BIH QUEST
Transforming Biomedical Research

BIH QUEST Center – Quality | Ethics | Open Science | Translation
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Achieving excellence in clinical trial reporting

A manual for European universities and university hospitals

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A growing number of universities and university hospitals across Europe want to ensure that the results of all their clinical trials are made available on trial registries, but often do not know where to start, or how to proceed.
This manual provides guidance, tips and tricks to make the journey easier.

The manual is based on interviews with 18 people who have been driving improvements in clinical trial reporting at 13 different institutions in six European countries. Some of these institutions have already made strong progress; others are still in the early stages of their journey.

While the manual primarily focuses on the European registry EudraCT, many of the approaches are transferable to ClinicalTrials.gov and other registries.

COMING NEXT: COLLECTION OF USEFUL RESOURCES
The BIH QUEST Center plans to collect resources developed by universities and university hospitals to improve their registry management in order to facilitate cross-learning between institutions. Examples include policies, training materials for researchers, Standard Operating Procedures, flowcharts, document templates, forms, checklists, and contracts. Please contact us if you have relevant resources – if you request confidentiality we will not make them publicly available.

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Workflow →

	FIRST STEPS	PAST & PRESENT TRIALS	FUTURE TRIALS
REGISTRY MANAGER	1 Designate manager 2 Create overview 3 Identify problems	1 Old EudraCT trials 2 Recent EudraCT trials 3. All other trials	*[Manage registry data]*
TASKFORCE	1 Set up taskforce 2 Choose model 3 Set expectations	1 Strengthen policies 2 Strengthen systems & processes	

INTRODUCTION

Legal, regulatory and funder requirements

Legal responsibility for uploading clinical trial results rests with institutions such as universities and university hospitals (the 'trial sponsors'), not with individual researchers or research funders.

- On the European registry EudraCT, institutions must upload the result for every trial within 12 months of completion (6 months for paediatric trials). This applies to every trial on EudraCT, including all Phase 1 trials and older trials that were completed over a decade ago. From 2022 onwards, when the EU Clinical Trial Regulation fully comes into force, institutions that fail to meet this requirement may face fines and other sanctions.

- On the American registry ClinicalTrials.gov, institutions must upload the results for some interventional trials within 12 months of completion. Institutions risk a fine of over $11,000 for every day of delay in posting a trial result. The applicable law (FDAAA) is complex, so it can be difficult to determine which of your trials are subject to it.

- On the other World Health Organisation (WHO) primary registries, such as ISRCTN and DRKS (full list here), there is usually no legal requirement to post results. However, some research funders already require their grantees to upload trial results within 12 months of completion, and many others are preparing to adopt similar rules.

  "The buck stops with the sponsor."
  Experienced registry manager

Scientific benefits

There are numerous good reasons why regulators, research funders and the World Health Organisation emphasise the importance of making trial outcomes available on registries, including:

- Posting results onto registries accelerates medical progress because the 12-month timeline permits far more rapid results sharing than the slow academic publication process allows.

- Posting results onto registries minimises the risk of a trial never reporting its results and becoming research waste.

- 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.

Registry publication versus journal publication

Many researchers still fear that rapidly making their trial results public on a registry could endanger subsequent publication in a journal. This fear is completely misplaced. Journals have clearly stated that they will never reject a manuscript for this reason – and they have kept that promise. (You can share this blog with your researchers.)

FIRST STEPS

> TIP: The slides of the BIH QUEST Center's 2019 clinical trial reporting workshop in Berlin provide an introduction to the challenges ahead, and tips and tricks for overcoming them.

Designate a registry manager

It is absolutely essential to formally designate one person as registry manager, and to write this role into their job description.

The registry manager creates and maintains an overview of the institution's trial portfolio, manages communications with regulatory agencies, and communicates with and provides support to individual researchers. Depending on the institutional setup, the registry manager may also directly upload some or all trial results.

Performing the role of registry manager may take up only a couple of hours a week at institutions with small trial portfolios; at large institutions, it can require a new part-time position to be created.

> *"The time taken to update each EudraCT record varied widely according to the availability and format of data, the challenges in posting it to the registry, and subsequent liaison with the EMA and MHRA to update the records. On average, each record took several hours to complete."*
> Experienced registry manager

The person assuming this role does not have to hold a senior position or have prior specialist skills. Some institutions have found that giving the role of registry manager to a statistician can simplify workflows.

> *"A willingness to learn and good communication skills are vital attributes."*
> Experienced registry manager

Once the initial backlog of unreported trials has been cleared, and strong policies, systems and processes have been put into place, keeping a trial portfolio up to date will require significantly less input.

> *"We currently have 54 ongoing trials listed on EudraCT. Managing these entries on EudraCT – including periodic updates and the posting of summary results – entails a total workload of around 20 hours per month across the team, on average."*
> Experienced registry manager

Create overview of all registry entries

The new registry manager should start off by searching clinical trial registries (all WHO primary registries used by your researchers, plus ClinicalTrials.gov) for interventional clinical trials sponsored by your institution. When searching the registries, try a variety of spellings, and also search for the name of your institution's home town. Create a spreadsheet of all registry entries.

> TIP: Some trials might have been registered on multiple trial registries (e.g. on EudraCT and ClinicalTrials.gov). Flag such trials as you go along, so you can later ensure that data are consistent across all registries.

Identify common problems

Next, review entries across all registries to gain a better understanding of the challenges you face (example here). For example, you are likely to discover that some researchers or even research unit at your institution have been registering trials independently, rather than using the institution's account, that many trials were only registered retrospectively, and that some trials that were needlessly registered on more than one registry, plus a lot of missing, outdated and inconsistent data. This information can help the taskforce (see below) to develop stronger policies, systems and processes.

Set up a taskforce

Set up a taskforce headed by a senior member of the management team. The taskforce should be composed of representatives of all units involved in running clinical trials (e.g. Clinical Trial Unit, research governance, legal department, finance, etc).

The taskforce's overall role is to ensure that changes to policies, systems and processes are fully coordinated and aligned across the entire institution. The taskforce should meet on a monthly basis to review and guide the efforts of the registry manager.

> *"The Head of Research Governance will now regularly review and provide updates at faculty board and committee level on how clinical trials researchers are making positive progress, as well as highlighting where further work is required to ensure compliance."*
> Experienced registry manager

Choose a model

Many institutions have already achieved excellence in trial registry management. Experience shows that a range of different models can ensure that registry entries are complete, accurate, and up to date, and that results are uploaded in time. The taskforce needs to choose a model that aligns well with existing structures and provides researchers with the best possible support.

> TIP: In some cases, several different institutions have pooled the trial registry management function in one shared unit. An example is King's Health Partners, which (among other things) manages trial reporting on EudraCT for a university, two hospitals, and a public body (case study here). Institutions that sponsor few trials might be able to achieve efficiency gains by outsourcing registry management to a larger institution.

The model should take into account the scope and role of the Clinical Trial Unit (CTU). For example, in many institutions, only some trials are run through the CTU, whose trial policies and processes may differ from those used by the wider institution. Options to consider include locating the registry manager function within the CTU, making CTU statisticians available to support the retrospective reporting of results on EudraCT, centralising some processes such as trial registration for all trials (within or outside the CTU), or even running all future interventional trials through the CTU. Institutions that do not have a CTU may want to consider setting up such a unit.

> TIP: In some institutions that perform strongly on trial reporting, the registry manager sits within the CTU (example here), while in others the registry manager is embedded within a central institutional Research Governance team (examples here and here) whose remit covers a broader range of research projects. Either approach can work well.

European universities and university hospitals have adopted at least four different models for trial registry management:

1. Decentralised model

In the decentralised model, researchers retain full control over the registry entries for their own trials. The registry manager oversees the portfolio as a whole, sends emails to remind researchers to update entries or upload results, and provides training and support on demand, for example by sitting with researchers when they enter data into registries.

2. Centralised model

In the centralised model (example), the registry manager assumes full and exclusive control over all trials in the institution's portfolio. When updates or results are due, the registry manager requests the necessary data from researchers, and then directly enters that data into registries.

3. Cluster model

One institution interviewed uses a cluster model. The registry manager has oversight of the overall portfolio. Each research cluster (or unit) within the institution has one designated point person who assumes control over all trials run by that cluster, and directly enters data for that cluster's trials into registries.

4. A la carte model

The a la carte model is similar to the centralised model, but researchers are given a choice between directly managing registry data for their own trials, or letting the registry manager perform that task for them (example).

	ADVANTAGES	**DISADVANTAGES**
1 DECENTRALISED	Low workload for manager Fast and easy to set up Builds staff capacity	Higher workload for researchers Low overall efficiency Uneven data quality
2 CENTRALISED	Researchers appreciate 'good service' Potentially very efficient High data quality Easier to upload results when researcher has left institution	High workload for manager Data requests usually require several iterations Manager may lack understanding of trials if portfolio is large
3 CLUSTER	Good 'fit' for decentralised institutions Data entry performed by person close to researcher Builds staff capacity	Potentially less efficient
4 A LA CARTE	Researchers appreciate 'good service' Builds some capacity	Hard to predict workload for manager Requires multitude of processes

> *"I let researchers choose if they want to upload the results themselves, or want me to upload them. If they want me to do it, I compile most of the information that needs to be uploaded into EudraCT from the trial protocol, and then send it to the researcher to review it for accuracy. It's a 'customer service' approach."*
> Experienced registry manager

Set clear expectations

Researchers running trials are typically overworked, and may assign low priority to emails from a registry manager urging them to update registry entries or provide data.

Senior management must therefore send a clear message that achieving excellence in trial registry management is an important institutional goal, and that all researchers are expected to contribute towards attaining this goal. A formal high-level decision setting out clear expectations can help to strengthen the registry manager's hand.

> TIP: Experience shows that most researchers are surprisingly supportive of efforts to improve registry management if the importance of doing so is explained to them (this blog provides some talking points), and if they are offered strong support throughout the process. In one institution offering centralised reporting, some researchers asked to directly enter their data themselves as they saw this as a valuable career-enhancing skill.

Prepare to face two challenges

Institutions in Europe commonly face two challenges:

- **Retrospective:** Upload the results for past clinical trials listed on EudraCT
- **Prospective:** Adopt and implement WHO best practices to ensure that reporting is timely and consistent across all registries (including but not limited to EudraCT) in future

> *"These are essentially two separate processes, but they can be run in parallel."*
> Experienced registry manager

> *"Be prepared and willing to undertake some intensive activity to bring your records up to date, perhaps devoting a dedicated 'task team' to address this swiftly and comprehensively. Subsequently, and critically, set the parameters, expectations and guidance for maintaining registries and communicate these clearly to the clinical trials community so that responsibilities are clear and progress can be maintained as a matter of routine in the future."*
> Experienced registry manager

UPLOAD MISSING CLINICAL TRIAL RESULTS ONTO EUDRACT

Your institution must upload the results for every clinical trial listed on the European trial registry EudraCT, even if that trial was completed many years ago, or if the researcher running it has left your institution.

Identify trials you are responsible for

Type your institution's name into the search window of the EU Trials Tracker and use the results to expand your existing spreadsheet (see above) of registry entries. The Tracker relies on registry data, so inaccurate data in the registry leads to inaccurate Tracker results. Frequent problems with registry data include:

- False ongoing trials. Some trials that were completed long ago may still be incorrectly marked as 'ongoing' in the registry, and are thus shown as 'not due' by the Tracker even though their results are overdue.
- Trials flagged by the Tracker as having 'inconsistent data'.
- Not our trial. The person registering the trial might have accidentally entered your institution's name as the trial sponsor, so you are falsely listed as being responsible for a trial you never ran.
- Unallocated trial. One of your own researchers may have entered an ambiguous sponsor name such as "Heart Clinic", so the Tracker does not list the trial under your institution's name even though you are legally responsible for it.

> *"The Tracker is very useful, but you should not rely on the Tracker alone to provide an overview of your [EudraCT] trials. You need to create a separate spreadsheet."*
> Experienced registry manager

Check for data accuracy

Check for data accuracy and flag incorrect data in your spreadsheet:

- Check all trials that are listed as 'ongoing' against your internal records. It is highly likely that some of those trials that have actually been completed.
- Click on the 'inconsistent data' tab within the Tracker to see what the problem is for each of those trials.
- Flag any trials that incorrectly list your institution as the sponsor.

Contact your national regulator

You cannot directly change the trial status (e.g. from 'ongoing' to 'completed') on EudraCT. Only your national medicines regulator can do this. Send a spreadsheet with the correct data to the regulator and ask the regulator to enter missing completion dates, correct inaccurate data, etc. If the trial was run in more than one country, you will have to request the regulators of all countries involved to update the trial status (contact details here).

> TIP: Sending a single spreadsheet to the regulator makes the workflow far easier than requesting corrections on a trial-by-trial basis. Make sure to regularly follow up with the regulator until all data on EudraCT is accurate. If there is more than one regulator in your country (e.g. BfArM and PEI in Germany), you can see which regulator ('National Competent Authority') is responsible for a trial in its EudraCT entry.

At the same time, ask the regulator to provide a complete list of trials that your institution is responsible for. The regulator has access to contact email addresses that are not publicly displayed on EudraCT, so it can help you to identify additional trials that your earlier searches missed. Once you have that information, change the sponsor name in the EudraCT entry and notify the Tracker team so they can correctly allocate it. (The regulator also has information on your institution's Phase 1 trials in adults, which are not publicly displayed on the registry.)

> TIP: Sometimes the Tracker does not allocate trials to the correct institutions. For example, it might aggregate trials belonging to a university and a university hospital, even though sponsorship for these trials lies with two legally separate institutions (or vice versa). In such cases, you can directly contact the Tracker team and ask them to correct the allocation. However, in all other respects, the Tracker exclusively relies on data listed on EudraCT. The Tracker team thus cannot make changes to trial completion dates or any other data points. These changes have to be made directly on EudraCT.

Triage trials by their completion date

It is mandatory for your institution to upload the results for each and every clinical trial that is listed on EudraCT, including trials that terminated early.

There are two possible ways of doing this:

- For trials involving adults only that ended before 21 July 2013, you can upload the results as an attachment. This is comparatively easy.
- Entering the full data set into EudraCT is the standard process. This can be complex and time-consuming. Full data sets are mandatory for all trials that ended on or after 21 July 2013, and for all paediatric trials regardless of completion date.

These two processes are described in more detail below.

> *"Many [old] trials… can have results posted very easily by uploading a publication or results document. I would suggest that these results are uploaded first, as this will familiarise users with the system before the more complex results data entries are attempted."*
> Experienced registry manager

Contact researchers

Regardless of whether you plan to centrally upload results, or expect researchers to upload their results themselves, you will need to contact the researchers who ran the trials. Experienced registry managers suggest a 'friendly but firm' approach – with an emphasis on 'friendly'. You should always combine reminder emails with links to relevant training materials and offer to provide them with assistance. Remind researchers of the obligation to upload their results long before results are due.

> TIP: The first time you contact researchers about their missing trial results, the email should come from senior management to underline that reporting results is an institutional requirement that is to be taken seriously. Referencing a formal faculty decision on the issue and/or to regulatory expectations can add additional weight.

> *"Our legal department sends out the reminder emails. That always gets researchers' attention. I then follow up with an email of my own offering support with uploading trial results."*
> Experienced registry manager

Become the 'primary user' of your institution's trials

To enter the results of a trial in EudraCT, users first need to apply for 'results user' status with EMA.

If you plan to centrally upload results for multiple trials, you first need to create an EMA account, then request assignment to become the 'primary user' for those trials, and then gain the 'results user' role for those trials. (You should also assign a colleague as a 'back-up user'.) The EMA's "Tutorials on posting results" and FAQ explain how to do this. You can ask EMA to assign up to 20 trials using the same request form; this will save time.

> TIP: Even the researcher who originally registered the trial has to obtain 'results user' status before being able to upload results. If you plan to adopt a decentralised approach in which researchers upload their own results, provide your researchers with guidance on how to obtain 'results user' status for themselves.

EMA generally processes 'primary user' assignment requests within one working day. The 'results user' role is automatically assigned through logging out of the application and then logging back in. (In case your credentials do not seem to work immediately, wait a few hours and then log back in.)

> TIP: If a request for assignment of a trial is automatically rejected by the system, it means that in the past, the trial was already assigned to a different primary user. Contact EMA in order to replace the primary user for that trial.

> *"Develop a small group of expert 'results users' within your team or department initially, and later roll out to other staff members."*
> Experienced registry manager

Upload results as an attachment (older trials only)

This option is available only for trials conducted exclusively with adults that ended before 21 July 2013. EudraCT is very flexible on which format you use to do this.

If a trial's outcomes have been published in an academic journal, you can simply upload a PDF of the journal article to the registry (example here). If you are worried about copyright violations, you may be able to upload a post-print provided by the author. Else, you can upload a file containing the text of the abstract plus a hyperlink to the full journal article. For experienced registry users, this process takes only 1-2 hours per trial.

If a trial's outcomes have not been published in a journal, ideally you use the standard process for entering the full data set in order to maximise utility for registry users. However, you can also present results in a narrative with tables and upload that (example here). If a study ended prematurely without recruiting any patients (example here), or terminated early after recruiting only a few patients (example here), a very brief statement is sufficient. You can upload results in a broad range of file formats, including PDF, XLS, DOC, and PPT.

> TIP: Once the summary attachment has been uploaded, you must click on "Post results" at the top right corner of the webpage. Otherwise, results will remain in 'draft' status and will never be posted.

Upload results using the full results data set

This option is mandatory for all trials that ended on or after 21 July 2013, and for all paediatric trials regardless of completion date. It is optional for adult trials that ended before 21 July 2013 (see above).

EudraCT is not user-friendly, so this can be a complex and time-consuming process. First-time users can take up to a week to enter the results for one single trial. However, there is a strong learning curve, and experienced users can typically enter results within 2-4 hours if the results have been pre-formatted in line with EudraCT data requirements (5-15 hours if not).

> TIP: If you receive a validation error or warning related to the results you are uploading, look up the problematic item in EMA's "Validation Rules" document (column on "rule description" for guidance on how to resolve it. The EMA's "Tutorials on posting results" and FAQ provide additional information. If you are unable to resolve the problem, contact EMA for assistance.

> *"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. 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."*
> - Experienced registry manager

> TIP: One institution is piloting the use of graduate students for entering the results of older trials whose lead researchers no longer work there. Whether this approach works well is not yet clear.

Overcoming technical problems with uploading results onto EudraCT

PROBLEM	SOLUTION
EudraCT requires specific data formats	For future trials, statistics should be prepared with results reporting on EudraCT in mind from the beginning. For trials that have already been completed, results sometimes need to be re-analysed to meet EudraCT data requirements. You need to ensure that the registry manager has access to support from a statistician when needed. Alternatively, appoint a statistician as the registry manager.
(Serious) Adverse Events	A key advantage of registry reporting is that it provides more data on SAEs and AEs. Often, researchers will have to go through old records, and/or get statistician support to get full AE data and analyse them.
Data required by EudraCT is missing	Consult multiple sources, including the trial protocol, ethics approval documents and Clinical Trial Unit archives. Never rely on just one data source.
The researcher no longer works at the institution	Contact the researcher, and if that is not successful, contact the other team members. Also check in your archives. According to one registry manager, "you will be surprised how many old trial results you will be able to recover". Once you have obtained the necessary results information from the researcher, ask EMA to assign you as the 'primary user' for that trial to upload its results.
The trial never recruited any patients	Contact your National Competent Authority and ask them to change the trial status to "prematurely ended". For older trials involving only adults, upload a PDF explaining why the trial never recruited patients. For more recent trials, see Module 6 here for a simple workaround. See also the FAQ by EMA and this blog by EBM Data Lab.
Trial sponsorship has been taken over by a different institution	Liaise with the new institution and the relevant National Competent Authority in order to have the name of the sponsor updated in EudraCT. Provide any details on the trial you hold to the new institution so that results uploading will be easier for them.
Other problems	Please refer to the FAQ by EMA. The FAQ regularly gets updated.

Useful guidance for uploading results onto EudraCT

GUIDANCE	DESCRIPTION
QUEST workshop	Modules 4-6 provide advice on how to gain results user status, enter data into EudraCT, and overcome common barriers and challenges.
EMA tutorials	This page details all the steps required to post your trial results in EudraCT.
AllTrials guide	A blog by the AllTrials campaign explaining how to upload results and update entries on two registries, EudraCT and ClinicalTrials.gov.

REVIEW YOUR TRIALS LISTED ON OTHER REGISTRIES

Review registry entries

Review the registry entry for each trial and flag problems on your existing spreadsheet of all trials (see above). Flag trials that do not have results available on registries. Flag errors and outdated information for later follow-up (example here). For trials listed on more than one registry, check for consistency of data between different registries.

> *"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 [our university's] account."*
> Experienced registry manager

Identify completely unreported trials

Studies suggest that the results of around half of all clinical trials are never made public; a recent review of German university trials found hundreds of trials that had not made their results public anywhere. These unreported trials endanger patients and public health. For example, American doctors inadvertently killed over 100,000 people over the course of a decade because the results of a single 'uninteresting' academic trial remained hidden.

For every trial that does not have results available on its registry entry, check whether its outcomes have been published in an academic journal. This requires manually searching PubMed for the trial ID number (such as NCT123456789), and if that fails, searching Google Scholar for the trial number, title, investigator name, and keywords. Review search hits carefully to ensure that they really contain trial outcomes (rather than just the trial protocol or an external reference to the trial). Upload the DOI of journal articles onto trial registries and mark the trial as reported in your spreadsheet.

Follow up on completely unreported trials

For trials whose results you could not find, email the lead researchers and ask them to provide you with a link to the journal publication. If the trial has not been published, flag it as being in acute danger of becoming research waste. Follow up with researchers until they have made the results public, either in a journal or on the trial registry. (It is very easy to upload results onto some trial registries; researchers can still publish results in a journal later.) No trial should be left completely unreported.

Correct and update registry records

Your review of registry entries (see above) will likely have identified many problems. Fixing every single problem is probably not feasible. Identify and prioritise the most important problems, and draw up a plan for fixing those. In particular, it is important for patients and for public health to update the registry entries for trials that are listed as 'ongoing', but in fact have been completed.

ADOPTING AND IMPLEMENTING WHO BEST PRACTICES

Why WHO best practices?

In order to achieve regulatory compliance and avoid drug trials remaining unreported on EudraCT in future, you will have to make changes to policies, systems and processes. Adopting WHO best practices means that you make these changes not only for drug trials listed for EudraCT, but for all interventional clinical trials as defined by the WHO, no matter which registry they are listed on. (This excludes observational studies and non-interventional studies.)

Adopting WHO best practices will bring your institution fully in line with scientific best practices and current regulatory, funder, and public expectations. It will ensure that your medical research helps to improve patient care by ensuring that all interventional clinical trials are pre-registered and rapidly report their results.

> TIP: Fully adopting WHO best practices now will save you work in the future. For example, some UK universities recently improved their trial reporting, but only for drug trials listed on EudraCT. Following changes in national regulations that mandate the reporting of all trials, these universities will now have change their systems again.

At least one university has gone even further – it now ensures that even observational studies registered on ClinicalTrials.gov post their results there in a timely manner.

Strengthen your policies

Assess your institution's policies on trial registration and reporting against WHO best practices using this checklist to identify the gaps that you need to address.

Different research groups and units (such as the CTU) within your institution may have different policies. Also, policies for drug trials registered on EudraCT (so-called 'CTIMPs') may differ from policies for other trials, or. You need to ensure that your assessment covers all policies related to interventional clinical trials. For example, if existing policies make pre-registration mandatory for drug trials, but not for other trials, that is a gap.

> TIP: Use the WHO definition of clinical trial to define the scope of your policy.

Draft new policies (examples here) that are consistent and easy for researchers to understand. Ideally, all policies should be contained within a single document.

> TIP: Does your institution have a policy on where clinical trials should be registered? If you do not have a clear policy, your researchers may unnecessarily register trials on more than one registry, which can create a lot of avoidable work in future. According to the WHO, every trial should ideally be registered on one registry only – either on one of the WHO primary registries, or on ClinicalTrials.gov. If a trial has to be registered on more than one registry due to regulatory or funder requirements, ensure that all trial registry ID numbers (example: NCT123456789) are entered as secondary identifiers on each registry (see page 5 here).

Strengthen your systems and processes

Policies are only as good as the systems and processes that ensure that people consistently adhere to them. Before designing systems to support your new policies, use your review of existing registry entries (see above) to identify current gaps and weak points.

> TIP: For each policy item, define who will monitor compliance and how. Experience shows that in many institutions, researchers do not understand, or do not follow, existing policies.

Appropriate systems and processes will need to be tailored to individual institutions' contexts. You may want to integrate some of the following innovations introduced by pioneering institutions:

- **Institutional registry accounts.** Some institutions have created a central account with all trial registries used by their researchers so that in future, trials can only be registered through that account. This enables the registry manager to ensure that all trial registrations are complete and accurate, and assists in the tracking and updating of registry entries.

  "The university decided to set up an institutional 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… Throughout this process, the Research Governance Team received support from the PRS team working at ClinicalTrials.gov, who were responsive and extremely helpful."
  Experienced registry manager

- **Budgeting.** Many institutions now routinely include a budget line for reporting trial results on registries in their grant applications. This includes statistician support for producing results that match registry requirements as well as the time required to upload results. You should also budget for producing a lay summary, which will become mandatory for all drug trials when the EU Clinical Trial Regulation comes into force. (Around the same time, producing a lay summary will also become mandatory for all interventional trials with a trial site in the UK.)

- **Trial design.** Developing a strong and very detailed trial protocol will make subsequent trial registration and reporting easier. Some registries (notably EudraCT, but also ClinicalTrials.gov) require trial outcomes to be analysed and reported in a specific way. Review trial designs at an early stage to ensure that they will produce outcomes in a registry-compatible format. In addition, ensure that adverse events are coded in a EudraCT-compatible format from the very outset.

"We have produced a Results Template that Investigators use to present their trial results to us once the trial data analysis is complete. We now give this Results Template to Investigators at the trial kick-off meeting... We have also introduced results awareness slides into our standard Good Clinical Practice (GCP) training and our specific training for Chief Investigators… [O]nce these newer trials reach End of Trial notification stage, the results will be presented to us in a way that will enable all compliance staff, once trained, to upload results…"
Experienced registry manager (centralised model)

- **Early warning.** At one university, the Ethics Committee notifies the registry manager as soon as a clinical trial has been given ethics approval. This enables the registry manager to support the lead researcher with identifying an appropriate trial registry and registering the trial there.

- **Early control over EudraCT trials.** In centralised models, the registry manager should apply with the EMA to get 'primary user' status as soon as the trial receives its Clinical Trial Authorisation from the national regulator, and also assign a colleague as the 'back-up user'.

- **Continuity planning.** When lead investigators have moved to a different job, institutions often struggle to secure and upload trial results. One institution ensures that a replacement lead is identified at the outset of each trial, and provides registry training to that person too. In addition, the Human Resources department immediately informs the registry manager of impending staff departures.

- **Clear responsibilities.** You have to clearly communicate to lead researchers that they are responsible for providing the data required for registry reporting (or for directly reporting on registries themselves). One institution has given this obligation legal force by integrating it into researchers' employment contracts. Another institution has incorporated it into its existing 'condition for sponsorship' document.

- **Checklists.** One institution has embedded registry tasks into existing checklists:
    - Trial initiation checklist: a study can only begin after a trial has been registered
    - Amendments checklist: the lead researcher has to confirm that the registry was updated to reflect amendments to the study protocol
    - Closedown checklist: the lead researcher has to confirm that results have been uploaded onto the registry

"Clear Standard Operating Procedures are key to driving the standardisation of processes across the entire institution. They can also drive improvements in research design and implementation."
Experienced registry manager

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