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How to tackle clinical trial transparency: University of Bristol case study

This case study from the University of Bristol (UK) explains the steps the university has taken to ensure appropriate clinical trial registration and reporting of results across three trial registries – Clinicaltrials.gov, EudraCT and ISRCTN. It describes how the university tackled the issue, discusses how it overcame various challenges along the way, and outlines future plans for embedding best practices in clinical trial transparency.

Key lessons learnt – at a glance

- **Start the process as soon as possible.** Cleaning up registry entries can be a prolonged process, and the results of this work can take time to become publicly visible.
- **Create a central account for the institution** from which clinical trial registration and the posting of summary results can be managed, with oversight and support from a core funded Research Governance Team.
- **Include registry maintenance in job descriptions** and ensure that this area is resourced appropriately. Uploading data onto trial registries can be difficult and time consuming, and often requires specialist skills.
- **Use the [WHO definition](#) to identify clinical trials** and ensure that trials are set up and run accordingly from the very beginning. This will avoid the need to retrospectively post summary results on EudraCT, as this often requires a time consuming statistical re-analysis of trial data to meet registry requirements.
- **Actively engage with the administrators of trial registries.** Active support from registry counterparts throughout the process can significantly help university staff in navigating the process.
- **Engage in best practice exchanges** and work collaboratively with counterparts, including regulators. Relevant fora in the UK include the [HRA](#), [NHS R+D Forum](#), [MHRA forum](#), [ARMA](#), and [UKRIO](#).

Background

The University of Bristol is a leading British academic institution. In any one year, its Research Governance Team supports about 1,200 active studies in addition to 2,000 that are reviewed via the university's Research Ethics Committees but do not require additional due diligence checks.

In 2010, the university put into place a [Research Governance and Integrity Policy](#) and appropriate clinical trial registration is indicated as a sponsor obligation and managed in line with the Standard Operating Procedure. The university has been actively tackling its clinical trial registry entries since 2014.

Registration of trials conducted at Bristol is distributed across three main registries: Clinicaltrials.gov, EudraCT, and ISRCTN. Some trials have an entry in more than one registry. For example, European Union regulations require every Clinical Trial of an Investigational Medicinal Product (CTIMP) to be registered with EudraCT, but sometimes [funders require](#) these same trials to also be registered with ISRCTN. In addition, some researchers register their studies with the American registry Clinicaltrials.gov, usually if their project is funded by an American funder requiring the study to be registered there.

Centralising and cleaning up registry entries on Clinicaltrials.gov

The university initially considered the American registry Clinicaltrials.gov to be the trial registry of choice as it enabled researchers to register their trials for free. However, when the university became aware of potential penalties for not updating registry entries in 2014, only researchers who received U.S. funding were encouraged to use this registry.

Historically, trials were registered by individual researchers naming the University of Bristol as their umbrella organisation (trial sponsor) without prior agreement by the university. This meant that the central Research Governance Team was unable to effectively manage the registration of trials associated with the university.

In 2014, the university decided to set up an institutional University of Bristol account on Clinicaltrials.gov that would be managed centrally by the Research Governance Team. In order to do this, the university had to take on responsibility for every study that named the university as the umbrella organisation. The account was set up in 2016, with a legacy portfolio of 16 studies that had named the University of Bristol as the sponsoring organisation.

Since then, the Research Governance Team has systematically worked through all older registry entries.

It contacted the principal investigators involved in these studies (interventional clinical trials as well as observational studies) to ensure that these studies were appropriately registered in line with Clinicaltrials.gov requirements. Throughout this process, the Research Governance Team received support from the PRS team working at ClinicalTrials.gov, who were responsive and extremely helpful.

“The Research Governance Team has systematically worked through all older registry entries.”

In some cases, the university had been incorrectly listed as the sponsor of a study, or different research team members had accidentally registered the same trial twice. After thorough due diligence, Clinicaltrials.gov removed these entries from Bristol's account.

The posting of summary results will probably not be possible for studies that closed prior to the setup of the university's central account in 2014, except in the case of one study, where it was possible to secure input from appropriately qualified statisticians with knowledge of the trial.

“Now that the university has assumed central control, the process is easy to manage.”

Looking forward, the university will ensure compliance with ClinicalTrials.gov requirements for all registrations made since the central university account was set up in 2014, including the timely posting of summary results on the registry for all studies, including observational studies.

Now that the university centrally controls who can get access to its registry account, the process is easier to manage. At present, the Research Governance Team is managing four such ongoing studies on the U.S. registry.

In line with WHO best practices, if a trial is registered on Clinicaltrials.gov, duplication of its registration with EudraCT or ISRCTN is discouraged unless specifically required by funders.

Posting summary results on EudraCT

The university currently actively manages 16 registrations on EudraCT, the European trial registry. (All of these are CTIMPs, a category of clinical trials defined by European Union regulations. CTIMPs must be registered on the European registry, and [must also post their summary results there](#) within 12 months maximum of the primary completion date. Trials that are not CTMIPs cannot be registered on the European registry.)

Of the 16 CTIMPs being actively managed, eight have already posted results. (Note that there is a time delay between validation by the national medicines regulator MHRA and public visibility.) Seven trials have obtained EudraCT numbers, but it has not yet been possible to assign these to the central university account to allow the posting of results. The university is working with the regulator to ensure that trials that are sponsored by the university are added to the central account to enable the university to manage upload of results. One study is in the process of being set up and will obtain a EudraCT number over the next few weeks.

In addition, there are six older CTIMPs that closed in 2009 or earlier that are also registered on EudraCT. Where possible, the Research Governance Team has worked with researchers to see if summary results can be uploaded for these trials, but in most cases, the original research team is no longer at the university.

Retrospectively posting the summary results of older trials poses significant challenges as EudraCT outcome reporting requirements had not been included in the original funding applications and research designs, so their statistical analyses had not been geared to EudraCT reporting purposes. (In the past, it had been sufficient to mail a trial summary or publication to the national medicines regulator on a CD.) Thus, for older trials, considerable input from researchers, statisticians and members of the Research Governance Team is required to address validation issues and manage the uploading of results.

“Retrospectively posting the results of older trials poses significant challenges.”

Today, the University maintains a central EudraCT account and actively monitors clinical trial registration and the uploading of summary results. During trial setup, researchers are made aware of trial registration and EudraCT summary results posting requirements, including its requirements for outcome reporting formats.

Resources invested

At the university, a central core funded Research Governance Team of six people is responsible for overseeing research that involves human participants, their tissues, and/or data. This includes managing clinical trial registry entries.

Since 2017, one member of the team has been responsible for clinical trial registration and the posting of summary results on EudraCT and Clinicaltrials.gov. This person manages the EudraCT account, including the uploading of results onto the registry, for all CTIMPs sponsored by the university. The same person also acts as [PRS Administrator](#) for Clinicaltrials.gov, and is responsible for ensuring that registry entries there are accurate and up to date.

This work usually takes up about one day per month. More input is required when summary results are being uploaded as the validation process, which typically involves multiple exchanges with registry staff, can be complex. As the university has a centralised Research Governance Team, this process can be managed within the existing support infrastructure with support from the research teams.

Future plans

The University of Bristol is in the process of installing a new Case Management and Award Management System and clinical trial registration and reporting fields will be added to the meta data fields to ensure that appropriate support can be offered to its researchers in relation to trial registration and the uploading of results.

“A new case management system will enable the university to track all clinical trials.”

The new system will enable the university to clearly identify and track studies that should be registered on a trial registry. Historically, the university was only able to flag CTIMPs in this way. Going forward, the University of Bristol will be able to ensure that all studies that fit the [WHO definition](#) of a clinical trial are tracked.

In addition, the university plans to extend its retrospective data clean-up operation to ISRCTN, the third trial registry it uses.

At present, different regulatory and funder requirements sometimes require the same trial to be registered on more than one registry. In these cases, the university cannot avoid duplicate registrations. This is a problem outside the control of the university, requiring reforms at a higher level. Members of Bristol’s Research Governance Team will contribute to resolving this issue by working collaboratively with major stakeholders, including Britain’s Health Research Authority and the MHRA.

*This case study was written by [Dr Birgit Whitman](#), Head of Research Governance at the University of Bristol. Till Bruckner of TranspariMED contributed editorial input.
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