On 4th December the Committee asked us for suggested questions to put to Minister of State for Universities, Science, Research and Innovation Jo Johnson when he appears before them. I have included as an annex here a letter sent to Secretary of State for Health Jeremy Hunt. It sets out how the UK led discussions and pressure on this issue in Brussels in 2103 and 2014. The Regulation EU No. 536/2014 comes into force in 2019 (probably after 29th March) and the provisions will not be captured by the Repeal Bill. It asks the question, what is the UK government going to do to ensure measures on increasing clinical trial transparency in the new EU Clinical Trial Regulation - measures which the UK government, UK organisations and British citizens, fought hard to get included into the Regulation - will be retained in UK law after Brexit? It would be useful for the Committee to ask Mr Johnson the same question.

There was a discussion at the evidence session on potential push back against more stringent transparency regulations, especially those that ask trial researchers to show their past behaviour. There has already been push back. In 2015 contract research organisation Richmond Pharmacology (they run early stage clinical trials on behalf of pharmaceutical company clients) launched a judicial review against the HRA to try to show that HRA’s moves to ask trial sponsors to declare that they had reported all past UK trials they sponsored was unlawful. Sense about Science obtained permission to intervene as a third party in the judicial review. The judge ruled that the HRA has a clear legal right to check researchers’ compliance with ethical and legal requirements to register and publish clinical trials. The only problem was that their website was not clear on the difference between ethical obligations and legal obligations. The judge ordered the HRA to clarify a few pages on its website.

This was a very narrow judgement that should not stop the HRA from pushing on with its plans to ask sponsors to declare they have reported their past trials. But since the judicial review was an annoying and costly process for them I would not be surprised if the HRA was feeling unsure about pursuing their plan. It would be enormously helpful if the Committee could encourage them to move ahead.

I am happy to have a supply more detail on ether of the above points.

December 2017
RE: Clinical trial regulation and transparency in the UK after Brexit

Dear Secretary of State

The UK has led international discussion on transparency in clinical trials and has shown strong global leadership on measures to increase clinical trial registration and reporting. The gains you have fought hard for over the past four years are at risk of being lost if the provisions on transparency in the new EU Clinical Trial Regulation do not move into UK law after 29th March 2019. What will the government do to ensure this does not happen?

I am writing on behalf of the AllTrials campaign for clinical trial transparency which was founded by Sense about Science¹ with the BMJ, Cochrane Collaboration, Dr Ben Goldacre and others in January 2013. The campaign is a global collaboration of 735 organisations who together represent more than 600 million people worldwide². The campaign calls for all clinical trials to be registered and results from them reported. Today, according to the best evidence available, around half of all clinical trials that have been carried out have not reported results³. This means that doctors, researchers, treatment assessment agencies, medicine payers and patients do not know what found out in trials of medicines we use today so cannot be sure they are making the best decisions and not unknowingly doing harm.

The UK government is committed to supporting clinical trial transparency

As Secretary of State in November 2013 you and the Department of Health announced that the UK government supports clinical trial transparency and the AllTrials campaign,

“The government supports the call for more transparency in clinical trial data. Transparency is important for patients, the public, researchers and the NHS, and can be achieved through ensuring that all clinical trials are registered on a public database such as the EU Clinical

¹ Sense about Science is the independent UK charity that campaigns on the misuse of evidence in public life. www.senseaboutscience.org
² http://www.alltrials.net/supporters/
Trials Register. This means that everybody can see what trials are ongoing, the results of all clinical trials are published, and data from all clinical trials are made available.”

In the government’s response to the House of Commons Health Select Committee inquiry into clinical trials in 2013 Earl Howe, then Parliamentary Under Secretary of State for Quality (Lords) said, “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.”

In June 2015 Prime Minister David Cameron committed the UK to leading the world on clinical trial transparency. Mr Cameron told the G7 meeting in Hamburg that, “The UK will be the first country in the world to require clinical trials and disease control operations to be fully transparent. From now on any UK-funded research, data or operation will be made openly available and the UK will look to develop an international agreement – via the G – that would see the publication of results of all clinical trials for vaccines for relevant diseases. The UK’s Chief Medical Officer will now work with the World Health Organisation (WHO) to develop a new, more advanced system to share data on a disease with health agencies and doctors and nurses on the frontline. “As a world we must be far better prepared with better research, more drug development and a faster and more comprehensive approach to how we fight these things when they hit. The UK will lead the way but we need a truly global response if we are to face down this threat.”

The UK government’s research regulator, the Health Research Authority, has shown global leadership in developing measures to ensure more clinical research is registered and results shared. When the HRA was established it was given a statutory duty to promote research transparency. In September 2013 the HRA made it a condition of gaining ethical approval to run a trial in the UK that the trial is registered on a publicly accessible database within 6 weeks of the first patient being recruited into the trial and the HRA is developing measures to increase reporting of clinical trial results. The HRA has truly been an inspiration to global research regulators who continue to look to the UK for leadership on this issue.

The UK medical and research community shaped the new European law on transparency
British medical and research organisations and individuals urged the European Commission and Parliament to include provisions in the Clinical Trial Regulation EU No. 536/2014 to mandate

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transparency of European clinical trials. These groups included us at Sense about Science, AllTrials partners, MRC, the Wellcome Trust, medical Royal colleges and academies, medical research charities, professional and learned societies, patient associations and UK universities. Their pressure resulted in an EU Clinical Trial Regulation that requires clinical trial registration and results reporting for European clinical trials. The UK government supported the amendments these organisations and thousands of UK citizens urged the European Parliament ENVI committee to adopt.

Indeed, the UK government was a leading advocate for provisions in the EU Clinical Trial Regulation to increase transparency of European clinical trials. In November 2013 the government said, “In its proposal for a Clinical Trials Regulation (2012/0192), the European Commission calls for a publically accessible EU database. This database will contain details of all trials submitted for authorisation in the EU and summaries of their results within one year after they have ended. The government is supportive of these proposals. … “The government also agrees with the European Parliament that once a regulatory decision has been made, the data in clinical study reports should not be considered commercially confidential.”

The NHS has supported increased clinical trial transparency. Elisabetta Zanon of the NHS Confederation said in 2014, “The extensive lobbying in Brussels – by the NHS European Office and other medical research groups – calling for the EU rules to be rewritten has, eventually, paid off. After extensive debates and negotiations at EU level, a new EU regulation on clinical trials entered into force in June 2014, bringing with it a number of positive changes. Addressing many of the shortcomings of the Clinical Trials Directive, the new EU regulation will:

• Improve transparency, by requiring the publication clinical trial results, whether positive or negative, so that both researchers and patients can be made aware of past trials and their outcomes, and avoid the same studies being repeated unnecessarily.”

UK pharmaceutical companies lead the world on transparency

British company GSK was the first global pharmaceutical company to join the AllTrials campaign and to make strong commitments to release information from its clinical trials that had not previously been available. On making these commitments GSK said, “We are pleased to sign up to the AllTrials campaign for clinical trial transparency and support its call for the registration of clinical trials and the disclosure of clinical trial results and clinical study reports. At GSK, we are committed to being transparent with our clinical trial data to help advance scientific understanding and inform medical judgment. We already publicly disclose a significant amount of information about our clinical trials. We register and post summary information about each trial we begin and share the results of all our clinical trials – whether positive or negative – on a website accessible to all.”

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9 The Health Research Authority, NICE, NHS Blood and Transplant and the NHS R&D Forum and several NHS trusts have joined the AllTrials campaign.
10 http://www.nhsconfed.org/blog/2014/10/momentous-changes-to-eu-rules-unleash-nhs-clinical-research-potential
GSK has led discussions on clinical trial transparency within the pharmaceutical industry. The initiatives the company has taken include building an online platform\textsuperscript{12} to share information from its clinical trials. Twelve other global pharmaceutical companies\textsuperscript{13} have now followed GSK’s lead and joined the data sharing platform including companies with a large presence in the UK such as Pfizer, Novartis and Eisai.

In 2017 the AllTrials campaign conducted an audit of global pharmaceutical companies’ policies on clinical trial transparency\textsuperscript{14}. We scored companies against a globally agreed gold standard for transparency and produced a ranked list of companies based on their score. GSK tops the list\textsuperscript{15}.

UK companies lead the world in publishing clinical trial results too. The TrialsTracker tool\textsuperscript{16} shows that UK-headquartered company Shire has published results for every Shire-sponsored trial on ClinicalTrials.gov\textsuperscript{17}. Shire is the only global company to show an 100% publication rate.

**Intergovernmental organisations have called for global government action on clinical trial transparency**

The United Nations, the World Health Organisation and the World Medical Association have all called on global governments to bring in measures to increase clinical trial transparency.

The World Medical Association following its 64\textsuperscript{th} General Assembly in 2013 in Brazil said,

“Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

“Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports.”\textsuperscript{18}

The WHO has long said that,

“The registration of all interventional trials is a scientific, ethical and moral responsibility.”

“There is an ethical imperative to report the results of all clinical trials, including those of unreported trials conducted in the past.”\textsuperscript{19}

\begin{itemize}
\item \textsuperscript{11} https://www.gsk.com/en-gb/media/press-releases/gsk-announces-support-for-alltrials-campaign-for-clinical-data-transparency/
\item \textsuperscript{12} https://www.clinicalstudydatarequest.com/
\item \textsuperscript{13} https://www.clinicalstudydatarequest.com/Study-Sponsors-Info.aspx
\item \textsuperscript{14} http://www.bmj.com/content/358/bmj.j3334
\item \textsuperscript{15} http://policyaudit.alltrials.net/
\item \textsuperscript{16} The online dashboard developed by researchers at the University of Oxford which pulls in information from the world’s largest clinical trial register ClinicalTrials.gov and from medical journals about trials sponsored by the world’s largest trial sponsors (commercial and non-commercial) and assesses which trials have published results. It displays ranked lists of trial sponsors’ publication rates based on this information https://trialstracker.ebmdatalab.net/#
\item \textsuperscript{17} https://trialstracker.ebmdatalab.net/#shire
\item \textsuperscript{18} https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
\item \textsuperscript{19} http://www.who.int/ictrp/results/reporting/en/\
\end{itemize}
In April 2015 the WHO called on governments to introduce measures to achieve full registration and reporting of future and past clinical trials and said,

“WHO calls for ethics committees, regulatory authorities, professional bodies, sponsors, investigators, and funding agencies to act in their jurisdictions to ensure results from all interventional clinical trials are reported and publicly disclosed.”

In September 2016 the United Nations Secretary-General’s High-Level Panel on Innovation and Access to Health Technologies said that,

“Governments should require that the unidentified data on all completed and discontinued clinical trials be made publicly available in an easily searchable public register... regardless of whether their results are positive, negative, neutral or inconclusive. To facilitate open collaboration, reconstruction and reinvestigation of failures, governments should require that study designs and protocols, data sets, test results and anonymity-protected patient data be available to the public in a timely and accessible fashion.”

Will the government retain the gains the UK has made on clinical trial transparency after Brexit?
The Clinical Trial Regulation EU No. 536/2014 is expected to come into force across EU member states in 2019. This will probably occur after 29th March 2019 and certainly will not be captured by the European Union (Withdrawal) Bill 2017 - 19. Therefore, the provisions in the Clinical Trial Regulation that UK organisations and the UK government fought so hard for will not automatically become UK law. What will the UK government do to ensure the provisions on clinical trial transparency move into UK law?

The provisions on transparency in the EU Clinical Trial Regulation would have been the UK government’s answer to the WHO and UN’s calls to global governments to bring in measures to increase registration and reporting of clinical trials. How will the government answer those calls?

I and my colleagues in the AllTrials campaign would be happy to discuss this further.
Yours sincerely

Síle Lane
Head of international campaigns and policy

20 http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001819
21 http://www.unsgaccessmeds.org/final-report/