Department of Health

Government Response to the House of Commons Science and Technology Committee Inquiry into Clinical Trials

Cm 8743

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Introduction

This document sets out the Government's response to the report on Clinical Trials by the House of Commons Science and Technology Committee, chaired by Andrew Miller MP. Detailed responses to each of the 35 recommendations contained in the Committee's report can be found from page 2 onwards.

Clinical trials play an essential role both in improving and promoting the health of the UK population and in contributing to the nation's economic growth. The Government is seeking to ensure a vibrant, world-class NHS platform for research investment by the life sciences industry and other major funders of health research as part of the *Strategy for UK Life Sciences*. We are also strongly supportive of transparency in the publication of clinical trial results.

We are making significant progress. Continued improvements to the clinical trials infrastructure by the National Institute for Health Research (NIHR) have led to a run of recent "global firsts", where trials being arranged over a number of countries were established first in England. Over 99% of NHS Trusts are actively recruiting patients onto trials and studies hosted by the NIHR Clinical Research Network (CRN), and more than 630,000 participants were recruited to trials and studies in 2012/13.

The Health Research Authority (HRA) is now well established and is collaborating with partners on a range of projects to improve and transform the health research process. The work of the HRA is making a vital difference to the NHS environment for clinical trials.

The Government welcomes the Committee's report which makes a number of helpful recommendations aimed at reducing barriers to conducting trials in the UK and increasing clinical trial transparency. The Government hopes that this response is clear in establishing how we will achieve those aims.

Earl Howe, Parliamentary Under Secretary of State for Quality (Lords)

1. Clarity in use of the term "clinical trial" is essential. The establishment of consistent terminology would be an important first step towards making the UK an easier place to conduct clinical research. We recommend that the Government agrees a set of simple definitions for the terms "clinical trial", "clinical study" and "clinical research" and ensures their consistent use across the Health Research Authority, Medicines and Healthcare Products Regulatory Agency, Medical Research Council, National Institute of Health Research and the NHS. (Paragraph 11)

The term "clinical trial" as it applies to trials of medicines is a legal term defined in EU clinical trials legislation. As described in the Committee's report, the legislation is currently under review and a proposed Clinical Trials Regulation is being negotiated. The UK Government is actively contributing to the negotiations and will seek to ensure clarity when these definitions are finalised.

The HRA has responded further to this recommendation.

2. We recognise the significant barrier to research posed by the European Clinical Trials Directive and welcome proposals for a new European Clinical Trials Regulation. However, we are concerned that a lack of clarity in the detail of the Regulation could lead to inconsistencies in its implementation across Member States, and we are not persuaded that proposals go far enough in ensuring that low-risk trials are regulated in a proportionate way. We urge the Government and MHRA to continue engaging at a European level to resolve these issues and to work together to ensure that, when the resulting legislation is introduced, the administration of clinical trials in the UK will be pragmatic and proportionate. (Paragraph 24)

The Government welcomes the European Commission's proposals for a Clinical Trials Regulation. Although the Clinical Trials Directive aimed to harmonise requirements across Europe, some Member States introduced additional requirements when implementing the Directive that have limited harmonisation and reduced the benefits of the Directive. The Regulation will be directly binding and should therefore dramatically reduce the scope for Member States to introduce national requirements.

The Government is working with other Member States to ensure that the legal text is sufficiently clear but at the same time not overly restrictive. The Government believes that the Commission's proposal for a Clinical Trials Regulation introduces a proportionate and risk-adapted approach to clinical trials by introducing the concept of low-intervention trials and risk-adapted monitoring of trials. In general, risk adaptation is not easily captured in legislation and the Government believes this is better done in guidance. The new Clinical Trials Advisory Group has a role in ensuring consistent implementation across Member States.

3. We commend the establishment of the Health Research Authority (HRA) and note that feedback on the HRA's performance to date has been largely positive. However, we are unable to judge whether the HRA has so far been effective in achieving its objectives, as the necessary performance indicators are not currently in place. We recommend that the HRA establishes and publishes a suite of relevant key

performance metrics and targets in its 2014/15 Business Plan, and monitors performance against these targets annually. We further recommend that a triennial review of the HRA takes place no later than December 2014, three years after its creation as a Strategic Health Authority. (Paragraph 31)

The HRA has set out an ambitious programme of work and recognises that it needs to deliver tangible improvement. It has had key performance indicators (KPIs) in place since its first full year of operation as a Special Health Authority (2012/13) and reports performance against the KPIs at quarterly accountability meetings and in its annual report. The KPIs are reviewed each year to ensure their continued relevance and are published in the HRA's Business Plan. We will continue to ensure that they are relevant and current (including that they take appropriate account of the findings of this inquiry) and we will support the HRA in achieving these objectives for 2014/15.

The Care Bill currently before Parliament would establish the HRA as a non-Departmental public body (NDPB) by spring 2015, meaning the Special Health Authority would no longer be needed, while the need for the NDPB would have been recently determined by Parliament. A triennial review of the HRA would then be undertaken as appropriate from its creation as an NDPB.

The HRA has responded further to this recommendation.

4. **Over a year after its creation, some stakeholders (including an academic health science centre, intended to be a centre of excellence for UK health research) remained unaware of the function, or even the existence, of the HRA. Although these stakeholders also bear some responsibility for their own awareness of such developments, we consider that the HRA should now place greater emphasis on engaging with the clinical research community and raising the profile of its work. The HRA should detail in its response to this Report how it intends to do this. (Paragraph 32)**

The HRA has responded to this recommendation.

5. **We welcome moves by the HRA to streamline NHS governance arrangements and stress the importance of this initiative, which, in our view, should be given the highest priority. Following completion of the feasibility study, we recommend that a timeline detailing the next steps be published as part of the HRA's response to this Report. The Government should assist the HRA in its efforts to meet this priority, including making additional resources available if necessary. (Paragraph 35)**

A key function of the HRA is to facilitate safe and ethical research and it is working with relevant partners to help create an environment where applying to do research is simpler and getting a decision is quicker. The feasibility study found that both study-wide and local NHS Research & Development assessments can be integrated into a HRA assessment, which itself includes research ethics committee (REC) approvals. We welcomed the findings and requested that the HRA proceed to develop a detailed business case with costed options on how the integrated assessment can be implemented. The business case was submitted to the Department of Health in October.

The HRA has responded further to this recommendation.

6. We are disappointed that the Government has failed to meet its own 2012 deadline for measuring NHS Trust performance against a 70-day benchmark for clinical trial initiation and we query whether this target is realistic in the short-term. We recommend that the Government updates us on current performance and on how many NHS Trust contracts now include this benchmark in its response to this Report. (Paragraph 37)

The Government wishes to see a dramatic and sustained improvement in the performance of providers of NHS services in initiating clinical research. Publication by providers of performance data on a 70-day benchmark to recruit first patients into clinical trials has been a condition of all new NIHR contracts for providers of NHS services since December 2011. The benchmark is now in place, and links to providers' data are available on the NIHR website[1]. By October 2013, 55 providers had become subject to the new NIHR contract.

7. We welcome changes designed to make the NHS Constitution more research focused and the launch of the Government's OK to Ask campaign. However, we are cautious of any suggestion that the system, as a result of this new onus, will automatically act to promote the existence of and encourage involvement in clinical trials. We recommend that the Government provides details of how changes to the NHS Constitution and the OK to Ask campaign have been communicated and promoted, both within the NHS and to the general public. In twelve months' time it should publish evidence on how the measures have affected both public and professional attitudes to, and participation in, clinical trials. (Paragraph 43)

8. We note the apparent lack of public confidence in the pharmaceutical industry and are concerned that this may increasingly pose a barrier to conducting trials in the NHS. Industry should act to regain trust lost through past examples of poor behaviour by engaging more effectively and transparently with the public in the future. In addition, Trusts need to do far more to educate patients about the benefits, both to them and to the wider community, of participating in research and allowing properly controlled sharing of patient data. (Paragraph 44)

The NHS England draft research strategy addresses the NHS Constitution pledge to inform patients of research studies in which they may be eligible to participate. Priorities in the strategy include the need to support partner organisations in their drive to promote participation of patients and their families in research.

The 2013 'Ok to Ask' campaign has provided important proof of principle data on the feasibility and importance of this sort of awareness-raising initiative from a public and patient perspective. In a follow-up survey with NHS staff, 80% said that the campaign helped generate momentum around research in their Trust, and 77% rated the campaign as excellent or good. Over 150 events were held across NHS sites in England. 'OK to Ask' continues to be promoted locally and there will be further rounds of activity for

1 http://www.nihr.ac.uk/systems/Pages/ClinicalTrialPerformance.aspx

International Clinical Trials Day in 2014 and 2015.

The pharmaceutical industry is an important partner in the Government's drive to improve health outcomes for patients and the public. We encourage the Association of the British Pharmaceutical Industry (ABPI) to work with its members on engaging with the public to regain lost trust.

The HRA has responded further to recommendation 8.

9. **We were impressed by the quality and accessibility of Cancer Research UK's trials database, which is reflected in the high volume of traffic that it receives. In contrast, while we are satisfied that the Government is working to improve and promote its own Clinical Trials Gateway, we were concerned to find that only 20% of its target users were aware of its existence as of mid-2012, and that the Minister was unable to give us a more detailed account of what was being done to improve this. The Government must improve the Clinical Trials Gateway and raise its profile with patients, clinicians and the general public. We recommend that the Government provides details about how it will achieve this, together with indicative timelines and targets, in its response to our Report. (Paragraph 50)**

10. **We consider it important that the information contained on the Clinical Trials Gateway is accessible to the lay person, which does not appear to be consistently the case at present. The Government should ensure that all trials listed on the Gateway include a plain language summary written specifically for a lay audience. Where such summaries are not already in existence, the Government must be prepared to commit the time and effort needed to create them. Taking into account the Gateway's current resource levels, we recommend that, where possible, preparation of a lay summary should be included as a requirement for publicly-funded trials, but that the Government remain open to the option of increasing the level of resource dedicated to the Gateway if necessary. (Paragraph 51)**

The UK Clinical Trials Gateway is being redeveloped and redesigned with a view to strengthening and improving its presentation of information and functionality from a public and patient perspective. We have identified an appropriate supplier for the technical work and are putting in place a multi-disciplined Project Board which will have oversight of the redevelopment work and which will also have a responsibility to clarify the vision and direction for the Gateway. The Board will be chaired by Simon Denegri, NIHR (National Institute for Health Research) National Director for Public Participation and Engagement in Research and Chair, INVOLVE.

The Government has previously identified, and considered, the extremely significant resource implications of re-writing the descriptions of all trials currently on the Gateway, and has concluded that even for a subset of its own funded studies these costs are prohibitive and would not represent a good investment. Therefore, the Government has focused on how to continue to improve existing data sources. The Gateway development team are working with the HRA to take forward work on how to make the Patient Information Sheets (PIS) more user friendly. They are also looking at other data sources such as medical research charities to see how information from these sources

might be used to augment the information available. They will seek to do this without compromising the quality of the information presented via the Gateway in order to retain the high level of public confidence held in the Gateway.

Since 30 September 2013, it has been a condition of a favourable ethics committee opinion that clinical trials are registered on a publicly accessible database. This will in turn increase the number of studies presented by the Gateway, increasing transparency and access to research.

INVOLVE – the national advisory group for the promotion and advancement of public involvement in research – has also conducted and released a report and recommendation on plain language summaries[2] that will be implemented across NIHR over the coming year.

11. Clinical trial transparency is important and greater transparency would be likely to provide a number of benefits, particularly if applied retrospectively. However, there are obstacles to achieving this and the drive for greater transparency must be balanced against other concerns, particularly the need to protect patient privacy. Greater disclosure does not necessarily equate to greater transparency if the information shared cannot easily be understood and we therefore recommend that efforts to increase the availability of clinical trial data focus on providing information that is accessible, assessable, intelligible and usable. (Paragraph 58)

12. We consider universal trial registration to be a crucial step in increasing clinical trial transparency and believe that all future trials should be included in a publicly accessible register. This is clearly not the case at present, even for trials conducted in the UK. We recommend that the Government take steps to ensure that, in future, all clinical trials conducted in the UK, and all trials related to treatments used by the NHS, are registered in a WHO-listed primary registry. (Paragraph 63)

13. Since the trials of treatments currently in use often occurred many years ago, retrospective disclosure is important if the benefits of clinical trial transparency are to be realised in the short to medium-term. Although retrospective trial registration will incur some cost, we consider that this will be outweighed by the public health benefit of having a complete picture of the trials conducted on treatments currently available to patients. The Government should support the retrospective registration of all trials conducted on treatments currently available through the NHS and should actively pursue policies to bring this about. (Paragraph 64)

The Government and its arm's length bodies including the MHRA and the HRA are committed to transparency in the area of clinical trials and will continue to work with partners in the UK and in the EU to ensure greater transparency in the dissemination of clinical trials information. We believe that the developments that are ongoing in the negotiations on the Clinical Trials Regulation provide the opportunity to address this important issue. We would agree with the view expressed by the Committee that such

2 http://www.nihr.ac.uk/files/Publications/UKCTG%20Report_Jan%202013.pdf

information should be disclosed via the appropriate channels, with suitable checks and safeguards in place to ensure patient confidentiality in particular is protected. We would also expect the principle of informed consent to feature.

As noted above, clinical trial registration on a publicly accessible database is now a condition of a favourable ethics committee opinion.

The Government considers that it would be unfeasible to ensure that all trials related to treatments used by the NHS are registered in a WHO-listed primary registry, particularly in view of the extent and diversity of treatments, and the considerable number of sponsors and funders internationally that support the trials relating to these treatments.

14. We consider that summary-level results should be made publicly available for all clinical trials and we welcome the many new media through which it is now possible to share this information. Nevertheless, peer review is vital to the reputation and reliability of scientific research and we deem it appropriate that journal articles remain the primary instrument for the publication of summary-level trial results. (Paragraph 68)

A model clinical trials agreement for pharmaceutical research has been agreed by the UK health departments, the ABPI and the BioIndustry Association. This agreement makes it a requirement for pharmaceutical companies to ensure that the results of a clinical trial will be published on a free, publicly accessible clinical trial results database within one year of the medicine first being approved and commercially available in any country. Where a clinical trial is under review by a peer-reviewed journal, the results will be posted on a database at the time of journal publication.

15. Many historic trials remain unpublished, which is far from ideal. However, retrospective publication of all trials of all treatments currently in use, while desirable, would almost certainly be unachievable given the likely time and resources that this would require. We therefore emphasise again the importance of retrospective trial registration as a means of providing a vital "index" against which individual cases of non-publication can be identified and, where of particular importance, pursued on an ad hoc basis. (Paragraph 69)

The HRA is already taking forward plans to promote transparency in research. As mentioned in our response to recommendations 9 and 10, it is now a condition of a favourable ethics committee opinion that clinical trials are registered on a publicly accessible database. The HRA will also:

- work with partners to understand what is meant by publication and to make sure that where research is undertaken, it is subsequently published according to plans agreed with the REC at the time of approval;
- undertake an audit of completed studies to more fully understand publication rates in the UK;
- look for further ways to monitor compliance to publish within the agreed conditions of REC approval; and
- explore means by which researchers, sponsors and funders will demonstrate good conduct.

16. Given recent changes to academic publication models, we do not recognise as legitimate the argument that it is not possible to publish "negative" results in a peer reviewed journal and we consider failure to publish on a timely basis to be poor scientific practice. However, we are sympathetic to the pressure that scientists are often working under and therefore we urge the Government and other trial funders to ensure that researchers are provided with the time and resources needed to meet their publication obligations. (Paragraph 70)

The Government already provide leadership on this matter via the NIHR Journals Library, which includes the *Health Technology Assessment* journal. The NIHR Health Technology Assessment programme has 98% compliance of publication in relation to the funded research. This includes "negative" results. It is considered as a bastion of excellent practice. The Government encourages other funders to apply the same rigor and compliance management to their funded research going forward.

17. We encourage academic publishers to remove "Ingelfinger" restrictions on the prepublication of summary-level results through media such as trial registries, in order to facilitate greater openness and faster access to important scientific data. (Paragraph 72)

The Government encourages academic publishers to remove these restrictions.

The HRA has responded further to this recommendation.

18. It would be unduly burdensome to mandate that clinical study reports (CSRs) be produced for non-commercial trials. We also consider that issues concerning the reliability of the information contained in academic journal articles should be dealt with at source, for example by strengthening the peer review process as recommended in our 2011 Report, rather than by effectively bypassing academic publication through greater reliance on CSRs. We therefore do not support any move to make it mandatory for non-commercial trials to produce a CSR, or any other document of an equivalent level of detail. However, we recognise that CSRs can provide a useful contribution to the scientific literature and, once a regulatory decision has been reached, we see no compelling reason why CSRs should not be placed in the public domain, with identifiable patient data redacted. (Paragraph 79)

On the issue of clinical study reports (CSRs), the Government welcomes the proposed amendments that have been made under the negotiations on the Clinical Trials Regulation which would provide a clear legal basis for public access to an EU database, which would include summaries of the results of all clinical trials. We do, however, consider it important that there is clarity about the data that should be included in CSRs to ensure that trial sponsors as well as the public can be reassured.

19. We are not in favour of placing anonymised individual patient-level data (IPD) in the public domain in an unrestricted manner, as we consider that the risk to patient confidentiality is too great and, for many past and current trials, this level of disclosure would go beyond

the confines of previously obtained patient consent. Nevertheless, we recognise the scientific value of IPD and consider these data to be currently underutilised. We agree with the Caldicott 2 Review that providing specific individuals with controlled access to personal confidential data such as IPD through carefully managed and secure "safe havens", together with contractual agreements about how that data can be used, is the best way forward. We also consider that access should be facilitated by an independent "gatekeeper", responsible for evaluating research proposals and ensuring that data is handled responsibly and in a way that makes a useful contribution to scientific knowledge. (Paragraph 88)

20. **The UK could take the lead in shaping how a global system for sharing IPD for non-commercial trials might operate and a national system covering all non-commercial UK trials would be capable of delivering potentially significant benefits. We consider that the Health Research Authority (HRA) could act as developer, administrator and gatekeeper for a central repository of IPD for non-commercial UK trials. In order to achieve this, template consent forms provided by the HRA should allow for and emphasise to trial participants the benefits of data sharing. Research Ethics Committees should also take into account any transparency restrictions imposed by patient consent forms when evaluating research proposals for clinical trials. (Paragraph 89)**

The Government agrees that controlled access to IPD via 'safe havens' is the right approach. The Government has responded to the Caldicott Review and is currently considering the criteria for accrediting 'safe havens', which will provide a useful mechanism to aid the implementation of recommendation 19.

The HRA has responded further to these recommendations.

21. **We support the development of the EU Clinical Trials Register (EU CTR) and hope it will also include summary-level results, as promised, by the end of 2013. However, we do not consider the register to represent a complete solution to the problem of non-registration of clinical trials, as it does not include all the trials that have been conducted on all medicines currently available in Europe. The Government should encourage the EMA to further increase the scope of the EU CTR, for example by including phase I trials and trials conducted outside of the EU. We also recommend that the Government monitor the EMA's fulfilment of its pledge to include trial results on the register and obtain an explanation if the EMA fails to do so by the end of 2013. (Paragraph 94)**

The European Commission's initiatives towards increased transparency include a commitment to develop the EU Clinical Trials Register (EU CTR) to include summary results for all registered interventional clinical trials by the end of 2013. The European Medicines Agency (EMA) which is developing the system on behalf of the Commission is currently piloting it and is on track to make the functionality live during Q4 of 2013. Although the EU CTR does not include adult Phase 1 trials the draft Clinical Trials Regulation that is

currently under negotiation in the EU Council and Parliament proposes to provide public access to the planned EU database (except in the case of personal or commercially confidential data) and this will include data on all trials including Phase 1 trials.

22. **As a major direct and indirect funder of clinical trials, the Government can influence behaviour across both the public and charitable sectors. This influence has not been wielded effectively to increase transparency, meaning that many publicly-funded trials remain unregistered and unpublished. We recommend that registration in a WHO-listed registry and publication of summary-level results in a peer-reviewed journal be made contractual requirements for all publicly-funded trials, including research supported by the Charity Research Support Fund. The wording of these requirements should be standardised across all contracts to ensure consistency. We also recommend that public funders of research rapidly put in place mechanisms to monitor compliance with transparency policies and ask the Government to detail in its response to this Report how and when this will be done. (Paragraph 99)**

23. **Since the Government has encouraged industry to disclose retrospectively the results of past trials, we think that it should be prepared to do the same for the major trials that it has funded. We therefore recommend a retrospective audit of all public phase III trial grants awarded since 2000, followed by action to ensure that any failures to register or publish the summary-level results of these trials are rectified within 12 months. Any failures to correct these mistakes should be taken into account when considering future grant applications from principal investigators of previously unregistered or unpublished trials. In future, for grants awarded to fund phase III clinical trials we suggest that the MRC and the NIHR allocate a small proportion of funding to cover the time and resource requirements of preparing a manuscript for publication, and withhold this funding until the results of the trial are ready to be published. (Paragraph 100)**

It is now a condition of a favourable ethics committee opinion that clinical trials, including publicly-funded trials are registered on a publicly accessible database. The HRA is taking forward a range of plans to promote transparency in research as outlined in our response to recommendation 15.

We have commented further on publication compliance in our response to recommendation 16.

24. **We suggest that the academic publishing industry put in place robust measures to ensure that unregistered trials are not just rejected, but that the trial sponsor(s) and funder(s) are notified that the trial has not been properly registered. (Paragraph 101)**

We encourage the academic publishing industry to address this.

25. **In mandating trial registration, publication of summary-level results and publication of CSRs for commercial trials, we consider that the European Parliament's ENVI**

Committee appears to have reached a reasonable decision regarding the transparency requirements of the proposed EU Clinical Trials Regulation. (Paragraph 104)

The Government supports the ENVI amendments on trial registration and publication of summary result data including a lay summary and clinical study reports of commercial trials.

26. The Government should clarify why Department of Health or MHRA officials were not present at recent discussions relating to the EMA's revised transparency policy. We hope that the Government will be more fully engaged in the next stages of the development of this policy. (Paragraph 106)

The Government is fully engaged in all aspects of this policy, and has recently responded to the EMA consultation on clinical trials data (the Government's response is appended as Annex A). Going forward, we will continue to work with the EMA and the Commission on the development of a clear and workable policy on the release of clinical trials data.

27. We agree with the Joint Committee that the Care and Support Bill should make the promotion of research transparency a statutory objective of the HRA and we recommend that the Government includes the necessary provision. (Paragraph 109)

In responding to the Joint Committee report on the draft Care and Support Bill, the Government explained that in meeting its main objective of facilitating the conduct of safe, ethical research, it will be essential for the HRA to promote transparency in research. The Government accepts that there is a powerful case for increasing transparency in clinical trials and has listened to the views expressed during the Committee stage of the Care Bill in the House of Lords and taken account of the Science and Technology Committee's recommendation. We have also discussed the HRA's role in promoting transparency with stakeholders and with the HRA itself. As a result, the Government tabled an amendment to the Care Bill at Report stage which made it explicit that the HRA's main objective of protecting and promoting the interests of participants, potential participants and the public by facilitating the conduct of safe, ethical research includes promoting transparency in research.

28. Research Ethics Committees should have a role in considering and monitoring compliance with transparency policies. As such, we welcome the HRA's new transparency policy and support, in principle, the proposals made in its May 2013 paper. We recommend that the HRA initially retains full responsibility for policing its own policies and ensures that all trials have been registered and published according to an agreed timeline, rather than performing checks on a sample basis. In addition, there must be penalties for non-compliance. We recommend that the HRA provides us with a progress update on implementation of its new transparency policy by the end of 2013. (Paragraph 110)

The HRA has responded to this recommendation.

29. We recognise the efforts of some members of the pharmaceutical industry, particularly GSK, to increase clinical trial transparency and hope that other companies will act in the same spirit in implementing

industry-wide principles for responsible clinical trial data sharing. We suggest that all companies endorsing such principles agree and report on a common set of clinical trial transparency metrics each year in their annual reports. (Paragraph 113)

We encourage the ABPI to work with its members to share and promote best practice in clinical trial transparency and data sharing as this will show leadership from the pharmaceutical industry in demonstrating that transparency is an important part of its business.

30. **We are supportive of the broad aims of the AllTrials campaign and agree that all clinical trials should be registered and their results reported. We suggest that the AllTrials campaign clearly set out what it considers a full trial report to contain, particularly when prepared for non-commercial purposes, so that its supporters can work together to achieve a specific set of common goals. (Paragraph 116)**

We recognise the importance of the transparency agenda and the significant interest this has generated. The HRA is fully committed to its established role to promote transparency in health research and seeks to improve public confidence in research in the UK. It already publishes research study summaries and the opinions of its research ethics committees and, as mentioned in our response to recommendations 9 and 10, the registration of clinical trials within an agreed timeframe has become a condition of research ethics committee approval. The HRA has signed the AllTrials petition and is working with research funders and other key stakeholders to agree what is meant by publication and dissemination, and to set common definitions and standards.

31. **Value-based pricing (VBP) is predicated on the idea that the Government is able to influence industry's behaviour through its spending power. We therefore consider VBP—and to a lesser extent the PPRS—to be tools that could also be used to encourage and reward industry for making its clinical trial data more transparent. The Government should consider ways in which clinical trial transparency could be incentivised in the future through VBP and the current renegotiation of the Pharmaceutical Price Regulation Scheme (PPRS). (Paragraph 118)**

The Government agrees that there is a need to promote greater transparency in clinical trial data and is already taking a range of measures to support this as described earlier. However, the Government considers that the pharmaceutical industry should aspire to greater transparency as an end in itself and does not agree that rewards or incentives for improving clinical trial transparency should be incorporated into the pricing system for NHS branded medicines.

32. **Increased transparency is unlikely to lead to improved medical outcomes unless mechanisms are in place to ensure that emerging evidence is quickly and effectively incorporated into clinical practice. Given the high degree of reliance placed on NICE's guidance by health professionals, we consider it essential that this advice remains fully up to date and that processes are in place to ensure that emerging evidence is rapidly incorporated. The Government should ensure that, as improved**

transparency leads to ever greater volumes of trial data becoming available, NICE continues to receive the resources it needs to assimilate emerging evidence into its guidance in a timely manner. (Paragraph 122)

We agree that it is important for NICE's guidance to be kept up to date. NICE has processes in place to periodically review its guidance to determine whether it should be updated to reflect significant new evidence and changes in clinical practice. For technology appraisals, NICE sets a scheduled review date at the time of publication of final guidance and the review can be brought forward if significant new evidence emerges. In common with all public sector organisations, NICE operates within a tight financial climate and it is important that it discharges its functions efficiently. It is also important to achieve the right balance between developing guidance on new technologies and reviewing existing guidance.

33. **We consider that more can and should be done to make the UK a more attractive location to conduct clinical trials. (Paragraph 123)**

34. **We are confident that the Government is aware of these problems and the need to resolve them, but its promises have yet to be matched by effective action. We strongly urge the Government to act on our recommendations and put an end to these long-standing issues, so that the UK can continue to make progress towards being the location of choice for the global life sciences industry. (Paragraph 124)**

35. **We call on the Government to take decisive steps, as outlined in this Report, to ensure greater transparency in all future trials conducted in the UK, in order to demonstrate to the rest of the world how effective solutions might one day be applied at a global level. (Paragraph 125)**

The Government welcomes the Committee's report including its recommendations on reducing barriers to conducting clinical trials in the UK and increasing trial transparency. This response sets out the actions the Government is taking to address these areas.

Annex A – Government response to EMA consultation on clinical trials data

EMA/240810/2013

SUBMISSION OF COMMENTS ON 'POLICY 0070 ON PUBLICATION AND ACCESS TO CLINICAL-TRIAL DATA'

Comments from:

Name and affiliation

United Kingdom Government (Medicines and Healthcare Products Regulatory Agency)

Please note that these comments and the identity of the sender (not contact details) will be published unless a specific justified objection is received.

When completed, this form should be sent in Word format (not PDF) to: ctdatapolicy@ema.europa.eu

General Comments

The Medicines and Healthcare Products Regulatory Agency (MHRA) on behalf of the UK Government, welcomes the opportunity to comment on the proposals in draft 'Policy 70 on publication and access to clinical-trial data'. The question of transparency has been gaining profile at a national level here in the UK as well as at EU level. Along with other parts of Government, the MHRA recognises the importance of transparency to public health and is committed to the transparency agenda. A range of initiatives have taken place in the UK including the recent Caldicott review which reviewed how best to balance the need to keep patient information secure with the need to share it among healthcare professionals for legitimate reasons. The MHRA has carried out a great deal of work to ensure that information about clinical trials that we receive is put in the public domain. The Agency publishes public assessment reports following the approval of new medicines providing details of the information on which a decision to approve a marketing authorisation was made. In addition, since July 2012, summaries of product characteristics of all UK approved medicines are published on the Agency's website. The MHRA is working closely with other parts of Government and its EU partners on the transparency agenda and will continue to do so going forward. The UK Parliament Science & Technology Committee has recently published a report into clinical trials and transparency, and has recommended continued work with the EMA and the European Parliament to ensure greater transparency in the dissemination of trials information, with suitable checks to ensure patient and to some degree commercial confidentiality, are embedded in European policy and legislation.

A number of specific comments are provided below. We also wish to make the following general comments:

- The UK Government is fully supportive of the broad principles of transparency. It is important for patients, the public, researchers and the NHS and can be achieved through ensuring trial registration and outcome publication as well as making data available through appropriate means. The UK Government welcomes the proposed amendments under the Clinical Trials Regulation (CTR) which provides a clear legal basis for public access to an EU database, which will include summaries of the results of all clinical trials. We will however seek clarity on what data would be considered confidential in the database to ensure that those sponsors with commercial interests, and the public, are reassured.
- The MHRA has done a great deal of work to ensure that information about clinical trials that it receives is put in the public domain. It is worth stressing that, as the regulator, the MHRA does not receive all the raw patient level data that results from clinical trials. This remains with the sponsor. What the MHRA does receive, in support of applications for marketing authorisations, is enough information (in the form of Clinical Study Reports) to allow a decision to be taken on the safety, efficacy and quality of a medicine.
- We have carried out an exercise to establish what data the MHRA holds in relation to the EMA Annexes, and the present status of such data. This also identifies some data that MHRA as a UK regulator receives that is not held by EMA (in respect of national and decentralised procedures and inspections for example). This exercise is part of a wider programme of work carried out by the MHRA and wider Government to develop proposals for greater transparency in respect of its own data holdings.
- We support the proposal for the EMA's policy to apply prospectively from 1 January 2014 and to apply only to new data submitted to the EMA on or after 1 March 2014.
- We consider that several areas of definition in the draft policy need to be clarified or tightened, or set in their legal context. This applies in particular to definitions of commercially confidential and patient/personal information. We also think that the legal position on ownership of data held by sponsors and that submitted to regulators, including the EMA, and subsequently released, should be clarified, for example, how this relates to the EU wide General Data Protection Regulation being considered by the LIBE committee, which will have implications for regulators, sponsors and trialists.
- We would welcome further clarification of the practical arrangements that are envisaged under the proposed policy for release of data that would fall under Category 3 and how those arrangements would apply in the case of orphan medicines, for example.
- In relation to information on clinical trials (primarily Clinical Study Reports) submitted to MHRA we should emphasise i) that if the MHRA, as opposed to the Sponsor, is requested to release such information, national legislation on data protection and freedom of information also applies and ii) these data are supplied in support of requests for marketing authorisations, and do not represent the totality of clinical trials information. Therefore, we consider it important that the policy makes absolutely clear where specific

responsibility lies for release of data and what requirements would apply in those cases where, for example, a national regulator is approached to release data that has been received via rapporteurship arrangements under the centralised procedure.

- We are aware of concerns expressed by a number of stakeholders on some of the proposals, in particular sponsors of clinical trials and their representatives. While we remain broadly supportive of the overall drive towards transparency set out in the policy, we consider that any final policy should ideally aim to reflect a consensus across all groups involved in the clinical trials process, and not just Government and regulators.
- We are aware of current legal challenges to the EMA position on disclosure of clinical trial information. We consider it is important to see what implications these cases hold for the future releases of data. A statement from the EMA on its position in the interim would be helpful.

Comments on text

Line number(s) (*e.g. 20-23*)	Comment	Proposed changes, if any (*If changes to the wording are suggested, they should be highlighted using 'track changes'*)
36-49	We strongly agree with the proposition that personal data should be protected. We agree with the concern expressed that technological advances could lead to the re-identification of such data and that any policy adopted should include robust measures for the avoidance of such unlawful disclosure. The policy should say more on the status of patient data and also on the principle, of informed consent. How will the EMA satisfy itself that such consent has been sought on any data it releases. Our preference in relation to personal data would be not to release this if it has not been proven beyond doubt that the person has consented to its use.	
49-51	The statement in relation to commercially confidential data is over-simplified – this occurs elsewhere in the document. There may be exceptions where clinical trials data could be commercially confidential. A precise, legally underpinned definition of commercially confidential information should be included.	
132	A definition of 'duly justified cases' is needed in relation to CCI. This does not appear to derive either from legislation or ICH guidance	
165-175	The descriptions and proposals for de-identifying data could be more detailed, and include minimum standards and reference to specific methods	
177-218	Controlled access – there could be more specific detail in this section regarding the plans and proposals for identifying the requester, the reasons for the request, and the purposes for which the information or analysis is to be used.	
285	We have a number of concerns with the proposal that persons carrying out work in respect of clinical trials, such as investigators, should be exempt from PPD considerations. While we accept the view that such persons have a role in public health and are acting in a professional capacity, the regulator has taken the view, in releasing data, that individual information about staff should not be released. This would be a departure from that practice, and we would need to consider it in the context of existing guidance and legislation.	

Please add more rows if needed.

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