

TITLE: POLICY ON CLINICAL RESEARCH TRANSPARENCY

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1 PURPOSE

Transparency in clinical research plays a critical role in advancing scientific knowledge, improving patient care, and facilitating evidence-based decision making. With this policy, KCE Trials aims to align itself with the highest standards in the field of medical research funding and contribute to the global efforts towards transparency and accountability.

The policy was developed following an [independent study](#) (1) that assessed funders' ability to comply with [WHO Best Practices in Clinical Trials Transparency](#). (2) Both documents have been used to check how KCE Trials, as a public funder of clinical research in Belgium, can improve its processes to ensure compliance with these guidelines. This policy also draws on the [NIHR Policy on Clinical Trial Registration and Disclosure of Results](#). (3)

Prospective trial registration and timely disclosure of results are essential to ensure full transparency of the results of clinical trials, including those funded by KCE Trials. These principles are also important from an ethical, moral, accountability, research integrity and waste reduction (by avoiding duplication of research) perspective.

This policy aims to improve the prospective registration and timely disclosure of results of KCE-funded trials, with the objective to increase the likelihood of impact of KCE-funded research through greater transparency.

This policy will be reviewed every three years.

2 SCOPE

This policy applies to all KCE-funded clinical trials with a funding Research Agreement signed after the implementation date (May 2023, i.e. the date on which our funding agreements were amended). Trials for which the Research Agreement was signed before May 2023 are strongly encouraged to follow this policy (where applicable, for example if registration is still technically possible).

3 ACRONYMS

- CTR: Clinical Trial Regulation
- CTIS: Clinical Trial Information System
- FPI: First Patient In
- IVDR: In Vitro Diagnostic Medical Devices Regulation
- LPLV: Last Patient Last Visit
- MDR: Medical Device Regulation
- NIHR: National Institute for Health and care Research
- SOP: Standard Operating Procedure
- WHO: World Health Organization

4 PRINCIPLES

The following principles have been incorporated in our funding Research Agreements and Standard Operating Procedures (SOPs), as detailed in the Appendix.

4.1 Clinical trials and their protocol must be registered before the first participant is enrolled

KCE Trials requires the registration of all clinical trials and their original protocol in a publicly accessible database prior to enrolment. This essential step prevents the risk of selective reporting, enables tracking of ongoing and completed trials, and allows stakeholders to be better informed. KCE Trials' preferred registry is www.clinicaltrials.gov, but other recognised registries may be appropriate or required by regulatory requirements (e.g. Clinical Trials Information System - CTIS). In such cases, KCE Trials will only require a single registration (as long as the registry is included in the WHO International Clinical Trials Registry Platform), and will therefore waive the requirement to register with www.clinicaltrials.gov. To ensure compliance with this principle, the registration status of the trial will be a necessary step for the release of the next milestone payment in the trial's funding plan.

The protocol should be uploaded as an electronic document in the registry. If the initial protocol is not uploaded within six months of the start of the trial (First Patient In, FPI), KCE may publish the protocol on its website. KCE Trials encourages chief investigators to publish their protocols in an open access journal. Fees payable to ensure open access are covered up to a predefined maximum amount by KCE Trials funding. Links to this publication can be mentioned in the registry, but do not replace the upload of the detailed protocol (as major amendments can still be made after the publication of the protocol).

This principle (protocol publicly available before FPI) follows latest recommendations on clinical research transparency (4) and are stricter than WHO best practice (protocol publicly available at results stage).

The responsibility for timely trial registration rests with the chief investigator receiving KCE Trials funds, only for trials with sponsorship in Belgium.

4.2 Study information in the registry must be kept up to date

Trial registry records should be updated, as necessary, to include the final number of enrolled participants, and the date of primary trial completion (defined as the last data collection point for the last subject for the primary outcome measure). Information such as the status of recruitment, estimated timelines for publication and results, and major protocol amendments should also be kept up to date.

The responsibility for updating trial information in a registry record rests with the chief investigator receiving KCE Trials funds, only for trials with sponsorship in Belgium.

4.3 Registering summary results should be done within 12 months from primary study completion

A summary of the clinical trial results should be made publicly available in the trial registry within 12 months of the primary study end date (Last Patient Last Visit – LPLV - of the primary outcome, unless otherwise specified in the protocol). This delay is consistent with the regulatory requirements for trials falling under the scope of the Clinical Trials Regulation (CTR 536/2014), the Medical Devices Regulation (MDR 745/2017) and the *In Vitro* Diagnostic Medical Devices Regulation (IVDR 746/2017). Posting trial results to

registries is usually much quicker than publishing them in a peer-reviewed publication and, importantly, does not prevent the results from being published in a journal at a later date.(5)(6)

The responsibility for timely disclosure of summary results rests with the chief investigator receiving KCE Trials funding, only for trials with sponsorship in Belgium.

4.4 Results should be published in an open access peer-reviewed journal or platform within 24 months from primary study completion.

Publication of results in a peer-reviewed open access journal or platform is a requirement of this policy. KCE Trials recognizes that publication in a peer-reviewed journal or platform is not entirely within the control of the research team and therefore sets an indicative timeframe of 24 months from the end of primary trial. Fees payable to ensure open access are covered by KCE Trials funding. The basic principle remains that results must be published as early as possible, and that the registration ID must be included in the publication, preferably in the abstract. To ensure compliance with this principle, the submission of a publication to a scientific journal is linked to a financial milestone in the trial's funding plan.

Results should be communicated to participants and others involved in the research as soon as the results are published and if they have indicated they wish to be kept informed.(7)

The responsibility for timely publication of results in a peer-reviewed open access journal rests with the Sponsor, and for trials with sponsorship in Belgium also with the chief investigator.

4.5 The Clinical Study Report should be made publicly available within 24 months from primary study completion.

As a peer-reviewed publication often requires a limited number of words to describe the results, not all endpoints and analyses can be included in the publication. A clinical study report, on the other hand, is a detailed document that includes the results of all planned analyses, including all secondary and exploratory endpoints. This is standard practice for regulatory submissions of pharmaceutical products. The CSR template can be inspired by the ICH E3 guidelines (Structure and Content of a Clinical Study Report), but can also be simplified. The advantage of a CSR over a publication is that there is no word limit and all endpoints can be reported, including health economic endpoints where appropriate. This may be useful for KCE if a health economic analysis follows the trial. To ensure compliance with this principle, the writing of a CSR is linked to a financial milestone in the trial's funding plan.

The timeframe for the final CSR is expected within 24 months from the end of primary study. CSR are uploaded as documents to the KCE website (and can also be uploaded to the trial's registry).

The responsibility for the timely production of CSRs rests with the chief investigator receiving KCE Trials funding, only for trials with sponsorship in Belgium.

4.6 Sharing research data after trial completion is encouraged

Research data is an important output and KCE Trials expects appropriate sharing and re-use of data, which can increase the impact of the study. In accordance with its contractual arrangements with the Sponsors, KCE Trials has very broad access to and rights to use the Study Data for research and healthcare purposes

after the trial is completed. In addition, after the study, our sponsors are contractually required to grant access rights to the Study Data to non-commercial third parties after the trial on a non-exclusive basis on fair and reasonable terms.

4.7 History of no publication of sponsoring organisation will be taken into account when reviewing applications for funding of new research studies

When an application is submitted to the KCE Trials programme for funding of a new research study, the KCE Trials team will check the sponsor's track record of timely publication of results from previous KCE Trials studies. If the sponsor has not published previous KCE Trials funded studies that have been completed, the new research study proposal will be put on hold in the selection process. The original WHO recommendation focuses on the applicant (rather than the sponsoring organisation), but this may be a sub-optimal sanction mechanism: we believe that focusing on institutional rather than individual track records may be more effective in getting trial results published.

4.8 KCE Trials will monitor and report on compliance with this Policy

Institutions receiving KCE Trials funding are expected to have a procedure in place to ensure compliance with their contractual obligations in relation with this KCE Policy. Compliance will also be monitored for all KCE Trials funded studies through regular follow-up calls with funded teams.

KCE Trials will publish a monitoring report on compliance with this policy on a regular basis (no more than every three years), highlighting details of compliance with registration and publication of reported results.

4.9 KCE Trials will provide a fully transparent and accessible portfolio of research

KCE Trials is committed to full transparency of funded trials. The [KCE Trials dynamic dashboard](#) is regularly updated and provides information on: status of funded trials, progress of recruitment *by recruiting site*, type of trial, link to key publications. The [“Funded trials” page of the KCE Trials website](#) provides information on the registry number, study summary, budget, etc. When results are available, a short lay summary of the results is also published in 3 languages.

KCE is responsible for keeping this information up to date.

5 APPENDICES

5.1 Documentation of compliance of KCE Trials with WHO best practice

In this section we document how we comply with the WHO best practice (11 item) + 4 other item that are not explicitly mentioned in WHO best practice but are also important for transparency in clinical research (data sharing plan, mention of CONSORT statement, costs of compliance covered in funding and clinical study report). The source of the text mentioned in the table below follows this hierarchy: first we refer to text in our funding Research Agreements (focusing on RA for studies with Sponsor in Belgium). If there is no mention in our RA, we refer to one of our internal policy/SOP. If there is no mention in an internal policy or SOP, we refer to another document.

The latest version of the KCE funding contract (Research Agreements) is always available on our website ([Calls/ Documents for the call](#)). SOPs are internal documents.

Domain	Item	WHO Joint Statement wording (2)	Text KCE Trials (and source = contract, SOP, etc..)
REGISTRIES	1. Prospective trial registration	“Before any clinical trial is initiated (at any Phase) its details must be registered in a publicly available , free to access, searchable clinical trial registry complying with WHO’s international agreed standards (www.who.int/ictrp). The clinical trial registry entry must be made before the first subject receives the first medical intervention in the trial (or as soon as possible afterwards).”	Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023) <i>“2.2.9 Registration of the Study and Protocol</i> (a) Contractor shall comply with all transparency obligations in accordance with applicable laws and regulations. (b) Without prejudice to the generality of Section 2.2.9.(a), Contractor shall register the Study and Study Protocol in a publicly accessible registry (such as clinicaltrials.gov) before the First Participant In.”
	2. Registry records kept up to date	“Clinical trial registry records should be updated as necessary to include final enrolment numbers achieved, and the date of primary study completion (defined as the last data collection timepoint for the last subject for the primary outcome measure). If clinical trials are terminated, their status should be updated to note the date of termination, and to	Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023) <i>“2.2.9 Registration of the Study and Protocol</i> (b) ...Any major changes to the Protocol should be updated on the same registry as early as possible.” Source: KCET-SOP-FU-002 How to follow clinical studies from First Patient In until Clinical Study Report. Version 1.1 March 2023

		report the numbers enrolled up to the date of termination.”	<p><i>“5.1.8 Registration information</i></p> <p>In case of protocol amendment, end of recruitment, end of study etc. KCE study lead should remind the sponsor to update the publicly available database (e.g. CTIS, Clinicaltrials.gov etc.) where the study has been registered, and check the update has been performed.”</p>
	3. Results posted onto registry within 12 months	“We will work towards a timeframe of 12 months from primary study completion (the last visit of the last subject for collection of data on the primary outcome) as the global norm for summary results disclosure. ”	<p>Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023)</p> <p><i>“8.4.1 Registration of the Study Results</i></p> <p>(a) Contractor shall comply with all transparency obligations in accordance with applicable laws and regulations.</p> <p>(b) Without prejudice to the generality of Section 8.4.1.(a), Contractor must have registered a summary of the Study Results in a publicly accessible registry (such as clinicaltrials.gov) within 12 months after the Study End Date as defined in section 1.48 of this Agreement.”</p>
	4. Protocol posted onto registry within 12 months	“Access to a sufficiently detailed clinical trial protocol is necessary in order to be able to interpret summary results. Therefore we also encourage development of requirements that the protocols are made publicly available no later than the time of the summary results disclosure as part of the clinical trial registry summary results information (including amendments approved by ethics committees/institutional review boards, and either as uploaded electronic document formats such as pdfs or links to the pdf).”	<p>Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023)</p> <p><i>“2.2.9 Registration of the Study and Protocol</i></p> <p>(a) Contractor shall comply with all transparency obligations in accordance with applicable laws and regulations.</p> <p>(b) Without prejudice to the generality of Section 2.2.9.(a), Contractor shall register the Study and Study Protocol in a publicly accessible registry (such as clinicaltrials.gov) before the First Participant In.</p> <p>Any major changes to the Protocol should be updated on the same registry as early as possible.”</p> <p>And <i>“16.14 Transparency</i></p> <p>16.14.5 Notwithstanding any other term of the Agreement, the Contractor hereby gives consent for KCE to (...) (ii) in the event the Contractor has not published the Protocol itself</p>

			within six (6) months from the Commencement Date, publish the Protocol, as approved by the appropriate ethics committee, on the KCE website and (iii) publish the Final Report, summary of the Final Report and Summary of the Study Results on the KCE website, provided that such documents shall not contain any (Pseudonymized) Personal Data."
JOURNALS	5. Results made public in journal	"Publication in a journal is also an expectation, with an indicative timeframe of 24 months from study completion to allow for peer review etc."	<p>Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023)</p> <p><i>"8.4.2 Dissemination and publication</i></p> <p>(a) Unless otherwise agreed between the Parties, Contractor must as soon as possible and with an indicative timeframe of maximum 24 months from the Study End Date as defined in section 1.48 of this Agreement, disseminate the Results owned by it and/or (where applicable) any Collaborator, by disclosing them to the public by appropriate means, including in scientific publications (in any medium). Contractor"</p>
	6. Trial ID included in all publications	"The Trial ID or registry identifier code/number should be included in all publications of clinical trials, and should be provided as part of the abstract to PubMed and other bibliographic search databases for easy linking of trial related publications with clinical trial registry site records."	<p>Source: see section 4.4 of this Policy. Results should be published in an open access peer-reviewed journal or platform within 24 months from primary study completion.</p> <p>"The basic principle remains that results must be published as early as possible, and that the registration ID must be included in the publication, preferably in the abstract."</p>
	7. Open access publication	"We are all supporters of open access policies, and consider that publications describing clinical trial results should be open access from the date of publication, wherever possible."	<p>Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023)</p> <p><i>"8.4.3: Open access to scientific publications.</i></p> <p>Contractor must ensure open access (free of charge, online access for any user) to all peer-reviewed scientific publications relating to the Results owned by it and/or the Collaborators."</p> <p>In practice, we follow-up for the main publication containing primary results but not for all scientific publications.</p>

MONITORING	8. Funder monitors trial registration	“We each agree to monitor registration and endorse the development of systems to monitor results reporting on an ongoing basis.”	<p>Source: KCET-SOP-FU-002 How to follow clinical studies from First Patient In until Clinical Study Report. Version 1.1 March 2023</p> <p>“5.6.3 Registration information</p> <p>KCE study Lead should remind the sponsor that study results in a scientific and lay languages should be posted on the publicly available database where the study has been registered, and check that the update has been performed.”</p> <p>Source : KCE Trials Funded Studies website</p> <p>The registry number for each study is available on KCE Trials funded studies website.</p>
	9. Funder monitors results reporting	“We each agree to monitor registration and endorse the development of systems to monitor results reporting on an ongoing basis.”	<p>Source : KCE Trials Dynamic Dashboard website</p> <p>The link to all peer-reviewed publications of all studies is available on KCE Trials Dynamic Dashboard (section Publications).</p>
	10. Monitoring reports made public	“We agree that transparency is important and therefore the outputs from the monitoring process will be publicly available”	<p>Source: see section 4.7 of this Policy. KCE Trials will monitor and report on compliance with this Policy.</p> <p>Our first transparency report is published with this Policy.</p>
SANCTIONS	11. Funder considers PIs’ past reporting record	“Reporting of previous trials realises the value of funding; therefore the contribution made from reporting previous trials, whatever their results, will be considered in the assessment of a funding proposal. When a PI applies for new funding, they may be asked to provide a list of all previous trials on which they were PI within a specified timeframe and their reporting status, with an explanation where trials have remained unreported.”	<p>This measure is not applied at level of individual PIs but at level of Sponsor organisation.</p> <p>Source: application form (call 2023)</p> <p>“Reporting of previous trials realises the value of funding; therefore the contribution made from reporting previous trials, whatever their results, will be considered in the assessment of your funding application. List all trials for which you (the chief investigator) were the principal investigator over the past 5 years and their reporting status, with an explanation where trials have remained unreported.”</p> <p>Source: Call text 2023 v1.0 May 2023</p> <p>“Before submitting a new application, a candidate Sponsor/BCC should have made results publicly available for all previous trials funded by KCE that are past 12 months</p>

			from primary study completion (the last visit of the last subject for collection of data on the primary outcome). If this condition is not met, KCE Trials will notify the investigator and the Sponsor/BCC who will have three months from then to comply.”
OTHER	Requires results sharing plan	“at the time of the initial grant submission, the plan for public disclosure of results should be included”	<p>Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023)</p> <p>“9. Access Rights</p> <p>..9.2. Results</p> <p>9.2.1. Access Right. (a) In furtherance of the main purpose and interests set forth in Section 8.3.1 above, Contractor hereby grants, and procures (where applicable) that any Collaborator grants, to KCE and any other Belgian federal or regional institution, body, office, public service and/or agency at the end of the Study, a non-exclusive, worldwide, irrevocable, unlimited, royalty-free and transferable Access Right to the Results, with the right to sub-license, for any non-commercial research purposes, public health care services purposes, and/or for designing, evaluating, and/or implementing policies or programmes in connection with or related to health care, health economics, pharmacoeconomics and/or social security.</p> <p>(b) Upon request of KCE after the end of the Study, Contractor shall grant, and procures (where applicable) that any Collaborator shall grant, non-exclusive and royalty-free Access Rights to the Results and to Contractor Background IP to use such Results, to EU or EU member state’s institutions, bodies, offices, public services and/or agencies, for any non-commercial research purposes, public health care services purposes and/or for designing, evaluating and/or implementing policies or programmes in connection with or related to health care, health economics, pharmacoeconomics and/or social security.</p> <p>...9.2.3 Access right to third parties. After the Completion Date, subject to the provisions of this Agreement (Section 5 and 6), Contractor shall use its best efforts to grant, and procures (where applicable) that any Collaborator shall grant, Access Rights to the Results to third parties on a non-exclusive basis and at fair and reasonable terms. In this</p>

			respect, Contractor shall establish a data access plan managing the access by third parties to the Results subject to the third party entering into a data use agreement with the Contractor (or the person appointed by it) providing the terms and conditions for such access. Contractor shall appoint a contact person that shall manage the third party access on its behalf. In the event Contractor and the relevant third party are unable to agree on the terms and conditions for the access to the Results, Contractor may request KCE to facilitate the discussions.”
	Cover compliance costs	Compliance costs (open access fees) made a “cost eligible item in clinical trial budgets”	<p>Publication open access fees for key publication (main publication of results and protocol) and are covered in the budget tool.</p> <p>Source publication Budgeting of non-commercial clinical trials: development of a budget tool by a public funding agency (8)</p> <p>“The publication of the main trial results should be accessible free of charge (open access), and any costs of publication are included in the fee.”</p> <p>The last version of our budget tool is available on our website (Calls/ Documents for the call)</p>
	CONSORT statement		<p>Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023)</p> <p>“4.2.2. Reporting</p> <p>c) The Final Report shall, with respect to its content and format, be in compliance with the ICH E3 Guidelines or similar format acceptable to KCE and with the CONSORT Statement (unless KCE has confirmed that said report(s) may be set up pursuant to adapted or simplified standards). The Contractor shall also provide, in a form to be agreed with KCE, a draft summary of the Final Report as well as a draft summary of the Study Results written in a manner that is understandable to the general public in English, Dutch and French. If within one (1) year of the Study End Date the Contractor has not produced the Final Report, the summary of the Final Report and the Summary of the Study Results</p>

			which satisfies KCE, KCE may prepare and publish, or arrange for the preparation and publication of such a report.”
	Clinical Study Report (CSR)		<p>Source: funding contract KCE Trials-Sponsor (version 6.0, May 2023)</p> <p>See above 4.2.2 Reporting +</p> <p>“16.14.5 Notwithstanding any other term of the Agreement, the Contractor hereby gives consent for KCE to (i) publish the Agreement in its entirety, including from time to time any agreed changes to the Agreement, to the general public, (ii) in the event the Contractor has not published the Protocol itself within six (6) months from the Commencement Date, publish the Protocol, as approved by the appropriate ethics committee, on the KCE website and (iii) publish the Final Report, summary of the Final Report and Summary of the Study Results on the KCE website, provided that such documents shall not contain any (Pseudonymized) Personal Data.”</p>

6 REFERENCES

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