

Clinical Trial Transparency in Belgium

Mapping unreported drug trials

Brussels (Belgium) and Bristol (UK), 21 January 2022



“We advocate full transparency of which clinical trials are ongoing and ensuring all results are disclosed in a timely manner... full transparency on results advances both scientific understanding and timelines for product development and ultimately enables access to essential medicines.”

Dr Tedros Adhanom Ghebreyesus, [World Health Organisation](#)

“Lack of transparency in clinical trials harms patients. The timely posting of summary results is an ethical and scientific obligation.”

[Transparency International and Cochrane](#)

“Legislation or supporting regulations [should include] sanctions if a clinical trial is not registered and/or results are not reported.”

[WHO Transparency and Accountability Assessment Tool](#)



1 KEY FINDINGS AND RECOMMENDATIONS

Obligation to report the results of all trials

Failure to report clinical trial results is not a harmless infringement. It has substantial negative consequences for patients and public health.

European Union (EU) rules adopted in July 2014 require the sponsors (organisations that conduct a trial) of each clinical trial registered on the EU Clinical Trials Register to post those trials' summary results to the registry within 12 months of trial completion (6 months for paediatric trials). These rules also apply to trials completed before 2014 and apply irrespective of whether a trial's outcomes have been published in the academic literature. Thus, all of the clinical trials identified in this report as missing summary results are in violation of European Union transparency rules that were designed to protect the interests of patients and taxpayers.

Key findings

This report discusses the clinical trial reporting performance of the nine Belgian non-profit institutions running the largest number of drug trials. These sponsors are responsible for a total of 804 drug trials.

218 clinical trials were verifiably completed more than a year ago and should therefore have results available on the European trial registry. Of these, 172 trials (79%) have made their results fully public on the trial registry. Results of the remaining 46 trials (21%) are still missing.

Overall, Belgian sponsors have made substantial progress. Four sponsors - *CHU Brugmann*, the European Organisation for Research and Treatment of Cancer (*EORTC*), *KU Leuven* and *Cliniques Universitaires Saint-Luc*, have completed or almost completed the process of uploading all due clinical trial results. Only one sponsor, *CHU de Liège*, has not made any visible progress to date. Belgium's national medicines regulator *FAMPH* has made efforts to encourage the publication of trial results.

Trial registry entries by Belgian sponsors continue to be riddled with inaccurate and out-of-date data. (See our [previous report](#) for details.) This makes it impossible to precisely determine how many trials are in violation of European transparency requirements (see next page). Unfortunately *FAMPH* has not made any visible progress in improving the quality of Belgian data on the registry.

Recommendations

- **Belgian trial sponsors** should continue or accelerate their efforts to make clinical trial results fully public as required by European Union transparency rules and WHO best practices. [See here for useful tools](#).
- **Belgian national medicines regulator FAMPH** should continue its efforts to contact trial sponsors whose results are overdue. More efforts are needed to ensure that data on the register are consistent and accurate (notably to decrease the number of trials incorrectly labelled as 'ongoing'). A mechanism for imposing sanctions needs to be developed and implemented.
- **Public and philanthropic research funders** in Belgium should sign up to the [WHO Joint Statement](#) and monitor whether the results of trials they fund are rapidly made public.

2 CLINICAL TRIAL TRANSPARENCY IN BELGIUM

This report captures the status quo and trends in clinical trial reporting by the nine largest non-profit sponsors in Belgium. It follows two similar reports from July 2020 (based on June 2020 data) and [May 2021](#) (based on April 2021 data) to document sponsors' progress over time.¹ This report exclusively focuses on non-profit sponsors because all Belgian industry sponsors already perform strongly.

The nine largest non-profit sponsors in Belgium have launched a total of 804 drug trials. European Union transparency rules require sponsors to make the results of virtually all of those trials public on the European trial registry within one year of trial completion.

218 clinical trials were verifiably completed more than a year ago and should therefore have results available on the European trial registry. However, only 172 of these trials (79%) have made their results fully public on the trial registry. The remaining 46 verifiably due trials (21%) are still missing results.

Note:

The available figure of 46 **verifiably** due trials missing results in Belgium is far lower than the **true** number of due trials missing results because many trials are falsely listed as 'ongoing' on the registry. (See our [previous report](#) for details.) The following estimates aim to provide a more realistic number of the true number due trials missing trials. We estimate that around half of all trials, 400 clinical trials total, were completed more than a year ago and should therefore have results available on the European trial registry. However, only 172 trials (43%) have made their results fully public on the trial registry. According to this estimate, 228 due trials (57%) are still missing results.

Belgian sponsors' estimated true combined reporting rate of 43% puts them far ahead of their peers in the Netherlands, whose reporting rate is [just 7%](#). However, they significantly lag behind their peers in Germany, whose reporting rate is already [around 60%](#).

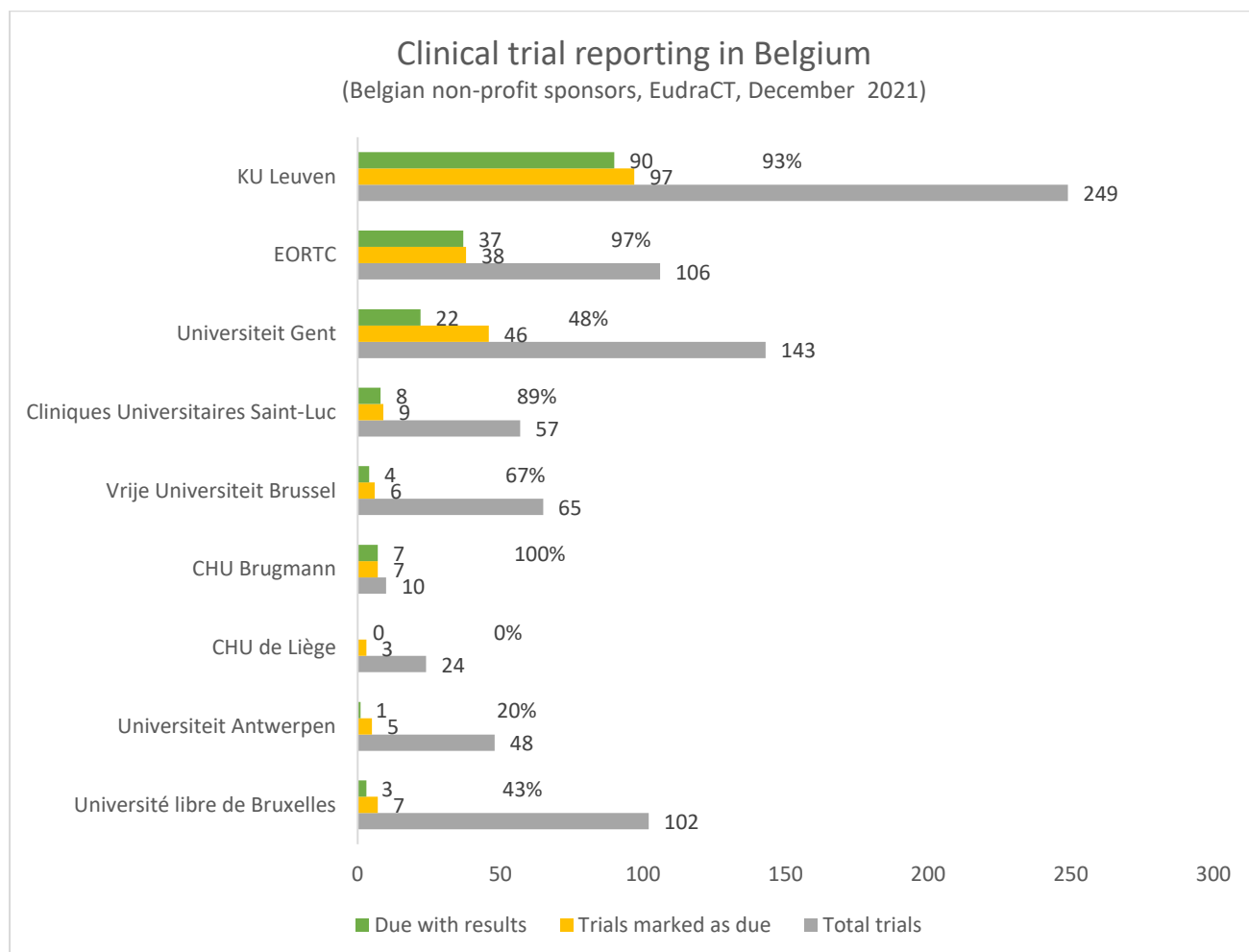
Overall, Belgian sponsors have been making substantial progress. Out of nine sponsors, four have already reported all (or nearly all) of their due trial results. As the next page shows, most other sponsors are also making progress, though at different speeds.

¹ The 2020 results were not published; they were sent directly to all listed sponsors to give them the opportunity to start improving their performance.

3 SPONSOR PERFORMANCE AND TRENDS

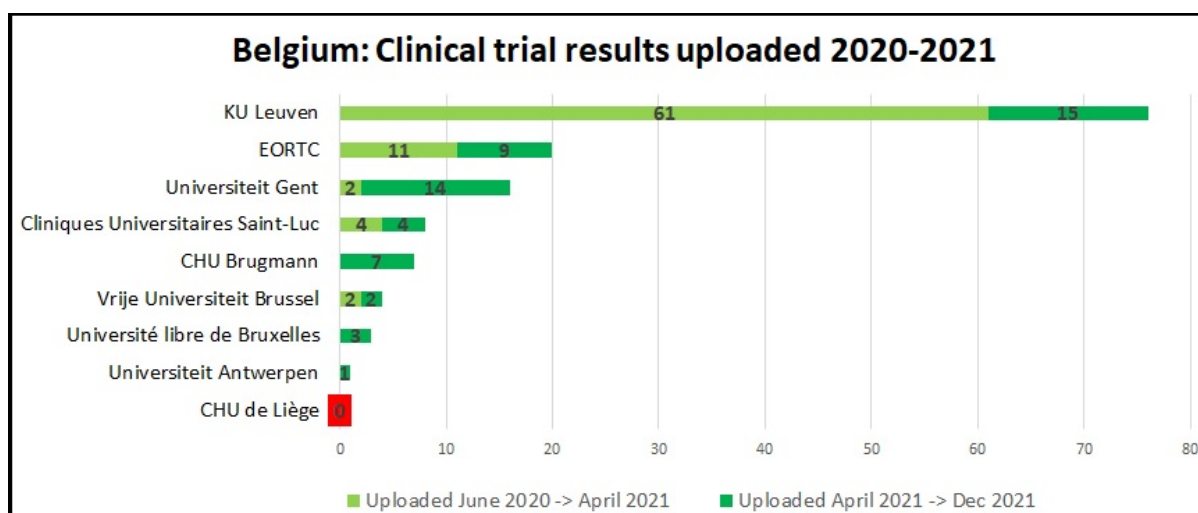
3.1. Current results

Four sponsors, **CHU Brugmann**, European Organisation for Research and Treatment of Cancer (**EORTC**), **KU Leuven** and **Cliniques Universitaires Saint-Luc** have completed or almost completed the process of uploading all of their due clinical trial results. The other sponsors still have – to a greater or lesser extent – a long journey ahead.



3.2. Evolution of reporting performance

The chart below shows that many institutions have considerably accelerated their trial reporting efforts during the second half of 2021. For example, **Universiteit Gent** has uploaded 14 due results since April 2021, compared to only two results during the preceding year. **KU Leuven's** reporting speed probably slowed down because nearly all of its due trials have already been reported.



The overall picture that emerges from the data is that Belgian sponsors fall into **three categories**:

- **Sponsors that have completed or nearly completed reporting all due trial results** (EORTC, KU Leuven, Cliniques Universitaires Saint-Luc, CHU Brugmann)
- **Sponsors that are making progress** but at different speeds.
 - Universiteit Gent, which within this category has the longest tradition of working on the reporting of clinical trials and which made big efforts last year;
 - Vrije Universiteit Brussel; Université libre de Bruxelles and Universiteit Antwerpen are also making progress
- **One sponsor that is making no visible progress** (CHU de Liège)

The table below provides the reporting performance percentage of the sponsors since June 2020.

Sponsor	% of due trials with results			Progress in % June 2020-Dec 2021
	June 2020	April 2021	December 2021	
KU Leuven	54	96	93	+ 39
EORTC	71	97	97	+ 26
UGent	18	21	48	+30
CU Saint-Luc	0	80	89	+ 89
CHU Brugmann	0	0	100	+ 100
VU Brussel	0	40	67	+ 67
UL Bruxelles	0	0	43	+ 43
U Antwerpen	0	0	20	+ 20
CHU de Liège	0	0	0	0

3.3. Data quality

Trial registry entries by Belgian sponsors continue to be riddled with inaccurate and inconsistent data. On one hand, as mentioned earlier in the report, many trials that were completed long ago are falsely still listed as ‘ongoing’. This means that more trial results are missing than is visible from registry data, and the percentages of due trials with results for many (but not all) sponsors stated in the table above overstate sponsors’ performance. For all but one sponsor, the percentage of due trials compared to the overall number is below 40% and in multiple cases less than 15%, which is unlikely to be true. On the other hand, data inconsistencies can also lead to sponsors’ reporting performance being understated: For some trials, sponsors have uploaded results, but because the trial status has not been updated from ‘ongoing’ to ‘completed, and/or the completion date is missing from the trial protocol, these trials are not listed as ‘due trials with results’. This is illustrated in the table below.

Sponsor	Trials with inconsistent data	Trials with inconsistent data that have reported results
CHU Brugmann	3	3
CHU de Liège	1	1
EORTC	29	22
Cliniques Universitaires Saint-Luc	12	10
KU Leuven	16	6
Universiteit Antwerpen	9	1
Universiteit Gent	45	5
Université libre de Bruxelles	13	9
Vrije Universiteit Brussel	7	3

Data can be inconsistent because (a) sponsors have failed to send updates to FAMPH, or (b) FAMPH failed to update registry records after receiving information for sponsors. Solving data inconsistencies is thus a shared responsibility of sponsors and FAMPH.² However, successful initiatives by the national medicines regulators in Austria and the UK show that regulators can lead effective efforts to remove data inconsistencies across entire national trial portfolios. (See this [case study](#).)

FAMPH should take a proactive role in resolving these inconsistencies (see next page).

² In the case of international trials, sponsors have to communicate with national medicines regulators in all relevant countries.

4. ACTIONS TAKEN BY FAMPH

Belgian medicines regulator FAMPH has made efforts to improve clinical trial reporting in Belgium.

Past communications with FAMPH

FAMPH in June 2021 informed us that it plans to improve clinical trial reporting and data quality by taking the following steps:

- By directly writing to sponsors, based on a list of due Belgian trials missing results provided by the European Medicines Agency
- By asking ethics committees to remind investigators of their reporting obligations
- By paying more attention to data inconsistencies in the trial registry

FAMPH efforts to improve reporting of clinical trial results

More recently, FAMPH informed us that in July 2021, they emailed all sponsors of trials without results. An updated list indicated that the number of trials without results had decreased. Another communication is planned for 2022. The Agency also published a news item on its website with relevant information about different aspects of clinical trial reporting³. Also, the Agency is organising information sessions about the new reporting rules and procedures⁴.

We strongly welcome these efforts by FAMPH, and encourage FAMPH to continue its efforts to contact sponsors during 2022.

FAMPH efforts to improve data quality

According to FAMPH, no efforts were made to improve data quality due to time constraints because of the COVID pandemic and preparations for the implementation of the new clinical trial regulation.

We encourage FAMPH to ensure that all data inconsistencies are removed before the end of 2022.

FAMPH plans to sanction sponsors that violate trial reporting rules

FAMPH clarified that sanctions are foreseen in Belgian national legislation, as well as the possibility of an amicable settlement, that can be applied once the EU Clinical Trials Regulation enters into force end of January 2022. According to the Agency, in practice, if an infringement is observed, FAMPH can propose an amicable settlement to the sponsor of the clinical trial (for a minimum amount of 4,000 Euros). If the offender does not accept the out-of-court settlement, the Public Prosecutor may initiate further proceedings.

³ https://www.fagg.be/nl/news/oproep_aan_alle_sponsors_om_de_resultaten_van_klinische_proeven_te_publiceren

⁴

https://www.fagg.be/nl/news/tweede_infosessie_over_de_nieuwe_verordening_voor_klinische_proeven_ctr_op_15_december_2021

5 WHY THIS MATTERS

Relevance to public health and clinical practice

Failure to report clinical trial results is not a harmless infringement. A 2017 [report](#) by Transparency International and Cochrane documents that a failure to fully report trial results has substantial negative consequences:

- Patients are harmed
- Public health agencies cannot make informed decisions
- Public health funds are wasted
- Medical progress is slowed down

Legal and regulatory framework

[European Union rules adopted in July 2014](#) require each and every clinical trial registered on the EU Clinical Trials Registry to post summary results to the registry within 12 months of trial completion (6 months for paediatric trials). These rules also apply to trials completed before 2014 and apply irrespective of whether a trial's outcomes have been published in the academic literature.

Thus, all of the clinical trials identified in this report as missing summary results are in violation of EU transparency rules that were designed to protect the interests of patients and taxpayers. Once the EU Clinical Trial Regulation comes into force, beginning of 2022, national regulators will have the power to fine institutions for not uploading trial results to the European trial registry.

Concerns about research waste

Unreported trials contribute nothing to progress in science and public health and are therefore costly [research waste](#). In the past, unreported clinical trial results have [caused public health losses amounting to billions of Euros and have led to the deaths of countless patients](#).⁵ For this reason, the Declaration of Helsinki has made reporting the results of every clinical trial a [universal ethical obligation](#) for all medical researchers worldwide.

While not all trials lacking results on the European trial registry are completely unreported, the best available evidence suggests that [around half of all trials missing results on the registry](#) have also not reported their results in academic journals. Thus, dozens of trials run by the universities covered in this report are in acute danger of becoming [research waste](#) unless their results are made public soon.

Universities should review their clinical trial portfolios across the EU registry, the US registry [Clinicaltrials.gov](#), and other WHO primary trial registries, identify those trials that have remained completely unreported, and ensure that their results are made public as soon as possible.

Global best practices

[WHO standards](#) require every sponsor of an interventional trial to post its results on every public registry where it was registered within 12 months of its primary completion date. Importantly, the WHO has explicitly stated that publishing trial results in the academic literature is [not](#) an acceptable substitute for posting trial results to public registries.

[Best practices jointly set out by Cochrane and Transparency International](#) also state that 'summary results for all clinical trials should be posted on the registries where they were originally registered

⁵ https://media.wix.com/ugd/01f35d_0f2955eb88e34c02b82d886c528efeb4.pdf

within 12 months of study completion'. The two health integrity groups note that retrospectively posting the results of all past trials to registries 'would improve healthcare delivery and government agencies' decision-making on resource allocations, as well as saving billions of dollars' worth of medical research from being lost forever'.

Similarly, the trial reporting benchmark set out by the AllTrials campaign states that '[a] summary of results (...) should be posted where a trial was registered within one year of completion of a trial'.

Why is posting trial results to registries so important?

There are good reasons why global best practices require posting the results of all trials to registries:

- Posting results to registries accelerates medical progress because the 12-month timeline permits far more rapid results sharing than the slow academic publication process allows.
- Posting results to registries minimises the risk of a trial never having its results reported and becoming research waste, which can happen when a principal investigator dies or leaves their post during the prolonged process of submitting an academic paper to a succession of medical journals.
- Research shows that trial results posted on registries typically give a more comprehensive and accurate picture of patient-relevant trial outcomes than corresponding journal articles do.
- Results posted on registries are easier to locate and are open access.
- Registry reporting facilitates the comparison of trial outcomes with a trial's originally stated aims and, thus, discourages harmful research malpractices such as HARKing, p-hacking and the 'silent' suppression, addition or switching of the selected outcomes.

Please see the report by Cochrane and Transparency International for further details and links to the relevant literature.

Uploading results to trial registries typically precedes publication in academic journals

There is no recorded case, ever, in which a manuscript was rejected by a journal because the trial results had already been uploaded to a trial registry.

Academic journals will accept articles reporting a trial's outcomes even if that trial's outcomes have already been made public in a trial registry. The International Committee of Medical Journal Editors has explicitly stated that the posting of summary results to trial registries is not considered prior publication by academic journals. Thus, because results reporting on registries is typically faster than academic publication, making trial results public on registries before they are published in an academic journal is becoming the new norm in scientific communications.

ANNEX: METHODOLOGY AND LIMITATIONS

Authorship

Report author: [Dr Till Bruckner](#) (Founder, TranspariMED) tillbruckner@gmail.com
The author does not have any potential conflicts of interest.

This report is published under a [Creative Commons BY 3.0 license](#)

Methodology

Cohort selection

The data in this report reflects data publicly available on the EU Trials Tracker as of 17 December 2021.

The main cohort for this study consists of all 9 non-commercial clinical trial sponsors headquartered in Belgium that had sponsored 10 or more clinical trials on EUCTR as of 01 June 2020. The same cohort formed the basis for two previous reports.

Measuring sponsor performance

Data on the clinical trial reporting performance of each of the 9 sponsors was manually extracted from the [EU Trials Tracker](#) on 17 December 2021.

The tracker data reflected trials results that were publicly available on EUCTR as of early December 2021. Due to delays by the European Medicines Agency in making public trial results submitted by sponsors, the tracker data might not include all trial results that were uploaded by sponsors during November 2021. Thus, the data in this report reflect sponsors' trial reporting performance as of early November 2021.

The EU Trials Tracker was built by the [EBM Data Lab](#), University of Oxford, and its methodology [published in a peer reviewed journal](#). The tracker is based exclusively on data that are publicly available on the EU Clinical Trial Register; the tracker is updated on a monthly basis. To the best of the author's knowledge, to date no instances of a trial incorrectly flagged as being due and missing results by the EU Trials Tracker based on registry records have been detected. The EU Trials Tracker individually lists every trial flagged as overdue, and includes a link back to the original registry entry for every trial. Thus, all data in this report is externally replicable.

Note: Estimates of the **true** number of due trials per sponsor were calculated by the author based on the conservative assumption that half of all trials were completed a year or longer ago. The same methodology has been used in numerous previous TranspariMED reports.

Limitations

Estimating the number of due trials

The EU Trials Tracker significantly undercounts the number of trials due to post results in Belgium because many trials are falsely marked as "ongoing" in the registry even though they were in fact completed long ago. The proportion of false "ongoing" trials in Belgium is unknown, and is impossible to precisely determine based on registry data.

Undercounting of results posted

Due to delays by the European Medicines Agency in making public trial results submitted by sponsors, trial results that were uploaded during late November 2021 may not have been captured by the EU Trials Tracker. In consequence, some trials whose results were only recently made public on EUCTR may have been counted as unreported. In TranspariMED's experience, the number of such trials is likely to be very low in a cohort this size. In addition, the Tracker lists trials with results that are not marked as completed and/or have no completion date in the protocol as having "inconsistent data"; such trials are not counted as 'reported' by the Tracker. These are listed in a separate table in this report.

Trials not listed on the EU Clinical Trial Register

The data in this report exclusively covers clinical trials that were registered on the EU Clinical Trial Register. Under EU rules, all clinical trials of investigative medicinal products (CTIMPs) conducted in the European Union *must* be registered on the EU Clinical Trial Register, and *must* post their results there within 12 months of trial completion.

Non-drug trials, including trials of medical devices (e.g. pacemakers) and non-drug treatments (e.g. surgery or physiotherapy), *cannot* be registered on the EU Clinical Trial Register and are thus registered on other trial registries. Such trials can be of even greater medical importance than drug trials, and sponsors are required to make their results public under global ethics rules. However, assessing Belgian sponsors' reporting performance for these non-drug trials is beyond the scope of this report.