDCG 2021-3 contains some examples of what is and is not a custom-made device. Under the UK's *The Medical Devices (Northern Ireland Protocol) Regulations 2021* s17, clinical investigations of custom-made devices are always required to submit to MHRA for authorisation, prior to commencement of the study. **Application for Authorisation required to be submitted to MHRA Devices under Article 62. Under National Provisions, all devices regardless of classification require an application.**
[5] [6]	**Investigated for Conformity Procedure – EU MDR Articles 62 to 81** Investigated for conformity procedure means clinical investigations that are carried out as part of the clinical evaluation for conformity assessment purposes, for one or more of the following reasons: a. to establish and verify that, under normal conditions of use, a device is designed, manufactured and packaged in such a way that it is suitable for one or more of the medical purposes listed in note [2] above, and achieves the performance intended as specified by its manufacturer; b. to establish and verify the clinical benefits of a device as specified by its manufacturer; c. to establish and verify the clinical safety of the device and to determine any undesirable side-effects, under normal conditions of use of the device, and assess whether they constitute acceptable risks when weighed against the benefits to be achieved by the device. MDCG 2021-6 (latest rev) (europa.eu) contains further guidance on devices being investigated for conformity procedure. If the investigational device is being investigated at any stage for clinical safety or performance data gathering where the data may be used for a manufacturer's conformity assessment, then it is being investigated for conformity procedure. In general, even pilot stage clinical investigations are conducted to gather preliminary safety and/or performance data, and a clinical investigation should be undertaken under Article 62. **If a device is being investigated for Conformity Procedure, then an application for Authorisation is required to be submitted to MHRA Devices**

	under Articles 62 to 81. Under National Provisions, all devices regardless of classification require an application.
[7]	**Not Investigated for Conformity Procedure** If a device is not being investigated for Conformity Procedure (as described above), then EU MDR Article 82 applies. **No application for Authorisation is required to be submitted to MHRA Devices under EU MDR Article 82, however the sponsor must ensure that the clinical investigation complies with the following provisions:** • **Article 62(2) and (3)** • **Article 62(4) points (b), (c), (d), (f), (h) and (l)** • **Article 62(6)**
[8]	**EU MDR Article 82 – Post-market studies within intended purpose** When the CE-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 activities as a post-market clinical follow-up (PMCF) investigation. EU MDR Article 82 applies to post-market (PMCF) studies where the device is being used under the exact conditions of it's CE-mark and there are no additional procedures that are considered invasive or burdensome. Please follow the guidance in MDCG 2021-6 (latest rev) (europa.eu) to assess whether the planned use of your device in the clinical investigation is within its intended purpose and for guidance on what is considered invasive and burdensome. **No application for Authorisation is required to be submitted to MHRA Devices under EU MDR Article 82, however the sponsor must ensure the clinical investigation complies with the following provisions:** • **Article 62(2) and (3)** • **Article 62(4) points (b), (c), (d), (f), (h) and (l)** • **Article 62(6)**
[9]	**EU MDR Article 74(1) – Post-market studies within intended purpose where additional procedures are invasive or burdensome** MDCG 2021-6 (latest rev) (europa.eu) contains guidance on post-market (PMCF) studies where additional procedures may be invasive or burdensome. Where the PMCF investigation would involve submitting subjects to procedures additional to those performed under the normal conditions of use of the device and those additional procedures are invasive or burdensome, EU MDR Article 74(1) applies.

	The sponsor shall notify the MHRA at least 30 days prior to its commencement and provide all the documentation listed in the article to the MHRA. If the sponsor is uncertain whether such additional procedures are considered invasive or burdensome, they should contact the MHRA prior to commencement of the investigation (see note below for contact details).
[10]	**Post-market studies where the device is being used outside of intended purpose** MDCG 2021-6 (latest rev) (europa.eu) contains guidance on studies where the device is being used outside of intended purpose. When the CE-marked device is assessed outside its intended purpose, EU MDR Article 74(2) states that the requirements for pre-market clinical investigation apply, i.e.: **Application for Authorisation required to be submitted to MHRA Devices under Article 62. Under National Provisions, all devices regardless of classification require an application.** If the clinical investigation is not performed as part of the clinical evaluation for conformity assessment purposes, EU MDR Article 82 applies i.e.: **No application for Authorisation is required to be submitted to MHRA Devices under EU MDR Article 82, however the sponsor must ensure the clinical investigation complies with the following provisions:** • **Article 62(2) and (3)** • **Article 62(4) points (b), (c), (d), (f), (h) and (l)** • **Article 62(6)**
	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?'. Once received, the MHRA Clinical Investigations team will reply to you to confirm. Please visit the Clinical Investigations Guidance webpage for more details on how to submit your clinical investigation Clinical investigations guidance - GOV.UK.

Version	Published	Changes
V1.0	December 2024	New guidance published