



Specialised Commissioning Group  
West Midlands



**Specialised Commissioning Group  
Commissioning Policy  
CP / 1 / 2008**

**NHS pick-up of company sponsored trials and  
treatments**

**FINAL VERSION  
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West Midlands Specialised Commissioning Group

<b>Document</b>	<b>Policy</b>
Title	NHS Pick up of Company Sponsored Trials and Treatments.
Release Date	June 2008
Author	Daphne Austin Consultant in Public Health Specialised Commissioning Team [West Midlands]
Description	This policy sets out the WMSG agreed position on how the treatments funded by PCTs on a collaborative basis will be managed if they form part of a clinical trial.
Circulation	West Midlands PCTs

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**1. The Commissioning Policy**

- 1.1 This policy applies to any patient who is the responsibility of a Primary Care Trust in the West Midlands Region and whose treatment is funded through a collaborative arrangement managed by the Specialised Commissioning Team (West Midlands) of their behalf.
- 1.2 West Midlands commissioners will not pick up funding of treatments at the end of clinical trials or when company sponsored funding is withdrawn without prior agreement of an NHS commissioning organisation (past or present). Providers trusts will need to provide evidence of any such prior funding agreement.
- 1.3 When a treatment is considered a low priority and is not generally funded, the SCG's view is that it is the moral responsibility of those initiating and sponsoring treatment to ensure ongoing access to treatment, when this is required.
- 1.4 If a provider is considering entering a patient into a trial and wishes to secure funding approval for post-trial pick-up, the clinician should submit a case, in writing, to the Specialised Commissioning Team (West Midlands). The trial protocol should be included.
- 1.5 In reviewing a request of this nature the Specialised Commissioning Team (West Midlands) in conjunction with the patient's PCT will consider the following: the strategic importance of the trial, the trial design (in particular the outcome measures used in the trial and duration of the follow-up) and affordability. Funding to support trials will be limited and generally be given low priority.
- 1.6 It is the clinician's responsibility to ensure that patients are fully informed of and agree to their management plan at the end of the trial. This includes making patients aware of this commissioning policy and, where relevant, any unsuccessful request for post-trial funding. Their consent should be documented.
- 1.6 Requests to pick up company sponsored funding (commonly called compassionate funding) will not be considered. Patients offered company sponsored treatment should also be adequately consented about their management plan following withdrawal of sponsorship.
- 1.7 In developing this commissioning policy the Specialised Commissioning Team (West Midlands) has given consideration to possible exceptional circumstances that might arise, when presented with a funding request for post-trial pick-up. It has not been possible to identify specific scenarios in which the NHS should take over funding responsibility. Exceptional circumstances are therefore not generally expected to occur.

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**2. The rationale for this policy**

There is no legal or policy requirement for commissioners to take over responsibility for ongoing access to treatment following a clinical trial.

Commissioners have a legal duty to allocate resources to optimum effect. In carrying out this responsibility it is essential that they have access to the full information derived from clinical trials and that they ensure that any new treatment is considered against other competing service developments through the normal processes.

In considering equity commissioners do not consider it ethical to give premature access to treatment to a minority of patients.

This policy should be read in conjunction with the following supporting document: The National Specialised Commissioning Group: *Funding of treatments for patients leaving clinical trials (March 2008)* which can be found together with this commissioning policy on the Specialised Commissioning Team's (WM) website: [www.wmsc.westmidlands.nhs.uk](http://www.wmsc.westmidlands.nhs.uk) .

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**FUNDING OF TREATMENTS FOR PATIENTS LEAVING CLINICAL TRIALS**

**1. Background**

The conduct of clinical trials is, of course, an integral part of NHS business and such trials make an important contribution not only to advancing knowledge and improving healthcare, but also to an important sector of the UK economy. However, Primary Care Trusts (PCTs) are regularly asked to pick up ongoing funding of treatments for patients who have participated in clinical trials. Such funding requests, which might arise either at the end of a trial or near the licensing date of a treatment, depending on whether or not there has been an extension to the trial, can present PCTs with difficult problems, and raise complex issues to which there are no simple answers. The National Specialised Commissioning Group has asked for the following guidance to be prepared and issued to Specialised Commissioning Groups, who can share it with their constituent PCTs as they wish. The circumstances in which particular requests are made to individual PCTs will vary widely, and there are unlikely to be universally applicable solutions. This note therefore aims to do no more than highlight the main considerations to be taken into account when assessing each case on its merits, and offer some generic advice on possible approaches.

The Director of the National Research Ethics Service (NRES) has also written to all Research Ethics Committees about their obligations in relation to continued treatment for research participants at the end of a clinical trial. A copy of this letter is attached to this note.

**2. The main points of context**

These are set out below:

**(a) The legal duties of PCTs**

Section 1 of the National Health Services Act 2006 <sup>1</sup> imposes a duty on the Secretary of State to '*continue the promotion in England of a comprehensive health service designed to secure improvement*'.... This duty has been delegated to PCTs.

Section 230 requires PCTs to ensure that their expenditure does not exceed their income.

Taken together, these provisions require PCTs, among other things, to have in place fair and robust processes for setting priorities and allocating resources to them in support of their overall duty of securing comprehensive healthcare for their population.

**(b) The need for PCTs to have robust and coherent processes for setting priorities**

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<sup>1</sup> The National Health Services Act 2006  
[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsLegislation/DH\\_413438](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsLegislation/DH_413438)  
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On these processes will rest policies which govern the commissioning (or not) of individual services or treatments. Each policy needs to be tested for its consistency with the underlying principles which it has been determined will govern the allocation of resources. There may, in particular circumstances, be good reasons for some divergence from these principles but, if so, PCTs must ensure that they are robust and clearly explained.

The following considerations will be particularly relevant:

- the need for comprehensive assessment of new treatments, including their place in disease management and issues relating to their implementation
- the need for all service developments to be subject to a review of their priority within the agreed framework. If this not to be the case, the reasons must be carefully argued.
- the need for a clear policy on exceptionality which, among other things, ensures that the reference group for assessing exceptionality is the relevant patient group.
- (c) The Declaration of Helsinki (see Appendix 1)

The World Medical Association's Declaration of Helsinki, which was revised last in 2000 and reviewed in 2004, is the main ethical framework for medical research. The paragraphs of particular relevance are as follows:

**World Medical Association's Declaration of Helsinki, which was revised last in 2000 and reviewed in 2004**

30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.

**With a clarificatory note by the WMA**

The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care **must** be described in the study protocol so the ethical review committee may consider such arrangements during its review.

These words leave some room for interpretation, which has not been helpful. However, one point is absolutely clear, and that is that "post-trial access arrangements or other care must be described in the study protocol..."

The main area of ambiguity arises from the words in the note of clarification which appear to qualify heavily the original statement by the addition of "**or access to other appropriate care**". The statement as a whole is usually interpreted to mean that if a treatment is considered to have efficacy then any patient in the trial should have continuing access to it, if it is thought to provide better outcomes than existing treatments. However, the qualifying words above must cast some doubt on this interpretation and, in this connection, it is important to note that what is identified as beneficial for a particular individual patient in the trial may be considered a *proven better treatment over all*.

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The note does not define who should be responsible for ongoing access. However, liability cannot rest on a PCT unless commitment is given by the PCT as part of the ethics approval process.

(d) The Medicines for Human Use (Clinical Trials) Regulation 2004 (Statutory Instrument 2004/1031)

These regulations incorporate the main points of the Helsinki Declaration into UK law and provide that

- a) exit strategies **must** form part of the trial protocol and
- b) Ethics Committees have responsibility to **ensure** that the exit strategy as described in the trial protocol is adequate.

**The Medicines for Human Use (Clinical Trials) Regulation 2004 (SI 2004/1031)**

**Schedule 3**

Particulars and documents that must accompany an application for an Ethics Committee Opinion:

**Part 1** An application document including the following information or, in each case, an explanation of why that information is not being provided...

(m) Details of -

(iii) the plan for treatment or care of subjects once their participation in the trial has ended;

[www.legislation.hmso.gov.uk/si/si20041031.htm](http://www.legislation.hmso.gov.uk/si/si20041031.htm)

Although the 2004 amendments to the Declaration of Helsinki are not expressly part of the 2004 Regulations, PCTs are entitled to take a policy decision to support the WMA approach

**3. Advice**

The application (for a clinical trial of an investigational medicinal product) is made to the appropriate Research Ethics Committee. These Committees are overseen by the National Research Ethics Service which is part of the National Patient Safety Agency.

Under the current legal framework there is no compulsion or legal requirement for PCTs to pick up the costs of patients' treatment post-trial, if this does not accord with their judgements about their priorities for their population, assuming these are robust and defensible. They may, of course, choose to do so.

The Declaration of Helsinki does not bind any specific organisation, body or individual to fund the treatment of patients post-trial. Nor does it follow that, given a failure of others to meet this cost, the responsibility to do so should sit with PCTs. Given the absence of more detailed guidance by the WMA and absence of direction

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by the Department of Health,<sup>2</sup> then PCTs should interpret it in a way which is consistent with the principles they have adopted for priority setting.

No external body can commit the resources of PCTs without their agreement. This being the case, neither a drug company nor and an NHS Trust can demand that the responsibility for post-trial pick-up costs lies with PCTs. PCTs should adopt an approach which makes it clear that they cannot be responsible for decisions to which to which they were not party.

Legally, the liability rests with the parties to the trial protocol: the Trust and the sponsor. In England these NHS organisations are separate legal entities from PCTs and therefore liability cannot be transferred. It is of course clear that where PCTs are trial sponsors then they should pick up funding.

Where PCTs have an agreed policy of not picking up post-trial costs, then considerations of exceptionality may be applied. The definition of exceptionality is no different in this setting than for others : namely that the patient in question has some unique (clinical) characteristics and that there are good grounds to expect that this difference will lead to greater than normal benefit compared to the relevant patient comparator group. The patient's ability to benefit per se is not a consideration.

It is difficult to anticipate what might constitute exceptional circumstances in trial patients. Being in a trial is not, of itself, unique; nor is benefiting from the treatment being studied. A range of beneficial effects will be normal. There will be many patients who will not benefit at all and, in those who benefit, there will be a range of health outcomes, with a few possibly considerable benefits. However this spectrum would be a common observation. To find one or two outliers who benefit significantly more than the group is uncommon. This is to be expected because the aim of many trials is to recruit a homogenous patient group. Further treatment would also be sought only if treatment had proved effective but that is not something that can be described as exceptional.

It is worth noting that the law of clinical negligence does not apply to PCTs making a funding decision as they owe no duty of care to a particular patient. The law relating to Corporate Manslaughter has recently confirmed this.

Thus, PCTs are entitled to agree to pick up trial funding but they are not required to do so unless they commissioned the trial or agreed to fund the patient(s) before they entered the trial. However, a further important consideration is the need to ensure that decisions do not have unintended consequences. In the event of an intention to agree to meet post-trial costs, careful thought would need to be given to the consequent pressure to fund the treatment more widely, in advance of any peer-reviewed assessment of the treatment or judgment about priorities.

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<sup>2</sup> In a communication of January 2008 from the Department of Health to the Faculty of Public Health, it was stated: *The NHS is under no obligation to pay for something just because the applicant told the ethics committee it would.*

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**4. Other issues**

(a) The implications of licensing

The granting of a marketing authorisation to a drug (by the Medicines and Healthcare Products Regulation Agency, an Executive Agency of the Department of Health) does no more than confer on the company the right to market the product in the UK. It has no effect whatsoever on the obligations on any NHS body with regard to the continuing access to treatment of a trial patient. The availability of a drug to patients is determined by the judgements of the relevant NHS bodies, either NIHC at the national level, or PCTs locally, acting in accordance with their agreed policies and procedures. Clearly, it is only when a drug is not made generally available, either nationally or within a PCT, that the question arises of the position of trial patients as a distinct group.

(b) An alternative approach to the protocol

Clearly, the requirement to agree an exit strategy within a trial protocol can be challenging, given the possible length of the trial, its unforeseeable outcome, and the uncertain circumstances of the relevant NHS bodies some years ahead. It has accordingly been suggested that a possible option for dealing with this is one of informing the patient that s/he will have no guaranteed right to receive (the experimental) treatment once the trial is over, the suggestion being that as long as the patient has consented to this, stopping it at the end of the trial is ethical. Whether such an option complies with the spirit of the Declaration of Helsinki is debatable, but the inclusion of words "or other care" in the note of clarification tend to support the view that it would do so.

(c) Policy tensions

There are clearly some tensions between different aspects of national policy. On the one hand, the Government wishes to create a favourable environment for the Pharmaceutical Industry and also to ensure that there is rapid dissemination of new treatments. On the other hand, such policies tend to conflict with the requirement of NHS commissioners to work within an annual cash-limited allocation and, accordingly, to ensure that the treatments which they provide are rigorously assessed for health benefit and value for money, within an overall framework of priority which will, inevitably, involve difficult decisions. PCTs, however, can do no more than focus on their legal duties, and ensure that they are discharged correctly. PCTs must not act ultra vires (beyond their powers).

**5. Conclusion**

PCTs are free to make their own decisions on trial pick-up costs. Those PCTs wishing to take a position of not generally funding trial pick-up costs or giving this category of funding request low priority can do so within a sound ethical and legal framework, providing they adopt a robust approach overall to setting their priorities. Critical to this is a good understanding of exceptionality.

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**APPENDIX 1**

**World Medical Association Declaration of Helsinki  
Ethical Principles for Medical Research Involving Human Subject**

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the

29th WMA General Assembly, Tokyo, Japan, October 1975

35th WMA General Assembly, Venice, Italy, October 1983

41st WMA General Assembly, Hong Kong, September 1989

48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996

and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000

Note of Clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002

Note of Clarification on Paragraph 30 added by the WMA General Assembly, Tokyo 2004

**Introduction**

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.
2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.
3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."
4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.
5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.
8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

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9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

**Basic Principles for all Medical Research**

10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.

16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

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20. The subjects must be volunteers and informed participants in the research project.
21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.
23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.
24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.
25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.
26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.
27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

**Additional Principles for Medical Research combined with Medical Care**

28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.

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29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.

31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.

32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

**Note: Note of clarification on paragraph 29 of the WMA Declaration of Helsinki**

The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:

- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or
- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

**Note: Note of clarification on paragraph 30 of the WMA Declaration of Helsinki**

The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review.

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APPENDIX 2

**ABSTRACT FROM NOTES ON NHS FUNDING IN SUPPORT OF TRIALS  
West Midlands Specialised Commissioning Team  
2007**

The Peckham Report in the early 1990s recommended increased R&D support through mainstream NHS funding.

In 1997 the Department of Health issued a series of documents which addressed NHS funding of service costs associated with non-commercial R&D. The most important of these is the Concordat between all the Department of Health in the UK and the Medical Research Council and other similar bodies which set out the obligations of the NHS to routinely fund the service costs related to non-commercial R&D.

Guidance was issued to the NHS in **HSG (97) 32 May 1997: Responsibilities for meeting patient care costs associated with R&D in the NHS.**

Detailed guidance sets out what is required of both commissioners and providers in relation to trials conducted under this concordat. In general it is expected that service costs, including excess treatment costs that are incurred as a result of the patient being entered into a trial, will be routinely funded. An element of discretion is specified in guidance in that the NHS can decline to fund a trial if it means creating new infrastructure that would be difficult to dismantled after the trial.

It should be noted that the Concordat and related HSGs constitute **guidance not directives**. At least one commissioning group has developed a commissioning policy ranking this type of funding as low priority.

The reality is, however, that most R&D related activity, is carried out under contract and commissioners are rarely directly approached for additional funding.

HSG (97) 32 also refers to R&D funded by health authorities and GP fundholders. Primary research commissioned by commissioners is acceptable practice. Indeed Peckham recommended that the NHS (both commissioners and providers) spent 1-2% of their budget on R&D.

The requests for N of 1 trials are increasing. It is probable that most are not genuine N of 1 trials as these require methodological robustness as any trial and therefore need a formal supporting research infrastructure. Many are therefore likely to fall into the 'pseudo-trial' category. PCTs must therefore satisfy themselves that the methodology of n of 1 trials is sound before funding is agreed.

Where a PCT has contributed funding to a trial, particularly those it has commissioned (e.g. IVAN) – the moral responsibility for trial pick-up rests with the NHS.

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APPENDIX 3



**National Patient Safety Agency**

National Research Ethics Service

Our Ref: JW/413/cd

13 March 2008

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Dear Chair

**RE: Continued treatment for research participants at the end of a clinical trial**

1. In December 2007, a joint statement was issued by the Association of Directors of Public Health and the Faculty of Public Health about the responsibility for ongoing funding of treatment for patients who have participated in commercially sponsored research. The statement was made in similar letters sent to the four UK Health Departments and other organisations, including NRES. A copy is attached.
2. In the light of the statement, RECs may wish to note the following guidance about the ethical review of post-trial treatment arrangements. The issue will arise mainly in the context of medicinal trials, but the same guidance applies to other clinical research such as devices investigations.

*Plan for post-trial treatment*

3. There is no legal or policy requirement to provide continued treatment to participants once they have completed a clinical trial. It is an issue to be considered on a trial by trial basis. However, the sponsor's plans must be made clear to potential participants before consent is sought. For medicinal trials, the Medicines for Human Use (Clinical Trials) Regulations 2004 require applications for an ethical opinion to provide details of:

*"The plan for treatment or care of subjects once their participation in the trial has ended"*

4. Information about post-trial treatment is sought in Question A25 of the Integrated Research Application System (IRAS). (The same question has previously appeared as Question A67 in the NRES on-line application form.)

*Ethical review*

5. Before giving a favourable opinion, the ethics committee should consider whether the proposed plan is ethical and ensure that it is accurately and clearly reflected in the participant information sheet. Depending on the circumstances of each trial, the following questions may be relevant:
  - Where the plan is for ongoing treatment costs to be funded by the NHS, has this been agreed with the relevant organisation(s)?
  - Who would carry the liability for provision of treatment outside the trial?

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- Will participants understand the arrangements at the end of the trial prior to agreeing to participate? Does the participant information sheet (see paragraph 11) make it clear whether the intervention will be available?

*Agreements on funding treatment*

6. It is not for the ethics committee to become involved in discussions between sponsors and NHS organisations about how treatment and care should be provided and funded. The post-trial treatment plan, and the funding of that plan, is ultimately a matter for individual negotiation between the sponsor and the care organisation(s). Those arrangements will form part of the specific clinical trial agreement. However, should that treatment plan differ from the plan contained in the application submitted to the ethics committee, then this would require notification of a substantial amendment to the REC.
7. Where assurance is given by the applicant that the arrangements have been agreed with NHS organisations, this should be accepted by the REC. *It is a criminal offence to provide false or misleading information when applying to an ethics committee or the MHRA to conduct a medicinal trial.* If a REC gives a favourable opinion on the basis of an application stating that the NHS has agreed to fund ongoing treatment when that is not the case, it should follow SOPs on the reporting of possible fraud or misconduct. In the case of a medicinal trial, the REC or its operational manager should notify the GCP Inspectorate under the terms of the Memorandum of Understanding with the MHRA.

*Multi-site studies*

8. In the case of multi-site studies, negotiations may not have been completed with all host organisations before the ethics application is submitted. It is also possible that the study will start at some sites before all the trial sites have been identified. This raises the possibility that the arrangements ultimately agreed with NHS organisations at some sites may differ from those stated in the original application.
9. It is proposed to amend the Clinical Trials Regulations to allow ethics committees, in giving a favourable opinion, to state conditions that must be met prior to the start of a trial. If and when this amendment comes into force, it would be open to an ethics committee, where appropriate, to include a requirement to agree post-trial funding arrangements with the relevant organisation before starting the trial at a site.
10. Where the agreement reached at a particular site differs from the plan declared to the REC and reflected in the approved PIS, the sponsor should submit a notice of substantial amendment prior to starting the research at the site. In some cases, site-specific variations in the PIS may be required; these should always be approved by the main REC.

*Participant information sheets*

11. Guidelines from the European Commission on medicinal trials state that the protocol and participant information sheet should include a description of the post-trial arrangements where additional care is necessary because of participation in the trial and where it differs from that normally expected for patients in routine care (see ENTR/CT2, Revision 1, February 2006, paragraphs 4.3 and 4.6, available at [http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/12\\_ec\\_guideline\\_20060216.pdf](http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/12_ec_guideline_20060216.pdf))
12. Unless a clear undertaking can be made by the sponsor or other organisation (e.g. PCT or NHS Trust), the PIS should emphasise that even if the participant has personally benefited from the intervention, there is no guarantee that it will be available to them at the end of the trial.

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13. Where the sponsor has indicated that a trial drug may be marketed following the trial, the information sheet should explain that marketing does not guarantee availability to participants. It may be some time before the National Institute for Clinical Excellence (NICE) and the Scottish Medicines Consortium (SMC) consider the drug and funding will not necessarily be made available in the interim.

*Guidance to applicants*

14. New guidance for applicants has been published in the form of question-specific guidance on Question A25 in IRAS.

With best wishes

Yours sincerely



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Encs