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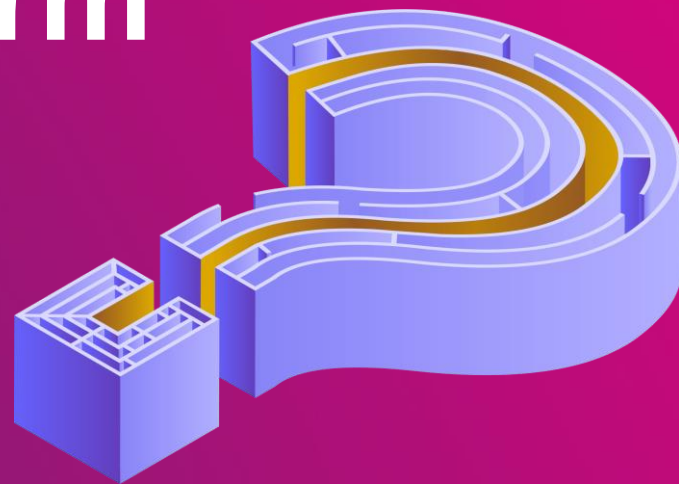


Barts Health
NHS Trust

Clinical trials regulations reform

Joint Research
Management Office

28th May 2026



Welcome

- 2025 amendment to regs came into effect 28th Apr 2026
- Biggest overhaul in 20 years
- Guidance not completed
- Discuss the changes, focus on those that may affect you
- Only affect CTIMPS
- GCP E6 revision 3 affects all

New definitions

- Non-investigational medicinal product (NIMP)
 - E.g. rescue medications, challenge agents
 - Treated mostly the same as IMPs
- Public registry
 - On or with World Health Organization
International Clinical Trials Registry Platform
- Notifiable trial (scrapping Type A-C)
 - Trial eligible for, approved via, notification scheme
 - MHRA approval (or rejected) within 14 days

Updated definitions

- Health care professional
 - Previously Dr/Dentist, now healthcare professional registered with professional body
- Coordinating Investigator (previously Chief)
 - Appropriate Health care professional (not just Dr/Dentist; e.g. Nurse). CI = PI for single site.
- Investigator
 - Previously Principal Investigator

Updated definitions

- Participant
 - Previously “subject” (or “patient”)
- Location
 - Previously “site” (locations aren’t always hospitals; wherever participants are seen / treated)
- Modification
 - Previously “amendment”
- Request for Further Information
 - Previously “Grounds for Non-Acceptance”

Approvals

- Combined review now legally mandated
- Notification scheme incorporated into law
 - Lowest risk phase 4 (and 3) approved in 14 days

Notifiable trials – inclusion criteria

Condition **A**

- IMPs authorized in UK, unmodified, used normally (no placebos)

Condition **B**

- Same as recent trial, but less risky (e.g. lower dose)

Condition **C**

- Trial approved in USA, EU, EEA (same protocol etc.)

Notifiable trials – exclusion criteria

Not aware of:

- Regulatory restrictions on IMP
- Similar, halted trials with/without USMs
- Important toxicology work incomplete
- Open serious breach with sponsor
- Impurities in IMP in healthy volunteer trials
- FIH, or FIH not complete
- Previous trials only used lower doses and/or don't reflect patient population

AND not ATMP, no participants under 18, pregnant, or breastfeeding

In Vitro Diagnostic (IVD) devices

Must identify all IVDs (e.g. pregnancy tests) using human samples (e.g. urine, blood, tumour block, saliva) to determine eligibility, stratify participants, or monitor their health in submission to MHRA.

Must confirm in cover letter that devices are a) UKCA / CE marked, and b) used according to their UKCA / CE marked licenced indication (or provide further information if not).

Modifications

1) Substantial Modification

- i. **Route A:** Substantial impact on participants or data (reviewed by MHRA)
- ii. **Route B:** no safety concerns (automatic MHRA approval, needs REC approval)
 - 1. Condition A
 - 2. Condition B
 - 3. Condition C

2) Modification of an Important Detail: Notify

3) Minor Modification: Non-notifiable, capture locally

Substantial modifications

- **Route A:** Substantial impact on participants or data (submit to MHRA)
- **Route B:** no safety concerns (usually automatic MHRA approval)
 - **Condition A:** Not first in human, same modification approved in USA, EU, or EEA (and nothing UK specific)
 - **Condition B (protocol changes):** Changes to primary endpoint/objective, end of trial criteria, patient interactions related to IMP, concomitant medication use, UK specific requirements, statistically significant trial design changes
 - **Condition C (IB changes):** New data no impacting safety, RSI increase frequency of ARs (no new terms), change not impacting safety profile, SmPC change related to undesirable effects

No concurrent substantial modifications, unless no overlap

Modifications

Modifications of an important detail (MOID)

- Doesn't impact safety or rights; not reviewed
- E.g. Trial extension (if no treatment change, change of PI, change of sponsor, adding sites)
- **NEW:** Date of recruitment of the first participant

Minor modifications

- Doesn't fall under the categories above
- E.g. Change in personnel excluding CI/PI, correcting typos, change in logistical arrangements, changing data capture method

Non-substantial modifications

- Notify MHRA and REC regularly about MOIDs
- Record Minor Modifications locally (e.g. TMF)
- IRAS updated; new modification tool deployed

**All modifications must be
approved by JRMO first**

Simplified (proportionate) arrangements for consent

Simplified arrangements if criteria are met

- IMP(s) authorised in UK and used according to authorisation
- Given during course of routine care
- No additional medications, interventions, or procedures specifically for trial

Aim to be proportionate, reduce burden, increase flexibility. HRA have task force to develop guidance & principles.

Pharmacovigilance

Written Urgent Safety Measures (USMs) 3 -> 7 days.

- Still need to call MHRA immediately

AEs (and SAEs) recorded “*from the signature of informed consent*” (unless protocol says otherwise, e.g. emergency scenarios).

- Includes medication errors, misuse & abuse of IMP

Important medical events (jeopardises participant or requires intervention to prevent SAE) also considered serious, require reporting.

Pharmacovigilance

Discussion of safety data and signal management replacing tabulated SAEs in DSUR.

SUSARs and annual safety reports no longer submitted to REC.

- MHRA will notify REC if they notice ethical issues in DSUR

Transparency

Register, and publish results

- Register trials on accepted registry
 - ISRCTN, unless elsewhere too (HRA requirement), within 90 days / before consent
 - Publish summary within 12 months*
 - Deferrals and waivers possible but unlikely to apply (e.g. IP related to medicine, DoD / national safety concerns)
- *6 months for paediatric studies

Transparency

Notify participants of results

- Must offer a lay summary of results to participants
 - To others if no capacity
 - Mandated for new trials, good practice for others
- Failure to update ISRCTN within 12 months may impact MHRA willingness to approve new studies

RECs

Unlikely to affect you

- Mandates a lay member
- REC must have 7 members to review
- 5 members (including lay member and chair) must be present to issue an opinion

Other changes

If you don't recruit within 2 years, MHRA approval lapses

- Need to re-submit trial for approval

Labelling requirements changing

- Liaise with IMP provider and sponsor pharmacist

Expert advice during approval process

- Mostly for novel compounds. Request expert advice when applying on IRAS, justify the trial and how it will be set up

Other changes

At the global end of trial:

- Notify MHRA and REC within 90 days (15 for terminations)
- Notify MHRA and REC where results have been published within 12 months

MHRA cover letters need a table of submitted documents, including version numbers and dates

Other changes

- Revise risk/benefit analysis for study if fatal or life-threatening event added to Reference Safety Info
- Abnormal lab results not AE if no change from baseline
- Agreement requires IBs sent immediately if changed
- Submit new IB with DSUR (even if no RSI changes)

Which regulations apply to me? Public registry

Will your study end after 28th Apr?

Before 28 th Apr 2026	After 28 th Apr 2026
Old	New

E.g. My study is ending but isn't registered on ISRCTN. Do I need to register it now?

Which regulations apply to me? Lay summary

Did you apply for approval for the trial



Before 28 th Apr 2026	After 28 th Apr 2026
Old	New

E.g. My study is ending. Do I have to offer a lay summary to my participants?

(...although the MHRA “encourage” you to publish in line with the new regulations if your trial ends sooner)

Which regulations apply to me? Modifications

Did you apply for the modification

Before 28 th Apr 2026	After 28 th Apr 2026
Old	New

E.g. My study has been running since 2019 but I need to submit a substantial modification. Do I submit the modification like I did previously?

Guidance

MHRA

- Guidance – from 28 April 2026
<https://www.gov.uk/government/collections/medicines-clinical-trials>
- <https://www.gov.uk/government/publications/clinical-trials-that-include-an-in-vitro-diagnostic-device>
- Modification classification flowchart
https://assets.publishing.service.gov.uk/media/68dbc85949e17d00a56ffc13/Fig1._Modification_types.pdf

HRA

- <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/clinical-trial-regulations-reform/guidance-on-changes-to-the-clinical-trials-regulations/>

Summary

- Changes to approving trials, submission of modifications, proportionality regarding consent, reporting AEs from consent, some definitions
- Principles of GCP, expectations remain similar
- Regulations closely mirror ICH GCP E6 R3

Thank you