Balancing transparency with protection of commercial confidentiality in meeting transparency requirements for UK phase I clinical trial data included in applications for EU clinical trials

The EU Clinical Trials Regulation (EU CTR; Regulation EU No. 536/2014), which was implemented on 31 January 2022, introduced new transparency requirements for clinical trial data included in applications to EU Competent Authorities (CA). This guidance explains how registration of UK phase I trials in the ISRCTN registry can meet those transparency requirements but protect commercially confidential information through deferral of publication of trial details.

Article 25 of the EU CTR requires that data submitted to an EU CA as part of an application dossier for clinical trial authorisation (CTA) or a substantial modification, submitted under the EU CTR, must come from a clinical trial that meets minimum transparency requirements. All new trials must be registered, *before the trial starts*, in a public register that is a primary or partner registry of, or a data provider to, the WHO ICTRP.

Data submitted in substantial amendment applications made to EU CA under the EU Clinical Trials *Directive* (EU CTD; Directive 2001/20/EC) do not have to meet the new transparency requirements. Also, the Article 25 transparency requirements do **not** apply to data in UK applications to the MHRA/research ethics committee (REC). While it is a condition of UK ethical approval that clinical trials be registered on a public registry, the Health Research Authority (HRA) allows sponsors to request deferral of registration[1] to protect commercially confidential information. Sponsors of trials with a deferral agreed by the HRA may satisfy Article 25 by registering limited information in ISRCTN as described below. Although it is not a UK requirement that sponsors register deferred trials before the deferral expires, the HRA has an expectation that sponsors will follow best practice and register deferred trials in ISRCTN with a minimum dataset, as described below, even if the sponsor does not intend to submit the data as part of an application made to an EU CA under the CTR.

The instructions below allow prospective registration of UK phase I trials in adults, in a WHO primary register, in line with EU transparency requirements under the EU CTR, but protect commercially confidential information.

The EU adopted its current transparency rules in October 2023 (*Revised CTIS Transparency Rules, EMA/263067/2023 dated 05 October 2023*). According to the rules, phase I trials fall into Category 1 (pharmaceutical development clinical trials). In recognition of the high commercial sensitivity of non-therapeutic clinical trials and the negligible benefit to the public of publication of details of those trials, the rules specify that Category 1 trials will be registered prospectively but *publication* of all but limited trial details will be deferred. Publication of full trial details and trial results will be at 30 months after the end of the trial.

Like the EU register, ISRCTN is a primary registry of the WHO ICTRP and allows deferral of publication of certain details of Category 1 clinical trials. The fields published at the time of registration mirror those published in the EU register at the time of the decision on the trial, and the maximum deferral period matches that in the EU transparency rules.

The following guidance summarises the *deferral process* for registering UK phase I trials in ISRCTN with delayed publication of all but limited details.

Prospective registration of new trials

New clinical trials must be registered prospectively if their data might be included in an application made to an EU CA under the EU CTR. If there is a deferral agreed by the HRA in

[1] Research registration and research project identifiers - Health Research Authority

place, ISRCTN allows sponsors to register their trials in 3 stages and defer publication of trial details and results, as follows.

1. **Initial registration –** publication of a minimal dataset: trial identifiers; very brief details of the nature, type and phase of the trial and of the number and type of participants; trial dates; details of the investigator, site and sponsor; date of submission of the MHRA/REC application; REC details; and justification for deferral of publication. For registration to be *prospective*, the dataset must be published *before* the recruitment start date provided in the dataset, so submission to ISRCTN just after MHRA/REC submission is recommended.
2. **Interim update –** publication of the date of trial approval.
3. **Final update –** publication of remaining trial details up to 30 months after the end of the trial. It is recommended, but not mandatory, that sponsors also post summary trial results at this time. Summary results can be posted in ISRCTN by uploading a file in the WHO format or providing a link to summary results on another registry, company website or repository.

If the sponsor has delegated registration, the sponsor takes responsibility for any future updates (eg details of any publications) after stage 3.

Retrospective registration of trials that started before implementation of the EU CTR

The Article 25 requirements are met for UK phase I trials in adults that started before implementation of the EU CTR if: (1) the trial had sites in EU Member States; or (2) the trial was a UK-only trial that was submitted under the rules of the EU CTD and finished before the end of the Brexit transition period – all those trials are considered to have been registered via EudraCT.[2] Trials that have been registered in other suitable registries (eg ISRCTN or clinicaltrials.gov) or published in a peer-reviewed journal also meet the requirements.

Unpublished and unregistered UK phase I trials in adults, with no EU sites, that meet either of the following criteria need further action to satisfy Article 25 before the trial data can be submitted to an EU CA in an application for a CTA or substantial modification made under the EU CTR:

- trial was authorised under the rules of the EU CTD but had not finished by 31 December 2020
- trial start date is between 1 January 2021 and 30 January 2022

For those trials, Article 25 can be satisfied by publication in a peer-reviewed journal or by retrospective registration in a public register that is a primary or partner registry of, or a data provider to, the WHO ICTRP, such as ISRCTN.

ISRCTN allows sponsors with an existing deferral agreed by the HRA to retrospectively register Category 1 trials and defer publication of all but limited details until up to 30 months after the end of the trial, as follows.

1. **Initial registration –** publication of the minimal dataset (as for prospective registration) and date of trial approval.
2. **Final update** – publication of remaining trial details, up to 30 months after the end of the trial. It is recommended that sponsors also post summary trial results at this time. Summary results can be posted in ISRCTN by uploading a file in the WHO format or providing a link to summary results on another registry, company website or repository.

As with prospective registration, sponsors who delegate the task of registration must assume responsibility for any updates to the registry entry after stage 2.

Some sponsors may prefer to fully register or publish their phase I trials. Detailed instructions are available on the ISRCTN website for sponsors who wish to take advantage of the deferral process.

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[2] 10c83e6b-2587-420d-9204-d49c2f75f476_en (europa.eu) Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation, May 2024, version 4.