Forthcoming practical framework for ethics committees and researchers on post-trial access to the trial intervention and healthcare

Neema Sofaer, Penney Lewis, Hugh Davies

When research concludes, post-trial access (PTA) to the trial intervention or standard healthcare can be crucial for participants who are ill such as those in resource-poor countries with inadequate healthcare, British participants testing ‘last-chance drugs’ unavailable on the National Health Service (NHS) and underinsured US participants. Yet, many researchers are unclear about their obligations regarding the post-trial period, and many research ethics committees (RECs) do not know what to require of researchers. Consequences include participants who reasonably expect but lack PTA to the trial intervention, unplanned financial liabilities for NHS Trusts forced to fund this, negative press and potential to undermine public trust.1-3

One reason for the lack of clarity is controversy over whether and when participants should have access, after the study, to the study intervention. At one extreme is the view that continued access need never be provided so long as non-availability of the study intervention post-trial was adequately disclosed when participants were invited to participate.4 There is also disagreement about when poststudy access to the study intervention should be considered beneficial for participants. The spectrum ranges from the view that the intervention should be regarded as beneficial for a proposed use only after the intervention has received regulatory approval, to views employing a lower standard of evidence.5 Another reason for lack of clarity may be the absence of practical guidance. Certainly, there are many international and national legislation and guidance documents on PTA to trial drugs, healthcare and information, but these are inconsistent, ambiguous or silent about many crucial details.6,7 Many reports with content on PTA that is relevant to research conducted in the UK are unlikely to be read by British RECs due to international focus and length.8 British regulations,9 which are weaker than international guidelines, merely require each application to a REC to include ‘details of the plan for treatment or care of subjects once their participation in the trial has ended’ or ‘an explanation of why that information is not being provided’; they prepare RECs neither to pre-empt issues about PTA to the study intervention nor to ensure adequate disclosures to participants of what PTA they will or will not have to the study intervention.

The discussion on PTA has focused mostly on research conducted outside resource-rich countries with universal healthcare. However, these issues arise worldwide, including in the UK,1,2,12 whenever participants want continued access to a study intervention that is unaffordable or otherwise unavailable. They are most pressing when participants are seriously ill and the study intervention has a better clinical profile than the standard treatment or is the only (remaining) option.

The UK Health Research Authority’s forthcoming document Care after research: A framework for NHS RECs13 (see online supplementary appendix 1) seeks to address RECs’ and researchers’ need for practical guidance in the face of various incompatible, yet often individually reasonable views. It prompts RECs to address specific questions about researchers’ plans for the post-trial period; ensure there are plans for transitioning sick participants to healthcare; examine any plans to ensure PTA to the study intervention; and verify that documents for participants explain what will (or will not) happen post-trial, and identify any uncertainty. It allows RECs to decide when PTA to the trial intervention may be feasible or appropriate but, to inform their deliberations, summarises important legal, ethical and practical issues, and key legislation and guidance.

Care after research results from a collaboration between two King’s College London academics and the Research Ethics Advisor of the Health Research Authority. With funding also from the Wellcome Trust and Brocher Foundation, these authors developed it iteratively via a 3-year international consultation that engaged major pharmaceutical companies, patient advocacy groups, the British Medical Association, Nuffield Council on Bioethics, National Research Ethics Advisors’ Panel, European Forum on GCP, Uganda National Council for Science and Technology, World Health Organisation, the Editor of the Indian Journal of Medical Ethics, a member and international panellist of the US Presidential Commission for the Study of Bioethical Issues, REC members and Chairs, members of the NIH’s Clinical Center Department of Bioethics, two heads of the NIH’s Fogarty International Center programmes in Bioethics, as well as prominent research ethicists. Care after research applies to the 79 British RECs,14 and so, indirectly, to the researchers who apply to them for permission to conduct research. Four consultation sessions that piggy-backed on large-scale training events for UK RECs should drive domestic adoption. It is too early to assess its impact on RECs.

There is a dearth of information on types, rates and mechanisms of care after research in the UK. However, limited UK information suggests that some REC-approved documents for recruiting participants lack appropriate plans, some participants expect but lack PTA to the study intervention, and some NHS Trusts have been forced to fund post-trial access to the study intervention (sources include examples of anonymised protocol and informed consent extracts from applications submitted to a North London REC and verbal reports made by many REC members and chairs involved in the consultation process). Wide variations in rates of reporting plans for post-trial access to the study intervention have been reported in informed consent forms and protocols for US-sponsored antiretroviral trials.4,5

Correspondence to Dr Neema Sofaer, Kings College London, Centre of Medical Law and Ethics, The Dickson Poon School of Law, London, UK

Received 25 June 2013; accepted 10 July 2013.15

1 Kings College London, Centre of Medical Law and Ethics, The Dickson Poon School of Law, London, UK

2 Correspondence to Dr Neema Sofaer, Kings College London, Centre of Medical Law and Ethics, The Dickson Poon School of Law, Strand, London WC2R 2LS, UK; neema.sofaer@kcl.ac.uk, neemaal@alum.mit.edu

3 These together reviewed 5560 applications between 1 April 2011 and 31 March 2012. Source: personal communication between NS and Health Research Authority staff.
researchers, and participants: Care after research came into force only in December 2012. However, participants should benefit at least from clearer and more complete information on care after research, and NHS Trusts and research sponsors should have fewer unplanned financial liabilities. The international consultation, intended to raise awareness of the consultation’s product, revealed support for the document’s practical approach and belief in its adaptability outside the UK. It will be important not only to foster and monitor domestic impact, but also to encourage international adaptations.

Acknowledgements We would like to thank Alex John London, Angus Dawson, Ruth Macklin and Ignacio Mastrolocco for their insightful comments on this editorial.

Funding A Wellcome Trust grant (088360) to NS funded (1) drafting Care after research and executing the consultation process; (2) the sixth consultation session; (3) a systematic review (written with Daniel Strench) and ethics research that informed various sections of the framework document; and (4) writing this Editorial. A Brocher Foundation grant to NS and PL funded the seventh consultation session. Two grants from Centre of European Law, King’s College London to NS for research assistance informed the briefing in the framework document on guidelines, legislation and position statements. Part of this work was undertaken by NS as a Caroline Miles Visiting Scholar at the Ethox Centre, University of Oxford. HD was Research Ethics Advisor to the National Research Ethics Service during the development of Care after research and the writing of this Editorial.

Contributors NS wrote and revised the drafts of this paper. PL and HD commented on the paper. All authors approved the final version.

Competing interests None.

Provenance and peer review Not commissioned; internally peer reviewed.

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and licence their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/3.0/

To cite Sofaer N, Lewis P, Davies H. J Med Ethics 2013;00:1–2. doi:10.1136/medethics-2013-101398

REFERENCES
6 Sofaer N, Strench D. Reasons why post-trial access to trial drugs should, or need not be ensured to research participants: a systematic review. Public Health Ethics 2011;4:160–84.
Forthcoming practical framework for ethics committees and researchers on post-trial access to the trial intervention and healthcare
Neema Sofaer, Penney Lewis and Hugh Davies

J Med Ethics  published online May 5, 2013

Updated information and services can be found at:
http://jme.bmj.com/content/early/2013/05/04/medethics-2013-101398

These include:

Supplementary Material
Supplementary material can be found at:
http://jme.bmj.com/content/suppl/2013/05/05/medethics-2013-101398.DC1

References
This article cites 3 articles, 1 of which you can access for free at:
http://jme.bmj.com/content/early/2013/05/04/medethics-2013-101398#BIBL

Open Access
This is an open-access article distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license. See: http://creativecommons.org/licenses/by-nc/3.0/ and http://creativecommons.org/licenses/by-nc/3.0/legalcode

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
Open access (108)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/