



Department
of Health &
Social Care

Government Response to the House of Commons Science and Technology Committee Report on Research Integrity: Clinical Trials Transparency

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Presented to Parliament
by the Secretary of State for State for Health and Social Care
by Command of Her Majesty

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Introduction:

This document sets out the Government's response to the House of Commons Science and Technology Committee's report on Research Integrity - clinical trials transparency.

The UK science and research sector is world class and one of which I am extremely proud. That world class reputation depends on adherence to the highest standards of research integrity. Unless research is conducted with integrity our outstanding scientists cannot build on the works of others, patients may suffer and money may be wasted repeating research that has already been conducted but not published.

Research findings must be communicated in ways that are timely, meaningful and relevant to evidence users. Only with a system which values transparency can we hope to improve patient care and support the sustainability of the health and care system through research. I therefore agree with the Committee that clinical trials transparency is vital to the integrity of research. The Government welcomes the opportunity to address the issues raised in this report.

Baroness Blackwood, Parliamentary Under Secretary of State for Health
(Lords)

Recommendation 1:

The Government should explicitly commit to introducing the clinical trials transparency requirements in the EU Clinical Trials Regulation that are expected to be applied in the EU shortly after Brexit. (Paragraph 16)

The Government and its arm's length bodies, including the Medicines and Healthcare Products Regulatory Agency (MHRA) and the Health Research Authority (HRA) are committed to greater transparency in the area of clinical trials.

In the Lord Patel amendment debate on the Withdrawal Bill on April 18th 2018, Baroness Goldie confirmed that the Government is committed to implementing all of the requirements of the Clinical Trials Regulation that are within its control.

Transparency measures will be increased under the new Regulation. The Regulation will require that, in addition to transparency requirements under existing legislation:

- All trials registered *via* the new EU central IT portal which will support the Regulation will be publicly accessible (including for example, the protocol, investigators brochure, notifications and assessment report), unless, for all or part of the data and information contained therein, confidentiality is justified on grounds defined in the legislation.
- When a clinical study report has been submitted in support of a marketing authorisation, this report will also have to be made available by the applicant within 30 days after a regulatory decision on the application.

The transparency requirements of the Regulation therefore mandate the registration of clinical trials and the posting of results *via* a new EU central IT portal. In the event of a negotiated agreement with the EU that allows the UK full access to the new EU portal, the UK will fully align with the transparency requirements of the Regulation.

If UK trial information and results are not part of European registers in the future, the Government will make sure this information could be published on a national basis.

Those running trials should, however, continue to use existing and established international registries such as EudraCT (EU), ISRCTN (International Standard Randomised Controlled Trial Number) registry, and clinicaltrials.gov (USA) to ensure that UK patients are aware of the trial. The UK will continue to make information about trials being conducted in the UK available to patients and clinicians *via* the UK Clinical Trials Gateway (www.ukctg.nihr.ac.uk).

Recommendation 2:

We recommend that the updated and strengthened Concordat to Support Research Integrity being developed by Universities UK should include requirements on universities to ensure that all trials are reported, and that efforts are made to share best practice in achieving compliance with reporting rules within the university sector. (Paragraph 19)

We note the recommendation and support Universities UK's (UUK) development of an updated and strengthened concordat. UUK has confirmed that they are strengthening the concordat by making its requirements explicit, so that it is very clear what the expectations are and what is necessary to meet those requirements. This will provide for greater transparency, including around clinical trials. There will be a specific requirement around the submission of data so that it will be easier to monitor take up of these commitments.

Recommendation 3:

It is particularly disappointing that trusted bodies such as Public Health England and a range of NHS Foundation Trusts are also failing to report results from clinical trials. Public trust in medicine could easily be eroded by failures in clinical trials transparency from such important parts of the health system. Public Health England should write to us with an explanation and the steps it will take to correct this (Paragraph 21)

The Chief Executive of Public Health England, Duncan Selbie, has written to the Committee regarding the clinical trials in question:

www.parliament.uk/documents/commons-committees/science-technology/Correspondence/181030-Public-Health-England-re-Clinical-trials-transparency.pdf

HRA has confirmed that it will be writing to the NHS trusts which have hosted the trials identified in the report, asking them for further action to ensure publication of the results of these trials. HRA will write to the Committee advising it of the outcome of that correspondence.

Recommendation 4:

We recommend that the Government explicitly re-commit to tackling clinical trials transparency, perhaps through a focused ministerial speech on this issue. This should set a clear time limit for institutions to fully comply with clinical trials transparency requirements and make clear what the consequences will be of failing to meet that deadline. (Paragraph 26)

The Government is committed to tackling clinical trials transparency through continued working with stakeholders, ALBs and other partners.

In addition to setting the legal framework around clinical trials transparency, the Government has also taken action to increase transparency by sponsoring the development of 'Model clinical trial agreements' (mCTAs) for pharmaceutical research, which include requirements to comply with all relevant laws and guidance relating to medicines and clinical trials including transparency.

The February 2018 revised model Clinical Trial Agreement (mCTA) and Clinical Research Organisation model Clinical Trial Agreement (CRO-mCTA) templates are designed to be used without modification for industry-sponsored trials in the NHS. They recognise that participating organisations have a responsibility to ensure appropriate publication and dissemination of clinical research for the benefit of patients and their peers. Publication should be done in an orderly way, usually in compliance with the publication policy set out in the trial Protocol. The model agreements state that sponsors shall ensure that the results of the Clinical Trial are published on a free, publicly accessible clinical trial results database within one year after the Investigational Medicinal Product is first approved and made commercially available in any country and within one year of trial completion. In respect of a clinical trial that is under review by peer reviewed journals which prohibit disclosure of results pre-publication, the results will be posted at the time of publication.

Prospective study registration and timely disclosure of results are already critical to ensuring transparency of clinical trials funded by the National Institute for Health Research (NIHR), through which DHSC publicly funds high quality health research. The NIHR is the first health research funder to publish comprehensive accounts of its research within its own publicly and permanently available journals. The NIHR Journals Library provides information relating to its research throughout the life of each project, on individual research pages. These pages also provide access to the published research in the NIHR's open access, peer reviewed series of journals, comprising *Efficacy and Mechanism Evaluation*, *Health Services and Delivery Research*, *Health Technology Assessment*, *Public Health Research* and *Programme Grants for Applied Research*.

The Medical Research Council recently strengthened its policy on clinical trial transparency which has an absolute requirement for registration and promotes publication of protocols: <https://mrc.ukri.org/research/policies-and-guidance-for-researchers/open-research-data-clinical-trials-and-public-health-interventions/>

The Government is considering what further action it, or relevant Arms Length Bodies, could take to further strengthen research integrity.

Recommendation 5:

We recommend that the Health Research Authority (HRA) should be provided with funding to establish a national audit programme of clinical trials transparency, including the publication of a single official list of which UK trials have published results and those which are due to but have not. In the first instance this should focus on providing information on whether any results have been published in an academic journal following global best practice, building on the automated methods already developed by others. We recognise that there are other dissemination routes for clinical trials results beyond academic journals that automated methods might not capture. Where alternative means have been used to publish information the HRA can use this process to *prompt* lead investigators to provide details of where the results have been posted so that the entry for that trial can be corrected as necessary. (Paragraph 36)

HRA is considering how best to gather definitive information about the registration of clinical trials and the publication of results arising from clinical trials. The HRA will be proposing how these aims will be achieved in its new transparency strategy requested by the Committee *via* Recommendation 9. Any resourcing implications will be discussed between HRA and DHSC as its sponsoring Department.

Recommendation 6:

We recommend that the HRA undertake further work to determine an accurate figure for the cost of such an audit and prepare a funding proposal for the Government to consider. The cost should be weighed against the potential public savings made by tackling mis-reporting, in terms of reduced 'research wastage' and the scope for better procurement decisions. If this model is pursued, then the results should be published trial-by-trial rather than simply at the summary level. (Paragraph 37)

As noted in the response to Recommendation 5, the HRA is considering the most effective way to both ensure that the public has access to a definitive register of UK clinical trials and ensure transparency of results from those trials. This may involve introducing an expanded audit function, but it may involve changing HRA business processes and introducing new functionality into HRA IT systems which are used to aid the approval and regulation of clinical trials. The cost of any potential HRA auditing activity must therefore be considered by Government in the context of HRA funding more generally. The HRA will outline the way forward in its new strategy which will be published in 2019.

Recommendation 7:

The Government should direct the HRA to publish information on trials that have received ethical approval but are not registered in a publicly-accessible register, on a trial-by-trial basis. (Paragraph 38).

Government will work with HRA and key stakeholders to determine the most effective way of achieving this. HRA currently publishes details of approved studies on its research summaries database, using information submitted by the applicant. This includes information about registration if the study was registered before submission but it does not capture subsequent registration or identify persistent non-registration. HRA already agrees that it should publish more information than it currently does and has had initial discussions with the Transparency Forum¹ about the possibility of expanding the research summaries database to include additional information such as final reports and publication details, so becoming a living record of the study.

Recommendation 8:

Echoing our predecessor Committee’s conclusions from 2013, we recommend that the HRA introduce a system of sanctions to drive improvements in clinical trials transparency, such as withdrawing favourable ethical opinion or preventing further trials from taking place. The Government should consult specifically on whether to provide the HRA with the statutory power to fine sponsors for non-compliance. (Paragraph 41)

The HRA, supported by Government, is committed to driving improvements in clinical trials transparency. Sanctions may play a role in driving improvements, but alternative actions or ways-of-working across the research ecosystem may also be equally effective in achieving this overall goal. HRA and Government are currently considering the right balance of measures to put in place to improve transparency. HRA will consult widely on this topic in 2019 before finalising the way forward in the new HRA strategy on transparency.

Recommendation 9:

We recommend that the Government ask the HRA to publish, by December 2019, a detailed strategy for achieving full clinical trials transparency, with a clear deadline and milestones for achieving this. We also recommend that the Government write to the HRA to clarify that it should interpret the Care Act 2014 to mean that it is responsible for driving improvements in clinical trials transparency—as opposed to ‘promoting’ transparency as a virtue. The performance of the HRA should then be explicitly measured on this basis through its annual

¹ The Transparency Forum is convened by the HRA and brings together funders, sponsors, research ethicists, clinical research organisations and publishers to promote research transparency.

report, including through specific measurable performance indicators. If further financial resource for the HRA is required to tackle clinical trials transparency then the Government should consider favourably such requests. (Paragraph 45)

The Government will ask the HRA to develop a new strategy in the timeframe proposed by the Committee.

Recommendation 10:

We recommend that the Government consult further with the HRA on whether it is capable of delivering the improvements to clinical trials transparency needed within its current remit. If necessary its remit should be extended through introducing legislation which amends the provisions of the Care Act 2014. (Paragraph 46)

The Government is consulting further with HRA and other stakeholders on how best to drive improvements in transparency and how this can be achieved in relation to the remit of the HRA.

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