The Health Research Authority

The Health Research Authority (HRA) was established in December 2011 in England to promote and protect the interests of patients and the public in health research. We strive, with partners, to make sure the UK is a great place for health research. Recognising that many members of the public want the opportunity to participate in research, we aim to ensure that health research involving them is ethically reviewed and approved, that they are provided with the information that they need to help them decide whether they wish to take part, and that their opportunity to do so is maximised by simplifying the processes by which high quality research is assessed. In doing this, we will help to build both public confidence and participation in health research, and so improve the nation’s health.

The Health Research Authority welcomes this Nuffield Council on Bioethics’ report; indeed the HRA’s National Research Ethics Advisors’ Panel (NREAP) commented that that it was “one of the best reports produced by the Nuffield Council on Bioethics”. We have disseminated the report to our research ethics committees for information and we will be taking it to our autumn regional Chairs’ Network Meetings for further discussion.

Recommendations

**Recommendation 3:** “We recommend that INVOLVE should collaborate with the National Institute for Health Research’s Research Design Service and relevant experts at the Medicines and Healthcare Products Regulatory Agency to explore how the design and regulatory scrutiny of clinical trials can take more account of the experience of young people who have previously taken part in trials, and of their families.”

HRA Response:

We note that whilst this recommendation is not directed at the HRA it does refer to the “regulatory scrutiny of clinical trials” and how this might take more account of the experience of young people and their families. As a regulator of clinical trials the HRA has a clear interest and role in the scrutiny of trial design and are committed to enabling patients and the public to have a say in decisions about the way health research is planned, designed, delivered, developed, evaluated, managed and regulated. Indeed the HRA has recently collaborated with INVOLVE (funded by NIHR) to produce a joint report examining “Public involvement in research applications to the National Research Ethics Service (NRES): Comparative analysis of 2010 and 2012 data” (published November 2014).

In addition, we have developed a strategy for how the HRA will involve patients and the public in our work and how we will use our influence to increase the amount and quality of public involvement in health research more widely. We have used the feedback to this strategy to develop an action plan to take the strategy forward in 2014 and 2015. The aims of the HRA’s Public Involvement Strategy are to:

1 NREAP Minutes 18/05/2015 [http://www.hra.nhs.uk/?p=199972](http://www.hra.nhs.uk/?p=199972)
• Improve the quality of decision making in the HRA by involving patients and the public in our own work, and
• Improve the quality of research the HRA approves by using its influence to ensure that more health research involves patients and the public

**Recommendation 4:** “We recommend that, whenever research ethics committees consider protocols relating to research with children, they should always ensure that they have timely access to expert advice from the relevant area of children’s and young people’s healthcare. Such expertise may need to be obtained through an external adviser co-opted for the particular decision.”

**HRA Response:**

In the case of clinical trials of investigational medicinal product (CTIMPs) involving children the HRA, in accordance with the Medicines for Human Use (Clinical Trials) Regulations 2004, requires that, where the REC does not have a member with professional expertise in paediatric care, it should “obtain advice on the clinical, ethical and psychosocial problems in the field of paediatric care which may arise in relation to that trial”. In other (non-CTIMP) studies the HRA currently ‘flags’ a number of REC for research involving children whose members include experts in paediatric healthcare and members who have attended training in the review of research involving children.

Currently there are a total of 68 RECs in England (88 UK-wide). Of these:

34 RECs in England (45 UK-wide) are flagged for research involving children
25 RECs in England (31 UK-wide) are flagged for both research involving children and CTIMPs

Submission of applications involving children to a REC flagged for such research is not mandatory but is normally expected. Where a non-flagged REC is allocated an application that would normally be reviewed by a flagged REC, the REC Manager and the Chair will consider whether the REC requires additional expertise to undertake the review, either through co-opting additional members or seeking advice in writing from a flagged REC or other referee.

**Recommendation 5:** “We recommend that the National Research Ethics Service, in cooperation with relevant Royal Colleges and other professional bodies, should establish a database of experts who are willing to act as REC advisors, from across the full range of potential clinical research areas involving children. The National Research Ethics Service might also consider ways in which researchers and research ethics committees might better communicate with each other with respect to any specialist areas of knowledge required to inform assessment of the protocol, for example through specific prompts in the online application form.”

**HRA Response:**

The HRA currently holds details of all REC members and their profession on the HRA Assessment Review Portal (HARP) database. Currently, over 40 REC members have clinical expertise in children’s healthcare and are available for either co-option to a REC reviewing research involving children or may be contacted to provide expert advice. In addition, a significant number of both expert and lay members will themselves be
parents/guardians and will have experience of the treatment of children and research involving children from a personal perspective. Others will have experienced treatment/research directly as children themselves prior to joining a REC. Such experience is difficult to capture and quantify but is undoubtedly present and brings a very important and valued perspective to REC review.

As noted above CTIMPs involving children must be reviewed by a REC whose membership includes a member with professional expertise in paediatric care. Where that expertise is unavailable the REC should always seek expert advice.

The HRA agree that REC review should be guided by appropriate and timely expert advice. We believe that expertise is largely present within the experts and lay members that make up the current REC membership. Where it is identified that appropriate expertise is not available within the REC or REC members more widely, then RECs have the option to seek external expert advice and are strongly encouraged to do so.

However, the HRA recognises that more can be done to ensure that timely access to, and use of, this immensely valuable resource is improved. To that end we will put out a call for REC members to be listed as expert reviewers who are willing to assist in the review of applications related to their specialty. In addition, the HRA Assessment and Review Portal (HARP) has been updated to assist REC staff in searching for members from a specific profession. This makes it much easier to identify members who could provide expert advice. The HRA also intend to update HARP to allow searching by sub-specialty as we recognise that there will be occasions when the paediatric expertise within a flagged committee may not be appropriate for the study being reviewed and more specific expertise will also be required.

Additionally, the HRA are currently piloting the “REC Application Review and Advice” function which involves staff proactively identifying where specialist advice might be required prior to REC review.

Notwithstanding the importance of appropriate expert advice immediately prior to and as part of REC review the HRA believe that involving patients and the public in health research, particularly early in the development of research process, will ensure it is relevant to the needs of patients and more likely to have an impact on their health and wellbeing.

The HRA consider that robust ethical review is facilitated by encouraging dialogue between researchers and research ethics committees (as well as other stakeholder’s including children and their families). This includes dialogue outside of the context of the committee meeting in order to explore and pre-empt ethical issues before they are the subject of formal ethical review. The HRA are currently setting up a workshop with REC members so that a group of researchers can present their proposed research along with guidance, evidence and results of previous discussion groups with other bodies to RECs in order to discuss the ethical issues involved and collate their views and opinions. It is hoped that, if this proves to be successful, that this model can be rolled out to encompass other areas of research particularly where these might be considered contentious or involve novel procedures.

The HRA also holds researcher training days providing important opportunities for researchers and REC members to meet. Furthermore, the HRA has presented at two MRC workshops to advertise the opportunity for researchers to contact RECs in order to request advice and assistance in developing research proposals particularly with regard to discussion of ethical issues.
Recommendation 6: “We further recommend that the National Research Ethics Service should keep under review the experiences of both research ethics committees and researchers with respect to the current system of ‘flagging’ committees as suitable for considering research with children and young people. If the evidence suggests any systematic difficulties with respect to the scrutiny of particularly complex or sensitive studies, the National Research Ethics Service should consider exploring alternative models, such as the creation of a limited number of expert research ethics committees, on the model, for example, of the Social Care Research Ethics Committee.”

HRA Response:

The HRA continually review and audit RECs to ensure that they are compliant with SOPs. In 2007 we established a three year rolling accreditation programme in order to audit UK RECs against agreed standards as detailed in our Standard Operating Procedures (SOPs) and Governance Arrangements for Research Ethics Committees (GAfREC). RECs are issued with an audit decision – full accreditation, accreditation with conditions or provisional accreditation coupled with action plans to ensure that the REC achieves full accreditation. HRA Operational Managers also undertake 6-monthly Quality Control checks on RECs against agreed standards. This includes an annual meeting observation of a REC meeting.

Complementary to this, and in line with the NCoB’s emphasis on “reflexive ethical practice”, the HRA also conducts a ‘Shared Ethical Debate’ (ShED) programme in which a single application is sent to a sub-group of RECs and their reviews analysed. Results and trends of the ShED exercises are shared with the RECs (enabling them to reflect upon their review in comparison to the other RECs), operational teams, the National Research Ethics Advisors’ Panel (NREAP), and the training department in order to identify issues and to develop HRA policies, guidance and training as necessary.

Furthermore, the Health Research Authority (HRA) is committed to routinely seeking feedback from its users to continually monitor and assess its performance, not only to identify strengths but also to recognise where improvements can be made, given the resources available. Feedback is routinely sought from users of HRA and Devolved Administrations Research Ethics Committees (RECs) and the Confidentiality Advisory Group (CAG) via an online survey (SurveyMonkey). This allows us to continually monitor and assess our performance and identify what is working well and areas for improvement. We produce bi-annual user satisfaction public reports of our work, highlighting actions or proposed actions from HRA Management based on feedback received. The latest report is available here.

The HRA are not aware of any evidence, either produced by the QA processes identified above, or from direct communication, that either RECs or researchers consider that there are “systematic difficulties with respect to the scrutiny of particularly complex or sensitive studies”. If the Nuffield Council on Bioethics has evidence, which could be appropriately shared with the HRA, that such difficulties exist we would be very grateful to receive this and review further.
Recommendation 7: "We recommend that the UK Departments of Health, NHS Employers, Universities UK and the Health Research Authority should jointly consider what steps they can take to protect the professional time needed for research ethics committees to work effectively."

HRA Response:

It has been reported informally to the HRA that expert members, especially clinicians, leave RECs before the end of their term of office due to workload pressures and lack of support from Trusts for their attendance at REC meetings. Where we are notified of difficulties with particular organisations the HRA writes to the Chief Executive drawing their attention to a joint letter signed on behalf of the GMC, CMO Scottish Government, CMO UK Government, Welsh Assembly, NHS (England), Department of Health and Social Services (Northern Ireland) which encourages organisations to release non-clinical work (including REC membership). It is important to state that whilst the issue of protecting professional time is important and a concern that the HRA shares, the HRA is not aware that this has impacted upon the quality of REC review generally or the quality of REC review of research involving children more specifically.

The HRA is not an employer of REC members and so is limited in the direct action that it can take to ensure that members are supported by their employers to enable them to contribute to the important work of RECs (which is an integral part of the statutory duty to promote research, and powers to support it, placed on the Secretary of State and on all levels of the NHS including NHS England, and Clinical Commissioning Groups by the Health and Social Care Act 2012).

The HRA will endeavor to support and influence any initiatives taken by UK Departments of Health, NHS Employers, and Universities UK in response to this recommendation.

Recommendation 9: "We recommend that research ethics committees should routinely require researchers to have involved children, young people and parents, as appropriate, in the design of their studies. Researchers who have not sought input in this way should be required to justify to the research ethics committee why this was not appropriate in their case, and be able to demonstrate an appropriate knowledge of relevant literature and guidance."

HRA Response:

As previously noted the HRA are committed to enabling patients and the public to have a say in decisions about the way health research is planned, designed, delivered, developed, evaluated, managed and regulated and have developed a strategy for how the HRA will involve patients and the public in our work and how we will use our influence to increase the amount and quality of public involvement in health research more widely.

Currently, the Integrated Research Application System (IRAS) application form asks applicants (Q.A14-1):

"In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?"

- Design of the research
- Management of the research
- Undertaking the research
- Analysis of results
- Dissemination of findings
- None of the above

Give details of involvement, or if none please justify the absence of involvement."

Thus applicants are routinely required to justify why patient and public involvement has not been sought and RECs will push back where such involvement may have usefully been sought.

However the HRA consider that to “require researchers to have involved children, young people and parents, as appropriate, in the design of their studies” in all cases would neither be appropriate nor proportionate. Such insistence would logically necessitate an unfavourable opinion to be given in all cases where such involvement had not been sought.

There will always be instances of research where the involvement of patients/public in the design would neither be practicable nor promote better research.

The involvement of patients and public in the design of research is always to be applauded where this is undertaken but it is not without associated cost. Some researchers, e.g. those conducting small scale Masters-level projects, will not always have the time or resources to do this. The HRA support and champion the involvement of patients and the public in the design of studies but recognise that the appropriateness of such involvement will always need to be considered on a case by case taking into account (amongst other factors) the complexity, intrusiveness and burden of the research upon the participants. Thus, a case for involvement to be a requirement is most likely to be justified in the context of CTIMPS involving children, but will always need to be considered within the context of the specific trial.

**Recommendation 13:** “We recommend that, where children and young people have sufficient maturity and understanding, but are not yet treated as fully ‘adult’ by the law of their country, professionals should, wherever possible, seek consent from both the children or young people concerned, and from their parents.”

**HRA Response:**

The HRA support the position taken by the NCoB that, where possible and appropriate, a shared approach to consent should be encouraged where the child has sufficient maturity and understanding but is not yet treated as fully ‘adult’ by the law of their country. However, in doing so we understand that the term “consent” is being used in this recommendation as an *ethical* rather than *legal* term.

The report very clearly and helpfully sets out the current legal position regarding the validity, or otherwise, of “consent” to research participation given by children under 16 years of age and the added complexity that parents in England and Wales retain the power to give consent to treatment on behalf of their children until the latter reach the age of 18.

The HRA understand both the complexity and uncertainty of the legal landscape in this area and expects RECs to take this into account particularly where the potential participants are children under the age of 16. In the majority of cases it will be unproblematic and good...
practice for both the child and their parent(s) or legal guardian(s) be involved in the decision making process so as to reach a joint decision regarding the child’s participation (even if documentation of the parental consent will be that relied upon to satisfy the law).

However, as the report acknowledges, there will be research involving participants under the age of 16 where, due to the nature of the research, parental involvement may not be appropriate. In such cases, whilst recognising that the legal position with regards “Gillick” consent is still untested in this area, the HRA fully supports any REC who, following a thorough consideration of the risks, benefits and scientific and public value of the research, reaches an opinion that seeking the ‘consent’ of a child under 16 to take part, without further parental consent, would be ethically appropriate.

**Recommendation 14** “We recommend that requirements in guidance and regulation to 'seek’ or 'obtain’ assent from children who are being invited to take part in research should be understood as requirements to involve children, as much as they wish and are able, in the decision about participation. In devising assent processes, researchers should primarily be concerned with how best to develop trusting relationships with children and communicate information appropriately throughout the research”

**HRA Response:**

The HRA support this recommendation which is reflected in HRA guidance:

“Children’s/young person’s wishes and assent

Even when a child or young person is deemed not competent to make a decision for themselves and in situations where legally they are not empowered to do so (e.g. in a clinical trial of an investigational medicinal product (CTIMP)), it is important that:

- You should give the child/young person information about your study, which is understandable to them and which explains what is involved and the potential risks and benefits.
- Staff with experience of working with children / young people should provide this information.
- You must consider the explicit wishes expressed by any child or young person who is capable of assessing the information and forming an opinion. This includes their refusal to take part, or to withdraw from the trial.

Whenever practical and appropriate, a child's assent should be sought before including them in your research.

When is it appropriate to seek assent from a child? You have to make an informed judgment to determine when seeking assent is appropriate; the age of a child can only be taken as a guide.

Consider also the child's developmental stage, knowledge of illness and experience of health care.

How are decisions usually made in the family? How much autonomy does the child normally exercise? From observation does the child wish to be involved in the discussions?
What are the parents' views and can they help with this decision? They know the child best.
Although there is a danger that children can be asked to exercise greater autonomy than normal, this must be balanced with the potential loss of trust associated with denying their assent.

Such judgment needs a framework of considerations for analysis, a record of observations and discussions and a documented decision.

In circumstances where seeking assent at the outset is not appropriate, you could provide the child with information as and when required (i.e. ‘drip feeding’).\(^2\)

**Recommendation 16:** “We recommend that, where a protocol indicates that children and young people may be recruited by a health professional responsible for their care, research ethics committees should explore with researchers the justification for this approach. Where such recruitment procedures are appropriate, research ethics committees may wish to assure themselves that there are support arrangements in place, such as access to another member of the research team to whom families can turn for additional information if they wish.”

**HRA Response:**

The HRA support this recommendation and note that RECs are required to consider the appropriateness of the proposed recruitment procedures, the individuals involved and any possible conflicts of interest. However, the HRA acknowledges that there is a tension between the need to be provided with accurate information and have a discussion with a knowledgeable and trusted individual (who may often be the care provider) and the need for that information and discussion to be independent and non-partisan. In many cases there will be a staged approach to recruitment and consent with the possibility of research participation being raised by the healthcare professional responsible for the patient’s care followed by further discussion with other members of the research team e.g. research nurses.

The HRA has recently undertaken a large scale public engagement exercise focusing on dialogue between members of the public and health researchers around ways of identifying people to take part in health research\(^3\). Whilst participants widely agreed that NHS employees should approach patients, and they should be identifiable by a uniform or badge there was a lack of consensus amongst the public over who should seek consent. Some participants favoured doctors while others felt research nurses would be acceptable as they would be able to talk knowledgeably about the research process. Many participants believed they would feel uncomfortable being approached by someone they did not know. It was important that the person approaching a patient was someone they could trust either because of their manner, the training they had received, their knowledge of the trial or their role within the hospital.

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