Health Research Authority

Agenda item:	8
Attachment:	A

HRA Board paper
10 December 2019

Title of paper:	Research transparency: final Make it Public strategy
Submitted by:	Juliet Tizzard, Director of Policy Naho Yamazaki, Head of Policy and Engagement Clive Collett, Ethics Policy Manager
Summary of paper:	To present the final Make it Public research transparency strategy for Board approval
Reason for submission:	For approval
Further information:	The paper covers: • How the strategy was developed • Its main elements • Decisions to be made by the Board (see section 9)
Budget / cost implication:	The cost of implementing the strategy is currently being carried out.
Dissemination:	In line with Cabinet Office guidance during the pre-election period, although the Consultation Report and Strategy are being shared with the members of the Board for their comments as part of the meeting on 10 December, they can only be published online once a new government is formed. The papers as presented to the Board will be added to the relevant section of the HRA website as soon as possible after this date. The strategy will be launched in late January.
Time required:	40 minutes

Research transparency: final Make it Public strategy

1. Introduction

1.1. The HRA has a statutory duty to promote research transparency. Transparency is central to good quality, ethical research and consists of:

- registration: making it public that a study has started
- reporting results: making it public what the study has found
- informing participants: letting those who took part know what the study has found, and
- sharing study data and tissue: enabling further research.

1.2. We have seen some improvements in transparency over recent years, particularly amongst commercially-sponsored research. However, university and NHS-sponsored research has a poorer record, particularly in reporting results.

1.3. This was highlighted by the House of Commons Science and Technology Committee in its report, *Clinical Trials Transparency*, published in October 2018. The report contained a number of recommendations, most of which were aimed at the HRA. One key recommendation was that the HRA develops a strategy to address poor performance in research transparency by December 2019. We accepted that recommendation and began developing the strategy in early 2019.

1.4. This paper describes how we developed the strategy and its key elements and draws out the key policy decision underpinning it.

2. How we developed the strategy

2.1. Effective engagement and consultation have been key to ensuring that we develop a strategy that improves research transparency in a way that is feasible and acceptable to both the public and those involved in conducting research. A full report on the consultation is at Annex B.

2.2. One key strand of our engagement has been the Research Transparency Strategy Group. Chaired by Professor Andrew George, the group includes sponsors, campaigners, funders and patients from across the UK. The Group worked with the HRA to develop a draft strategy, named Make it Public, which was put out to public consultation between 17 June to 6 September 2019. The consultation consisted of:

- An online survey
- Five open workshops
- A webinar for Research Ethics Committee (REC) members
- A focus group for patients and the public
- A series of workshops for HRA staff

2.3. The survey was open to anyone to respond and a total of 481 individuals and organisations took part. Of the 399 individuals responding, 21% were researchers, 32% patients, patient advocates and research participants and 16% research managers.

2.4. To complement the survey and explore issues in more depth, we held five open workshops, in London (16 July), Manchester (25 July), Cardiff (31 July), Belfast (12 August) and Edinburgh (6 September). The workshops outside England were organised jointly with colleagues in the devolved administrations.

2.5. The workshops were open to anyone and a total of 161 people attended, with similar attendance numbers at each location. When registering to attend the workshop, we asked participants to indicate their role in research (they were able to choose more than one category). Of the 161 participants, 25% were patients, patient advocates and research participants, 18% research managers and 17% researchers.

2.6. The Research Transparency Strategy Group met in September and October to consider the feedback from the consultation and to agree a recommended final strategy. Since then, we have discussed the main elements of the strategy with key stakeholders, to ensure support and early warning.

3. The strategy vision and approach

3.1. Based on feedback received during the consultation and advice from the Group, we have updated the Make it Public strategy. The strategy sets out a vision for research transparency:

> "Our vision for research transparency is that trusted information from health and social care research studies is publicly available for the benefit of all"

3.2. The HRA alone can't achieve this vision. We hope others in the research system will champion the strategy. However, the HRA has a key role to play:

- to make transparency easy – through clear guidance, an easy-to-use research approvals system and ongoing reminders about requirements
- to make transparency the norm/business as usual – aligning expectations across the system, rewarding good practice and highlighting poor practice, taking action where appropriate
- to make information public – ensuring clinical trials are registered and making information about studies easily accessible to the public.

3.3. The overall aim of the strategy is to bring about a significant improvement in research transparency by enabling good practice, calling out poor practice and increasing public visibility of individual research studies. The proposed focus is on better monitoring and enforcement of existing requirements, rather than to introduce new ones.

3.4. To do that, the strategy sets out planned changes and activities in three key areas: registration, reporting and communicating results to participants.

4. Registration

4.1. Principle 10 of the *UK policy framework for health and social care research* states:

> Information about the research: In order to avoid waste, information about research projects (other than those for educational purposes) is made publicly

available before they start (unless a deferral is agreed by or on behalf of the research ethics committee).

4.2. This applies to all health and social care research. For clinical trials, it is a condition of a favourable opinion from a UK research ethics committee that a clinical trial is registered before recruitment starts (or at least six weeks afterwards).

4.3. It is possible for applicants and sponsors to submit a request to defer registration of clinical trials on a publicly accessible database where there is commercial sensitivity around the study (this applies mainly in Phase I trials including healthy volunteers).

Current compliance

4.4. The MHRA enters clinical trials of interventional medicinal products (CTIMPs) onto the EU Clinical Trials Register on behalf of researchers. So for these studies, which make up around half of clinical trials, registration is currently 100%. For other types of clinical trials, researchers must register the study themselves. However, our audits suggest that only around 70% of these clinical trials are registered.

Feedback from the consultation

4.5. During the consultation, we asked for views about three different options for reaching 100% registration for all clinical trials. Of those responding to the survey:

- 34% thought the HRA should become a registry itself:
- 27% thought researchers must register their study before seeking approval
- 23% thought HRA should supply data directly to a registry

Recommendation from the Research Transparency Strategy Group

4.6. The Group agreed that it would be preferable for the HRA to register clinical trials (other than CTIMPs) on behalf of researchers. It also felt that it would be preferable for all health and social care research studies to be registered by the HRA, or at least made public on its website. However, given that the future of registration is reliant upon systems and resources and will have an impact on existing registries, the Group did not make a recommendation to the HRA about whether HRA should become a registry itself or supply data to a registry.

5. Reporting results

5.1. Principle 11 of the UK policy framework for health and social care research states:

> Accessible findings: Other than research for educational purposes and early phase trials, the findings, whether positive or negative, are made accessible, with adequate consent and privacy safeguards, in a timely manner after they have finished, in compliance with any applicable regulatory standards, i.e. legal requirements or expectations of regulators.

5.2. The EU Clinical Trials Directive (2001/20/EC) places additional requirements on clinical trials of medicines beyond those in the UK Policy Framework. In relation to

reporting results, a summary of the results of all clinical trials of medicines must be posted to the EU Clinical Trials Register within 12 months of the study completion. For paediatric trials, the deadline is reduced to six months.

5.3. The EU Clinical Trials Regulation (EU No 536/2014), which is due to be implemented in early 2021, will require sponsors to post a lay summary of the results on the EU Clinical Trials Register within 12 months of the end of the study.

Current compliance

5.4. According to data published on the EU Trials Tracker tool, sponsors of UK CTIMPs perform better on average than elsewhere in the EU. As of June 2019, 75% of UK sponsors reported results on time. A recent report by Sense about Science for the Science and Technology Committee suggested that university and NHS sponsors have increased their reporting rates to the European Clinical Trials Register by a third. Reporting rates for other types of clinical trials are not currently measured.

Feedback from the consultation

5.5. In the consultation, we presented a package of measures to improve the reporting of results. These included:

- making it clearer to applicants at the time of study approval that they have to submit an end of study report within 12 months after the study has ended
- taking a more proactive approach to prompt researchers and sponsors to keep their study information up to date and submit an end of study report, through systems improvements and monitoring
- publishing the information we receive.

5.6. When asked to what extent respondents thought that these steps will improve the reporting of results from clinical trials, 81% said they either believed or believed very strongly that these steps will do so.

Recommendation from the Research Transparency Strategy Group

5.7. The Group agreed that these approaches will improve the reporting of results. It agreed with our proposal that greater emphasis be placed on the end of study report, currently requested to be sent to the research ethics committee within 12 months of the end of the study (see section 8: Changes needed to implement the strategy).

6. Communicating results to participants

6.1. Principle 11 of the *UK policy framework for health and social care research* also states:

> Accessible findings: In addition, where appropriate, information about the findings of the research is available, in a suitable format and timely manner, to those who took part in it, unless otherwise justified.

6.2. It is an expectation that participants of all types of research receive information about the study findings in a suitable format and timely manner.

Current compliance

6.3. Although a large majority of applicants say that they intend to communicate the results to participants, only minority of participants actually receive that information.

Feedback from the consultation

6.4. Many of the responses to the consultation strongly supported the importance of communicating the results to participants and a number of research participants who attended the workshop reported that they had never received information of this kind.

6.5. It was pointed out that feedback is an ongoing process and participants should be kept informed of the trial's progress throughout, with many emphasising that the onus should not be placed on the participants to seek out this information. One patient captured the real importance of feedback in acknowledging the contribution made by research participants pointing out that "it can be very frustrating to take part in something and not really know how you actually contributed or what results related to you".

6.6. At two of the workshops, some wondered whether increasing research transparency might inadvertently lead to a false sense of hope for some patients. Others said that information needs to be clear, but also easy to access and to understand.

6.7. To ensure better feedback to participants, we plan to:

- change the question we ask applicants from whether they will share study results with participants to how and when they will share them
- ask sponsors to submit a lay summary of the study results to the HRA, possibly as part of the final study report, which we will then publish on the Research Summaries Database.
- produce new guidance on how to inform participants about study findings, tailored to different study types.

Recommendation from the Research Transparency Strategy Group

6.8. The Group felt that communicating results to participants should be a key area of the strategy. It also agreed that whether and how results have been communicated should form part of the reporting requirements in the end of study report and contribute to performance measurements.

7. Taking action in cases of non-compliance

7.1. Enhancing our monitoring of reporting results, communicating results to research participants and registering trials (other than CTIMPs) ourselves are the main elements of the strategy. However, we also need to consider what we action we will take if, despite efforts to enable good transparency practice, non-compliance persists.

7.2. In the consultation, we sought views about three sanctions for non-compliance:

1. Publish an annual ‘transparency league table’ highlighting individual studies which have information that is overdue
2. Taking into consideration the extent to which researchers/sponsors have fulfilled their transparency responsibilities in relation to their previous studies, when reviewing new studies for approval
3. Fining sponsors with very poor transparency compliance rates (this would require a change in legislation)

Views from the consultation: publishing an annual league table

7.3. The benefit of league tables is that they drive better behaviours by introducing an element of competition – a desire to be the best, or at least better than one’s peers. They also tap into the desire to have a good public reputation, whether amongst peers or wider groups. Any league table would need to report on something that the community cares about and understands to be a good thing. It will also need to be based on sound data with a fair adjudication system underpinning it, which itself is transparent. This will avoid unfairness and challenge.

7.4. When asked during the consultation to what extent a league table would be appropriate, 69% of online respondents considered that this approach was either appropriate (37%) or highly appropriate (32%) with only 24% disagreeing (‘Not Appropriate = 19% and ‘Not at all appropriate’ = 5%).

7.5. Those who supported the publication of a league table thought it would be a good way to incentivise compliance, prompt allocation of more resources to support transparency and increase accountability. Some suggested that it should be used to highlight good performance and good practice rather than identify poor performers.

7.6. Those who opposed the publication of a league table felt that this could deter patients from taking part in research at certain institutions and thus should only be visible to professionals. There was concern at some workshops that league tables could lead to game playing with the fear that ensuring a good showing in the table could become more important than actually making real improvements.

Views from the consultation: taking past performance into account

7.7. The benefit of considering track record is that most researchers and sponsors carry out research on an ongoing basis. Most research transparency requirements apply after the research study is complete, at a time when taking action in relation to the original research approval would have little effect. Focussing on future applications allows us to take action that is focussed on what researchers and sponsors really want: approval for their next study.

7.8. Like league tables, taking action on the basis of track record needs to be based on sound data with a fair adjudication system underpinning it which itself is transparent. This will avoid unfairness and challenge.

7.9. When asked during the consultation to what extent they thought considering track record would be appropriate, 75% of online respondents considered that this

approach was either highly appropriate (41%) or appropriate (34%) with only 19% disagreeing ('Not Appropriate = 13% and 'Not at all appropriate' = 6%).

7.10. Those supporting the consideration of past transparency performance when reviewing new studies for approval considered this to be a strong motivator and an important catalyst for compliance. Feedback from sponsor representatives suggested that preventing studies from being approved at an organisational level would give them increased weight in managing investigators.

7.11. Those who thought that this approach would not be desirable felt that blocking future approvals would result in less valuable research being undertaken which, in turn, would adversely and unfairly affect potential participants and patients.

7.12. At the workshops, opinion was split on who should be held responsible i.e. the sponsor or the individual researcher. Several of those in favour of this sanction suggested a 'red card' or 'traffic light' system, rather than an all or nothing approach, so that there was an opportunity for improvement before approval was withheld.

Views from the consultation: imposing financial penalties

7.13. The HRA does not currently have the power to fine non-compliant sponsors, so this would require a change to the law. The threat of a financial penalty could be a powerful incentive to comply with transparency requirements.

7.14. When asked during the consultation whether fining sponsors with very poor compliance rates would be appropriate, 39% considered that this approach was either highly appropriate (21%) or appropriate (18%). By contrast, 47% indicated that this option was either not appropriate (32%) or not at all appropriate (15%).

7.15. Those supporting the use of fines thought that this would concentrate minds, emphasise where the responsibility for meeting transparency requirements lay and highly motivate sponsors by showing that there are consequences for non-compliance. This, some felt, would best protect research participants.

7.16. Those opposing the use of fines thought that there was little evidence that fines would promote compliance. Rather they are a harsh, ineffective punishment that would alienate the research community and destroy good will in the system. Some felt that the imposition of fines might result in the UK becoming a less attractive place to do research. Many felt that fines should only be considered after other, less punitive, methods for facilitating compliance had been tried.

7.17. The patient focus group thought, initially, that the introduction of fines was reasonable but following lengthy discussion of the associated issues, everyone agreed that whilst the publication of league tables and taking into account past performance were appropriate, the imposition of fines was not.

Recommendation from the Research Transparency Strategy Group

7.18. The Group felt that there was merit in making information public to highlight poor performance and encourage behaviour change. However, many in the Group were concerned that a 'league table' could actually normalise poor performance, whilst one member argued that it would lead to improvement. Most felt that an alphabetical

list, rather than a ranked table, might be more appropriate. There was also a suggestion that we produce individual reports for sponsors. The Group agreed that the HRA needs to ensure it has the resources to be able to be fair, robust and allow people to know what will be published about them.

7.19. The Group agreed that past transparency performance should be taken into account for new research applications. However, there were split opinions on whether this should be applied against the individual researcher or the sponsor. Similarly, the Group felt that there should be further consideration about whether the review should sit with the Research Ethics Committee or whether this should be done at desk level by HRA staff. The Group recommended that a working group should be brought together to consider the practicalities of this measure.

7.20. The Group agreed that fines should not be introduced as a sanction. One member argued in favour of financial penalties but noted that if the new EU Clinical Trials Regulation applies in the UK in the future, the MHRA would be able to implement financial sanctions. Overall, the Group felt that removing money from research is ethically problematic, especially when the effectiveness of fines on increasing transparency compliance is unclear. Similarly, the Group noted that the impact of this sanction is likely to vary significantly between commercial and non-commercial organisations and so sanctions which will have more equal impact are preferable. The Group was also concerned that fines could result in the wrong person being punished (the institution rather than the researcher or sponsor). There was also a feeling that imposing fines, although if it is effective to some degree, would have the potential to deter some from conducting research in the UK.

7.21. The Group agreed that withholding approval was more likely to work as a sanction rather than a fine on a study that is already completed or in progress.

8. Discussion

8.1. It's clear from the feedback to the draft strategy received during the consultation that there is strong support for the HRA leading a system-wide effort to significantly improve registration, reporting results and communicating the result to participants. There was also strong support for the steps that we had already committed to carrying out, particularly around using technology to make it easier to comply and providing clear guidance and learning support to the research community. We also have a steer from the consultation and from the Strategy Group around sanctions.

8.2. The Research Transparency Strategy Group has considered the feedback from the consultation and reviewed and approved the final 'Make it Public' strategy (see Annex A). When considering whether to adopt the proposed strategy, the Board will need to consider wider questions of funding and negotiations with other organisations and service providers in the research ecosystem for implementation. The Group recognises that.

8.3. In order to achieve significantly better compliance with research transparency requirements in future, we need to enhance our approach to monitoring. We know from the experience of audits that the act of monitoring, where it involves interactions with sponsors, improves compliance. Monitoring will also give us data on which to take action. However, it will require an investment of resources, a clear escalation

policy and a framework for deciding whether there are mitigating circumstances for individual cases of non-compliance.

8.4. If the Board accepts the Group's recommendation to introduce both an annual performance report (as opposed to a league table) and consideration of past performance when considering new studies for approval, our recommendation is that we use the requirement to submit an end of study report as a basis for measuring performance and taking these actions. This is an existing reporting requirement with which researchers and sponsors are already familiar, although the reporting rate is currently around 50% [further analysis happening to firm this up].

8.5. The Strategy Group has recommended that the metric should not be whether the report has been submitted on time, as this does not necessarily indicate whether appropriate reporting and communicating has happened – only whether a report has been submitted. Instead, the metric should take account of whether these transparency activities have taken place.

8.6. As part of the implementation programme, we recommend working with stakeholders to define a dataset for the end of study report and determine what information we will publish in the annual performance report and use as the basis for considering past performance.

8.7. It should be noted that it may be some time before we are able to take action against non-compliance. We need to give the research community due warning that we will be measuring compliance against the submission of the end of study report and we would need to design a robust process for adjudicating individual requests for extensions. We would also need to resource this.

9. Summary of recommendations to the Board

9.1. Does the Board agree with the recommendation that, in principle, clinical trials should be registered by the HRA in future?

9.2. If yes, does the Board agree that we develop this idea further in collaboration with other stakeholders?

9.3. Does the Board agree that we should focus our attention on the submission of the end of study report as a mechanism for ensuring better reporting of results, communication of results to participants and to allow us to collect information to publish on the Research Summaries Database?

9.4. If yes, does the Board agree that we should start work with stakeholders to define a dataset for the end of study report?

9.5. Does the Board agree that communicating the results of studies to participants should be a key area of the strategy?

9.6. If yes, does the Board agree that we should start work with stakeholders to improve our guidance in this area and incorporate this area of research transparency into the end of study report?

9.7. Does the Board agree that we should measure performance on information collected in the end of study report and use this as a basis for taking action against poor performance?

9.8. Does the Board agree that we should use this performance data to produce an annual research transparency performance report?

9.9. Does the Board agree that we should use this performance data to inform review of future studies from the same sponsor or researcher?

9.10. If yes, does the Board agree that we should start work with stakeholders to define how the data collected in the end of study report should be used to produce the performance report and to inform review of future studies?

10. Next steps

10.1. Once the Board has finalised the Make it Public strategy, the immediate next steps are to:

- share it with policy leads in the devolved administrations to seek ministerial or permanent secretary sign-off
- prepare a business case to Government to fund the implementation of the strategy
- send it to the House of Commons Science and Technology Committee (when Parliament returns, and a new committee is formed)
- hold a public launch of the strategy in late January

10.2. We will then form working groups comprised of internal and external stakeholders to take forward the work to implement key aspects of the strategy.

10.3. Continued communications and engagement will be crucial. We are reviewing the role and purpose of the Transparency Forum in discussion with members of the group and will hold an annual meeting to celebrate success and share best practice for improvement. We are also developing a plan for continuing to use Make it Public as a campaign to keep the issue live and ultimately influence behaviour in the community.