**Note of HRA Meeting 3/12/2015**

**“Point of Care” trials: Their importance for public and patients and helping RECs review them fairly**

**Background**

This note summarises a workshop, hosted and funded by the Health Research Authority (HRA) in December 2015, aimed at gaining a wider understanding of the potential of Point of Care trials (PoCTs) – one of the forms of ‘pragmatic trials’ - in achieving better health care. The workshop explored the issues raised by PoCTs, both to inform developing HRA policy and guidance on proportionate consent and to provide a training and learning opportunity for members of Research Ethics Committee (REC) and other stakeholders. Video footage from the day will be used to develop further materials for training and awareness to support the effective design, review and conduct of PoCTs.

The HRA aims to give more patients the opportunity to take part in research studies and feel safe when doing so. PoCTs are an important component of an overall commitment from the HRA to ensure effective and proportionate regulation and governance of health research. The HRA is a signatory to The Lancet’s REduce research Waste And Reward Diligence (REWARD) campaign.

**Introduction**

In many cases we do not always know (due to a lack of evidence) which of the large number of treatments routinely used in the NHS is best for an individual patient, or group of patients with similar health problems. Clinical trials conducted for licensing purposes may focus on short term outcomes such as biomarkers rather than long term outcomes. It is important, therefore, to compare medicines and other treatments used in order to better inform clinical care. Indeed, a recent survey conducted in Scotland found that 97% of general public participants agreed that the National Health Service “has a duty to determine the safety and effectiveness of the medicines its doctors prescribe”[[1]](#footnote-1). Such general consensus places a duty upon:-

* Healthcare professionals, working with patients and researchers, to address uncertainties about the relative merits of treatments routinely offered in the NHS
* Research Ethics Committees (RECs) and other research regulators to facilitate research to help resolve such uncertainties

Point of Care Trials (PoCTs) are a simple and cost effective way of addressing uncertainties about the relative merits of different treatments in common use. They compare the effectiveness of alternative treatments in routine clinical practice. They do not withhold effective treatment; rather they compare accepted or licensed interventions / therapies in current use and do not involve extra interventions or measurements beyond routine care. Trials similar to PoCTSs are sometimes referred to as ‘simple trials’, ‘pragmatic trials’, ‘comparative effectiveness trials’ or ‘low-intervention clinical trials’ under the forthcoming EU Clinical Trials Regulation.

Unlike traditional clinical trials, it may be possible to not blind the interventions where the interventions offered are similar and the participant is unlikely to have a preference. This means participants can receive an actual prescription and the pack insert provided with this. Information covered in the pack insert does need to be repeated in the Patient Information Sheet provided for the trial.

Like all interventional research studies PoCTs require patient consent but the methods for seeking that consent need to be proportionate to the relatively low risks and levels of burden inherent in this type of research.

Background papers on ‘Current evidence (or lack thereof) on clinical treatments in use’ and ‘Patient and public opinion on point of care trials’ were circulated before the meeting.

**Speakers**

**Hugh Davies**, Chair Oxford A REC, welcomed delegates (attendee list attached) and outlined the purpose of the day. He explained that PoCTs are a cost effective way of reducing uncertainties regarding the effectiveness of treatments in common use.

Hugh introduced **Iain Chalmers** from the James Lind Alliance who chaired the morning and afternoon sessions. Iain explained the principal differences between PoCTs and routine clinical care and the similarities and differences between PoCTs and standard clinical trials (Appendix 1).

**Tjeerd van Staa** from Manchester University explained what PoCTs are, emphasising their benefits for both patients and clinicians and comparing them to other trials. He described his research on statins to illustrate the benefits and barriers to conducting this type of research.

**Matthew Hyde** from Imperial College, London, also highlighted the potential benefits of PoCTs to help improve routine clinical practice and their cost-effectiveness compared to other trials. He also presented data on RECs’ decisions when asked to review the same paediatric PoCT involving opt-out consent procedures. Matthew stressed that research is essential to reduce variability in clinical practice and pointed out that paediatric oncology has the best record of enrolling children in trials. This, he explained, has contributed directly to the dramatically improved prognosis for children with leukaemia.

**Ben Goldacre** from the Department of Primary Care, Oxford University, reinforced the message that PoCTs have the potential to improve patient care significantly at a fraction of the cost of Randomised Control Trials. He explained that there is an urgent need for research evidence to allow both clinicians and patients to make more informed, and therefore better, decisions. He also pointed out that marginal differences in effectiveness can add to substantial cost differences over a large patient population. However this means the trials themselves also need to be conducted on a large sample size in order to demonstrate relatively small differences.

**Kirsty Wydenbach** from the Medicines & Healthcare Products Regulatory Agency (MHRA) explained the current UK Clinical Trials Regulations, the MHRA’s risk adapted notification scheme for lower-risk trials (known as ‘Type A’ trials[[2]](#footnote-2)) and the forthcoming EU Clinical Trials Regulation[[3]](#footnote-3).

**Marion Cumbers**, a lay member of the Trials Steering Committee for PoCTs described by Tjeerd van Staa, provided a patient perspective on these trials and underlined the inconsistency in ethical standards applied to research compared to those applied in routine clinical practice. She highlighted barriers to the conduct of PoCTs, namely the additional paperwork and training requirements for conducting routine clinical activities in a research context.

**Amanda Hunn** from the HRA outlined the public engagement work using a deliberative approach on pragmatic trials and simplified consent which was supported and part funded by Sciencewise. She explained the general public supported a simplified consent approach including a shortened PIS. The public identified those elements of the PIS which need to be retained and which could be dropped. The public also specified the reassurances they would need to be in place for proportionate consent to be acceptable.

**Clive Collett** also from the HRA explained that existing HRA Guidance already advocates a proportionate approach to seeking consent but emphasised that compliance with legal requirements is essential. Details of these legal requirements can be found in the HRA draft guidance “[Seeking informed consent for simple and efficient trials in the NHS](http://www.hra.nhs.uk/documents/2014/10/seeking-informed-consent-simple-efficient-trials-nhs-draft-guidance-comment.pdf)”. He explained that the outputs from the Workshop will feed into future HRA Guidance on proportionate consent procedures for all types of research.

**Discussions at the Workshop**

Delegates discussed and agreed with the following conditions under which PoCTs may be carried out:

* Any treatments to be compared must be licensed or broadly accepted and/or in routine use
* PoCTs must only recruit patients who require the intervention under investigation
* As with other trials, PoCTs must not withhold effective treatments when these are available
* As with other trials, PoCTs must address uncertainties, demonstrated through rigorous review of current knowledge, about the relative merits of the forms of care to be compared.
* If either the clinician or the patient has a good reason for preferring one of the alternatives forms of care being compared (for example, a known allergy to one of them), this preference must be respected.

The benefits of PoCTs were discussed:

* Meeting public expectation that their health care is based on robust evidence.
* Promoting evidence-based reduction in variations in clinical practice
* Providing large scale, cost-effective research studies to detect small but important effects of treatments used routinely within the NHS
* Assessing treatment effects using treatment outcome measures relevant to patients and professionals
* Analysing additional data, for example on side effects, collected as part of routine care
* Providing greater flexibility in discovering ‘unintended’ treatment outcomes
* Providing the capacity for longer term follow-up than is usual with conventional studies
* Potential to contribute to a ‘Learning Health Care System’ (e.g. The U.S.-based PEDSnet[[4]](#footnote-4))

Delegates also discussed real and perceived barriers to undertaking these trials:

* Burden of governance procedures (form filling, additional training for routine clinical activities as well as research methodology leading to drop-outs and resource wastage)
* Non-compatibility among Information Technology systems
* Variable quality and accuracy of data collected primarily for audit purposes
* Public concerns about data protection and privacy
* Excess treatment costs
* Inconsistency in research ethics committee review[[5]](#footnote-5)

Delegates considered appropriate and proportionate procedures for seeking consent and noted that the HRA already advocates a proportionate approach in its guidance[[6]](#footnote-6). They acknowledged the public support for simplified consent procedures but also noted the strong emphasis placed by the public on the need for full consent procedures where the procedure is invasive or new or unproven treatments are involved.

**Further points discussed at the meeting**

* The need to address proportionate research regulation and review
* The nature of consent: what are the consequences of requiring specific and explicit consent in health care and research?
* Incentivising doctors to take part in PoCTs
* What duties do doctors have to contribute to resolving treatment uncertainties? (It was noted that the duty to “*help to resolve uncertainties about the effects of treatments*” has been removed from latest GMC “Good Medical Practice” (2013))
* Different consent standards applied to routine clinical care and research
* Role of the MHRA in facilitating PoCTs
* HRA/Research Ethics Committees role in facilitating PoCTs
* The appropriate relationship between research and clinical care and the HRA and RECs’ role in this?
* The need to include the public’s and patients’ voice in setting priorities, designing studies and ensuring fair and proportionate consent.

**Next Steps**

* Disseminating this meeting report
* Providing a summary ‘bulletin’ to collect and record delegate comments
* Developing HRA guidance on applying proportionate approaches to seeking consent in all types of research
* Developing training materials for REC members to support HRA guidance
* Preparing a fuller, academic report for publication based on this meeting
* Identifying interested parties for future collaboration/discussions.

**APPENDIX 1**

**What is the principal difference between PoCTs and routine clinical practice?**

The principal difference between PoCTs and routine clinical practice is the way that a treatment is selected from among alternatives of uncertain relative merits. In routine care, a number of factors may lead to the selection of a particular choice (tradition, whether a professional is aware of relevant research evidence, influence of advice, etc). In a PoCT the basis on which a treatment is selected from among alternatives will usually be random allocation, to ensure fair comparisons of the alternative treatments. Whatever the basis for recommending one of several alternative treatments, patients are entitled to be informed about the grounds for a recommendation, whether this is random allocation to help reduce uncertainty, or on some other basis, which usually does not contribute to a reduction of uncertainty.

**What are the principal similarities and differences between PoCTs and standard clinical trials?**

PoCTs and standard clinical trials must both be designed to address uncertainties about the effects of the treatments they are comparing. The principal difference between these two types of trials is that the former address uncertainties about the effects of treatments that have already been adopted in routine practice and for which there is already knowledge about adverse effects; whereas the latter address uncertainties about new, often unlicensed treatments, or treatments used in non-standard ways, for which there are uncertainties about safety and efficacy. Differences in consent to treatment and data collection should reflect these differences. This means, for example, that patients in trials assessing new treatments will usually receive detailed information explaining uncertainties about the effects of the untried treatments, whereas in PoCTs, patients can receive actual prescriptions for treatments, together with the regular package inserts describing what is known about them.

Iain Chalmers, Coordinator of the James Lind Initiative

1. Mackenzie IS, Wei L, Paterson K, MacDonald TM. Cluster randomised trials of prescription medicines or prescribing policy – public and general practitioner opinions in Scotland. British Journal of Clinical Pharmacology 2012 Aug;74(2):354-61. doi: 10.1111/j.1365-2125.2012.04195.x [↑](#footnote-ref-1)
2. In Type A trials the risk to the patient from the drug under investigation is considered to be no greater than that of standard medical care. For certain Type A trials the trial may go ahead after 14 days from receipt of notification if no objections have been raised by the MHRA. [↑](#footnote-ref-2)
3. <http://ec.europa.eu/health/human-use/clinical-trials/regulation/> [↑](#footnote-ref-3)
4. PEDSnet is a paediatric learning health system dedicated to discovering and implementing new ways of providing the best care and improving health care outcomes. <http://pedsnet.info/> [↑](#footnote-ref-4)
5. See <http://www.hra.nhs.uk/documents/2014/10/consistency-rec-review-2-may-2014.pdf> [↑](#footnote-ref-5)
6. HRA ‘Consent and Participant Information Sheet Preparation Guidance’ <http://www.hra-decisiontools.org.uk/consent/style.html> [↑](#footnote-ref-6)