NHS
Health Research Authority

CARE AFTER RESEARCH:
A FRAMEWORK FOR NHS RECs

Care after research is for participants after they have finished the study. Often it is NHS-provided healthcare for the medical condition that the study addresses. Sometimes it includes the study intervention, whether funded and supplied by the study sponsor, NHS or other party. The NHS has the primary responsibility for care after research. However, researchers are responsible at least for explaining and justifying what will happen to participants once they have finished. RECs are responsible for considering the arrangements.

There are ethical and practical issues, in particular when participants may wish to continue on the study intervention after the study. There are also various guidelines and legislation. This document presents a framework of questions to help NHS RECs and their applicants. Information on this document's development is here.

Question	Comments
1a. What care after research is relevant to this study?	Most protocols should describe arrangements for care after research. Such arrangements are part of responsible transition at the end of a study.
1b. Does the REC need to consider continued access to the study intervention?	This question is irrelevant when there is no study intervention. The REC needs to consider continued access, at a minimum, when: • It is reasonable to expect that it will be possible to give the study intervention safely after the study; • It is reasonable to expect a clinically important benefit; • The intervention is not available through the NHS locally; and • Treatment options are limited. Further information about when to consider continued access is here. Ethical and practical issues about continued access to the study intervention are here.
2. Information for potential participants	A Participant Information Sheet should explain, in appropriate language, what care after research will be available. In particular, when participants may wish to continue the study intervention after the study, these documents should say whether this will, will not, or may be available. Also, when the study intervention will or may be provided: • Which participants will or may be offered it; • Any waiting time between the end of participation and (possible) start of the study intervention; • Any uncertainty; and • When any remaining decisions are likely to be made. The REC should check this information will not mislead participants about the safety or benefits of the study intervention.

If there are plans, even if provisional, for some participants to continue taking the study intervention after the study:

Question	Comments
3. Which participants?	The group of participants must be identified.
4. In what circumstances?	The conditions for access must be outlined and justified. In particular, when access depends on whether the study succeeds (or benefits the participant or group), the protocol should state the success (or benefit) conditions.
5. How will the study intervention be provided?	RECs should be aware that there are limits on the information that can be provided when research has yet to commence. However, information should be provided to the extent possible. Note: • Different outline plans may be needed for different contingencies; • Control-arm participants who transition to the study intervention must be appropriately monitored; • If researchers rely on other parties to provide or fund the study intervention, for example healthcare purchasers, the sponsor, or the participant's doctor, the REC must receive suitable assurances that such parties are willing to act accordingly, or would be willing should continued access to the study intervention turn out to be appropriate; and • When the study intervention will be unlicensed after the end of the study, information must be provided on the provisions should participants be harmed.

If the REC determines from Question 1b that it needs to consider continued access to the study intervention, but there is no plan for such access:

Question	Comments
6. Why is there no plan?	Reasons should be given for not planning continued access. Acceptable reasons may include serious logistical obstacles e.g. with ensuring appropriate monitoring, making predictions and advance commitments, timing, supply limitations and maintaining a blind. There may also be insurmountable legal barriers.

Study intervention

Interventions here include drugs or devices, whether licensed or unlicensed, and also care delivery pathways, complementary therapies, physiotherapies, dietary manipulations and lifestyle changes. Interventions may include services as well as products.

We avoid the common phrase *post-trial access to the study intervention*, because some people understand *post-trial access* to mean only *sponsor-funded* supply of the study intervention after the study. However, care after research is broader than this: it also includes the study intervention when supplied or funded otherwise as well as standard healthcare that the participant may need after the study.

Most protocols

Aftercare should be addressed whenever participants will still need treatment or preventive measures after the study. Aftercare plans are particularly important when the study intervention is not available through the NHS locally, treatment options are limited, or the condition addressed is serious.

Arrangements for care after research

The nature of care after research depends on many factors, including whether the study intervention is available locally on the NHS. In the UK, arranging aftercare will usually mean referring participants to the NHS, where they will continue taking the study intervention (when available), start a different intervention or return to their pre-study intervention. Sometimes study staff will refer participants to another study. In fewer cases, which raise the hardest issues, the sponsor supplies the study intervention, usually when the intervention is unlicensed. The intervention may be supplied in various settings, and may or may not be sponsor-funded.

Responsible transition

The responsible transitioning of participants out of the study includes:

- Making arrangements for aftercare;
- Ensuring safety;
- Communicating with caregivers;
- Sharing information with participants: aggregate results and, as appropriate, individual results and incidental findings;
- Showing appreciation; and
- Resolving any deception.[1]

When the REC needs to consider continued access to the study intervention

The REC need not consider access to the study intervention when reviewing early studies designed primarily to address safety, pharmacokinetics, interaction potential with other drugs, or effects on biomarkers other than clinical efficacy. However, RECs should be aware that access to the study intervention after the study may become an issue in a small number of other phase I and II studies; in particular, when participants are seriously ill but have limited treatment options.

When participants may wish to continue the study intervention after the study

The potential for conflict and disappointment arises whenever participants believe that they would be better off continuing to take the study intervention after the end of the study, whether their belief is justified or not. It is thus often crucial to address the issue of continued access to the study intervention in the Participant Information Sheet.

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[1] The “Responsible transition” section is closely based on a slide presented by Dr Christine Grady on December 15 2011 at a two-day workshop at the Brocher Foundation on post-trial access to trial drugs (www.ptaworkshop.wordpress.com).

Which participants?

For example:

- all participants;
- participants who completed the study; or
- active-arm participants.

Unclear or difficult notions (for example benefit, active-arm participant) should be explained.

RECs should be aware that there are limits on the information that can be provided when research has yet to commence. However, information should be provided to the extent possible.

Any uncertainty

For example:

- Whether there will be a sufficient supply of the study intervention;
- Whether there will be sufficient safety data;
- Whether there will be sufficient efficacy data;
- Whether additional safety issues may be detected post-study, leading to withdrawal of the study intervention; and
- For how long the study intervention will remain available.

A global issue

The issue of post-study supply of the study treatment arose in the context of research sponsored from resource-rich countries and conducted in resource-poor countries. In that context, lack of plans for post-study supply can mean that ex-participants have no aftercare. Worldwide, post-study supply of the study treatment is an issue whenever participants want continued access and the study treatment is expensive and/or unlicensed; in particular, when participants are seriously ill and the study treatment is the only (remaining) option.

An additional issue in the UK is who should pay for continued access to the study treatment when it is licensed but unavailable on the NHS in the participant's area; the answer may depend on whether NICE has issued its recommendation and what it has recommended.

Ethical and practical issues regarding continued access to the study intervention

There is a strong moral obligation to ensure that participants transition after the study to appropriate care. However, controversy continues over whether and when participants in a successful study should have access, after the study, to the study intervention, particularly when the intervention is superior to standard treatment. At one end of the spectrum is the view that it is necessary to ensure continued access to the study intervention when it has turned out to benefit the individual participant or has proven safe and effective for the participant population, irrespective of cost and burden. At the other end is the view that continued access to the study intervention need never be provided so long as this was adequately disclosed when participants were recruited.

There is also disagreement about when the study intervention is beneficial. The spectrum ranges from the view that the intervention is beneficial for a proposed use only if regulators accept that this is the case, to views that employ a much lower standard of proof. It is difficult to justify the view that a participant's mere perception of benefit entitles the participant to continued access to the study intervention.

This section summarises some ethical reasons commonly given on either side. Whether the reasons are relevant and what they show depends on the particular case. Some reasons depend on factual assumptions for which there is little evidence and/or on questionable moral assumptions.

Reasons given why aftercare should not be required or need not be provided have included:

Assessing benefit and safety

- Many studies do not show the efficacy of the intervention, even when their results are combined with other findings, or offer definitive proof that their intervention is the "best".
- Even when the study succeeds, further research may be needed to show that the intervention is safe and effective in a healthcare context and to identify guidelines for use.
- An individual participant may experience benefit from an intervention even when the study provides no evidence of benefit for the participant population. Often, there will be no solid evidence that the individual in fact benefited and so would benefit from continued access to the study intervention. Views on what counts as sufficient evidence differ.
- Conflict can arise when a participant (rightly or wrongly) perceives benefit and requests continued access to the study intervention, but the intervention is not shown to work in the entire participant group.

Making predictions and advance commitments

- Before a study of an unlicensed intervention, it is often very difficult to say whether it will be possible or desirable for participants to continue after the study ends.
- Funders may be unwilling to commit to pay for an intervention that has not yet been shown to be safe, effective and better than alternatives.

Timing

- Even when the study leads to an intervention that becomes available on the NHS, much time may pass after an individual has finished participating before the intervention becomes licensed; and between licensing, NICE approval and NHS availability.

Supply limitations

- Continued access to the study intervention may be financially or logistically very difficult, particularly for small companies, when the only batch of the study intervention runs out.

Legality

- There may be legal barriers to continued access to the study intervention, particularly when the study intervention is not licensed. However, the fact that a intervention is not licensed for the relevant use is not necessarily a barrier to access: doctors sometimes prescribe licensed interventions to address conditions for which these interventions are not licensed.[2]

Monitoring participants post-study

- Participants who continue on the study intervention must be appropriately monitored, in particular placebo-arm participants who start taking the study intervention after the study. The possibility of transitioning placebo-arm participants to the active treatment within the study should be considered. Reasons not to give continued access to the study intervention to placebo-arm participants include genuine inability to provide or arrange for adequate monitoring.

[2] Such off-label use should not be encouraged.

Maintaining a blind

- In a double-blinded study, neither the participant nor the investigators know if the participant is taking the study intervention or a control. When a participant completes the study before the end of data collection, arrangements for providing the study intervention will usually require finding out if the participant took the intervention or a placebo. A correct data-handling protocol should be used to prevent jeopardizing the study data.

Researchers' role (narrow view)

- Researchers' primary obligation is to generate scientific knowledge, although in its pursuit they must protect participants and not exploit them.

Incentives for conducting research

- Requiring sponsors and/or researchers to fund or provide aftercare will weaken incentives to conduct research.

However:

- The cost of facilitating aftercare through referral may be low, and so requiring facilitation may have little or no effect on incentives.

Inappropriate or inefficient use of resources

- When sponsors of research provide continued access to the study intervention, this comprises an inappropriate use of resources (because sponsors should aim to develop new interventions) or inefficient use (because health care providers supply care more efficiently).

However:

- Sponsors might nonetheless be morally obliged to provide it.
- Sponsors may be efficient at providing the study intervention to small groups.

Compromising judgment

Promises of aftercare at recruitment may:

- Foster false beliefs about the benefits of taking the study intervention (therapeutic misconception).
- Compromise a person's ability to judge whether or not participation is in their best interests (undue inducement).
    - Even if so, bad judgement will not often endanger the person, because the REC carefully examines a study's risk-benefit profile before approving the study.

Ethical reasons given why the study intervention should be given or required have included:

Health need (when former participants need access to the study intervention to sustain health benefits from the study)

- Participants' health status after the study must not be worse than it was during the study.

However:

- Obviously, this reason does not apply when there are comparable standard interventions.
- It is unclear whether participants have a greater claim on the study intervention than other needy people who did not participate.
- It is unclear if the relevant comparison is with participants' health during the study or before the study, or with their health had they not participated.

Avoiding psychological harm

- Former participants may feel distressed and abandoned if they cannot continue on the study intervention. This is likelier in long studies, and when the individual did not fully understand, at recruitment, that there would not be aftercare or the implications of lacking it. Harm may occur *even*

if the individual participated knowing that there would be no continued access to the study intervention.

However:

- It is unclear that the need to avoid psychological harm requires provision of the study intervention when all reasonable measures have been taken to ensure that potential participants understand and remember that they will not be able to continue taking the study intervention after the study.

The above two reasons – health need and psychological harm – are most likely to support continued access to the study intervention when it is licensed or close to licensing, and when alternative interventions are inferior or unavailable.

Exploitation

- Research participants should not be exploited. Some have claimed participants are exploited when they are used in a study with little or no chance that the successful intervention will subsequently be made available to them.

Recognition and reward of participants' contribution

- Participants' assumption of the burdens and sometimes risks of participation enables improvements in health care and health, and so should be recognised and rewarded**.**

Reciprocity

- Participants deserve to receive benefits in return for their contribution.

However, some think that participants unable to continue on the study intervention are not exploited if they receive fair benefits and that study staff can recognise and reward contribution, and reciprocate, without ensuring continued access to the study intervention. Others maintain that no further benefits are required in addition to any promised to participants.

Researchers' role (broad view)

- Researchers are obliged to look after the health of those who participate in the research.

Maintaining public trust

- The public may lose trust and refuse to participate in research if former participants are perceived to suffer due to lack of access to the study intervention after the study.

Incentives

- Offering continued access the study intervention to the study intervention, even if conditional on for example the success of the study, may be necessary to recruit sufficient participants. Whether this is necessary will vary from study to study.

Promises

- Participants were promised continued access to the study intervention, if the intervention turned out to be beneficial, during recruitment.
    - Obviously, this reason applies only when such a promise was made.

Guidelines, legislation and position statements from other bodies

Declaration of Helsinki

The Declaration is published by the World Medical Association. The 1996 version, the one recognised by UK, does not mention continued access to the study intervention. The current, 2008 version stipulates that:

> "At the conclusion of the study, patients entered into the study are entitled…to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits."
> (World Medical Association 2008), Article 33

Regarding “Medical research involving a disadvantaged or vulnerable population or community”, the Declaration states that

> “[this] is only justified…if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.” (Article 17)

Report by the US National Bioethics Advisory Committee (NBAC)

Though this committee no longer exists, the report continues to be influential (National Bioethics Advisory Commission 2001). Recommendation 4.1, regarding former participants, is:

> Researchers and sponsors in clinical trials should make reasonable, good faith efforts before the initiation of a trial to secure, at its conclusion, continued access for all participants to needed experimental interventions that have been proven to be effective for the participants. Although the details of the arrangements will depend on a number of factors (including but not limited to the results of the trial) research protocols should typically describe the duration, extent and financing of such continued access. When no arrangements have been negotiated, the researcher should justify to the ethics committee why this is the case.

Recommendation 4.3 regarding the country that hosts research is:

> Wherever possible preceding the start of research, agreements should be negotiated by the relevant parties to make the effective intervention or other research benefits available to the host country after the trial is completed.

NBAC allows RECs in some cases to approve research whose investigators do not believe that the host country will receive the benefit of approved interventions:

> In cases in which investigators do not believe that successful interventions will become available to the host country population, they should explain to the relevant ethics review committee why the research is nonetheless responsive to the health needs of the country. *(Recommendation 4.2)*

The Report requires pre-trial discussion of continued access to the trial drug except in some circumstances, and requires the consent form to describe availability of the study intervention post-study or lack thereof. NBAC mentions the issues of who or what should provide or fund the continued access to the study intervention (when there is continued access to the study intervention) and how long it should last, but does not take a stance.

The UK Nuffield Council on Bioethics’ report

The Nuffield Council on Bioethics endorses NBAC’s recommendation regarding continued access to the study intervention for participants (Nuffield Council on Bioethics 2002):

> We…endorse the US National Bioethics Advisory Commission (NBAC) recommendation that researchers should endeavour before the initiation of a trial to secure post-trial access for effective interventions for participants in the trial and that the lack of such arrangements should have to be justified to a research ethics committee. *(Paragraph 9.31)*

The Council requires both pre-trial discussion of continued access to the study intervention and the description in the consent form of continued access to the study intervention arrangements or lack thereof.

CIOMS’ guidelines

The Council for International Organizations of Medical Sciences (CIOMS) is “an international, non-governmental, non-profit organization established jointly by WHO and UNESCO in 1949” based in Geneva.[3] It has published influential guidelines on research ethics (CIOMS 2002).

CIOMS strongly encourages continued access to the study intervention in some cases and identifies the agent responsible. For example, it requires the “sponsor” to provide “an investigational drug [that] has been

[3] http://www.cioms.ch/Jan2009cioms_web_what_is_cioms.pdf (accessed 28 August 2009)

shown to be beneficial" to former participants until it has been approved "by a drug regulatory authority" (Commentary on Guideline 10). It also requires, though with some exceptions, continued access to a successful study intervention for former participants.

Regarding the host population, Guideline 10 specifies that

> Before undertaking research in a population or community with limited resources, the sponsor and the investigator must make every effort to ensure that:
>
> > …any intervention or product developed, or knowledge generated, will be made reasonably available for the benefit of that population or community.

Concerning the timing of continued access to the study intervention, the commentary on guideline 10 adds that

> The sponsor is unlikely to be in a position to make a beneficial investigational intervention generally available to the community or population until sometime after the conclusion of the trial…

Guideline 21 also states that external sponsors should ensure the availability of

> health care services that are a necessary part of the commitment of a sponsor to make a beneficial intervention or product developed as a result of the research reasonably available to the population or community concerned.

While these requirements are stronger than any of those presented above, there are inherent contradictions. The commentary on Guideline 10 also states, regarding continued access to the study intervention for the host community:

> The issue of "reasonable availability" is complex and will need to be determined on a case-by-case basis. Relevant considerations include the length of time for which the intervention or product developed, or other agreed benefit, will be made available to research subjects, or to the community or population concerned; the severity of a subject's medical condition; the effect of withdrawing the trial drug (e.g., death of a subject); the cost to the subject or health service; and the question of undue inducement if an intervention is provided free of charge.

This suggests that, like NBAC and the Nuffield Council on Bioethics, CIOMS permits some research that will not provide continued access to the study intervention to host countries.

Like the Nuffield Council, CIOMS requires both pre-trial discussion of continued access to the study intervention and the description in the consent form of arrangements for continued access to the study intervention or lack thereof.

International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)

The IFPMA has no guidance on continued access to the study intervention.

Medicines for Human Use (Clinical Trials) Regulations, UK (2004)

Regarding continued access to the study intervention, the Regulations mention only that applications for an ethical opinion must provide details of "The plan for treatment or care of subjects once their participation in the trial has ended" (Schedule 3, Part 1, 1, (m) (iii)).

Statement on the responsibility for ongoing funding of experimental treatments for patients who have participated in commercially funded research, 2007

Issued jointly by the UK's Faculty of Public Health and the Association of Directors of Public Health, this statement takes the 2004 Regulations summarised just above to imply that "if ongoing commercial funding [for an experimental treatment beyond the end of the trial] has not been agreed then either: subjects must have consented to participation in the knowledge that their trial treatment will not be funded beyond the end of the trial, or local agreement should be reached that any ongoing treatment costs will be picked up by the NHS."

Association of the British Pharmaceutical Industry (ABPI)

The ABPI's position is found in the minutes of the Access Strategy Group (ASG), which convened at the ABPI in July 2006. The position is that all companies and ethics committees should ensure that an exit strategy is clearly defined at the beginning of a trial and communicated to patients before they sign the consent form. The ABPI considers that the nature of the exit strategy should be left to individual companies.

The National Research Ethics Service guidelines on information sheets and consent forms (NRES staff 2009)

The guidelines include the following:

> "The arrangements after a therapeutic trial must be given, particularly if this differs from that normally expected for their medical condition. It must be clear whether the participant will have continued access to any benefits or intervention they may have obtained during the research. If the treatment will not be available after the research finishes, this should be explained to the participant with information on what treatment will be available instead.
>
> You should consider whether and when it may be possible to tell participants which arm of the study they were in.
>
> The researcher and reviewer should agree one of 5 options
>
> - No therapy available after the trial.
> - Therapy available to all those in the trial already taking it.
> - Therapy available to all participants.
> - Therapy available to patients on a named patient basis with SAE reports. [A SAE report is a report of a Serious Adverse Event.]
> - Drug available on an open label basis for a cohort observational study."

Development of this document

This document has been developed from a document on information sheets and consent forms written by the NRES Research Ethics Advisor (NRES staff 2009). It has been informed by a letter issued by the NRES Director to REC Chairs[4] and the legislation, guidance and statements summarised above, and a broad variety of literature in philosophy, ethics and law. To keep the document readable, we decided not to cite individual authors but instead to cite works that would be useful as further reading.

Successive drafts were reviewed by three different groups of REC members and Chairs at NRES meetings in 2009 and 2010. The resulting draft was reviewed, at a fourth consultation session, by the National Research Ethics Advisors' Panel, in October 2010. At each of these meetings, delegates were informed of practical and ethical issues regarding continued access to the study intervention, and of key guidance, before the draft was presented to them. The fifth consultation, in November 2010, was with a large group of REC Chairs from all over the UK, who had received the draft document and reading questions beforehand. An informal transcript was made of each session and minutes written. The draft reviewed at the session was revised in the light of delegates' comments and extensive discussion within the author team.

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[4] Re. Continued treatment for research participants at the end of a trial. Letter sent 13 March 2008 from Janet Wisely to REC Chairs. Available at http://www.nres.nhs.uk/applications/guidance/clinical-trials/?entryid62=66929, which is on the guidance page of NRES's website: http://www.nres.nhs.uk/applications/guidance/clinical-trials/ [both links were last accessed 14 August 2012]. Wisely's letter gives guidance that remains relevant on the topic of procedural issues, such as the need to make a "notification of a substantial amendment to the REC" when the "plan [for post-trial treatment] contained in the application to the ethics committee" differs from that in the "clinical trial agreement" (point 6).

The sixth consultation session convened various stake-holders in research, including representatives of pharmaceutical companies, patient advocacy groups, the European Forum for GCP, the British Medical Association and the Nuffield Council on Bioethics, and academics in medical law or ethics. This session was held at the King's College London Centre of Medical Law and Ethics in January 2011. A recording and transcript were made of the session. Written comments were solicited from delegates, including from an additional patient and participant representative who did not attend the session. Many written comments were submitted and one organisation, the Association of the British Pharmaceutical Industry, submitted a document to aid discussion of the issues. A summary of verbal and written comments was produced, with comments on the same question or section grouped together, and then used to revise the draft. After this session, we decided to change the key term in the document from *post-study access to trial interventions* to *care after research*, because delegates at the session understood *post-study access to trial interventions* differently; furthermore, we thought that the document should also cover access, after the study, to standard interventions that address the study condition, and to health care more generally. The resulting draft was reviewed at a seventh consultation session, in December 2011, by a panel of international experts on continuing care at the Brocher Foundation in Geneva. It was then modified in the light of pre-, in- and post-session comments.

Relevant works

The literature on continued access to study interventions focuses on research conducted from resource-rich countries in resource-poor countries; however, various issues it discusses are relevant to the UK context. For the most comprehensive review of the reasons why continued access to the trial drug should, or need not be ensured, see (Sofaer and Strech 2011). For more readable presentations and critiques of a range of reasons, see (Macklin 2004; Grady 2005; Lavery 2008). For critical analysis of individual reasons, see (Merritt and Grady 2006; Ezekiel J. Emanuel and the participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries 2008; Hawkins and Emanuel 2008).

CIOMS (2002). International Ethical Guidelines for Biomedical Research Involving Human Subjects. http://www.cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm [last accessed 1 December 2011]. Geneva, Council for International Organizations of Medical Sciences.

Ezekiel J. Emanuel and the participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries (2008). Addressing exploitation: Reasonable availability versus fair benefits. Exploitation and Developing Countries: The Ethics of Clinical Research. J.S. Hawkins and E.J. Emanuel. Princeton & Oxford, Princeton University Press**:** 286-313.

Grady, C. (2005). "The challenge of assuring continued post-trial access to beneficial treatment." Yale Journal of Health Policy, Law, and Ethics **5**(1): 425-435.

Hawkins, J. S. and E. J. Emanuel, Eds. (2008). Exploitation and Developing Countries: The Ethics of Clinical Research. Princeton and Oxford, Princeton University Press.

Lavery, J. V. (2008). The obligation to ensure access to beneficial treatments for research participants at the conclusion of clinical trials. The Oxford Textbook of Clinical Research Ethics. E. J. Emanuel, C. Grady, R. A. Crouchet al. New York, Oxford University Press**:** 697-710.

Macklin, R. (2004). Double Standards in Medical Research in Developing Countries. Cambridge, UK, Cambridge University Press.

Merritt, M. and C. Grady (2006). "Reciprocity and post-trial access for participants in antiretroviral therapy trials." AIDS **20**(14): 1791-1794.

National Bioethics Advisory Commission (2001). Ethical and policy issues in international research: Clinical trials in developing countries. Bethesda, MD, National Bioethics Advisory Commission. **I and II**.

NRES staff (2009). "Information Sheets & Consent Forms. Guidance for Researchers and Reviewers. Version 3.2."

NRES staff (2009). Information Sheets & Consent Forms. Guidance for Researchers and Reviewers. Version 3.5. May 2009. Page 167 of 195.

Nuffield Council on Bioethics (2002). The ethics of research related to healthcare in developing countries. London.

Sofaer, N. and D. Strech (2011). "Reasons why post-trial access to trial drugs should, or need not be ensured to research participants: A systematic review." Public Health Ethics. **4**(2): 160-184.

World Medical Association (2008). World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. http://www.wma.net/en/30publications/10policies/b3/ [last accessed 1 December 2011]. Ferney-Voltaire, World Medical Association.