PRIFYSGOL
BANGOR
UNIVERSITY

Healthcare and Medical Sciences

Academic Ethics Committee

ETHICS GUIDANCE AND

PROCEDURES

2015-16

Contents

1. INTRODUCTION

Research carried out in the Schools of Healthcare Sciences and Medical Sciences (HCMS AEC) require ethical approval from the Healthcare and Medical Sciences Academic Ethics Committee (AEC) as part of the process governed by the University Research Ethics Committee (UREC) as specified in the UREC Ethics Policy (2015). Following approval by HCMS AEC where appropriate, the Ethics Committee of any external host organisation in which the study takes place as well as NHS R&D may need to receive an application. All staff and students conducting investigative studies abroad also need to seek approval from the Healthcare and Medical Sciences Academic Ethics Committee.

The electronic system was developed in partnership with the School of Psychology and the HCMS AEC continue to work collaboratively with the ethics committee at the School of Psychology to improve its effectiveness. As part of the continuing developments at Bangor University through UREC, it will be evaluated and subject to continued modification.

2. SUBMITTING YOUR ETHICS APPLICATION – PROCEDURE AND APPROVAL PROCESS

The policy includes guidance for applicants regarding the processes of electronic system, the framework for governance as part of the sponsorship arrangements for clinical trials and a range of relevant information on ethical issues for applicants, such as a consideration of PPI and secondary data analysis.

The ethics review process is largely conducted as an expedited process unless those submitting applications request a full review by the committee. Exceptions include (i) if the HCMS AEC reviews raises concerns regarding the application or (ii) the applicant decides to appeal the decision made on the basis of the initial expedited review. In general these are exceptional circumstances.

The **expedited review** is centered on two blind reviews and the recommendations (if any) are forwarded electronically to the applicant for action. If there are differences in the feedback or recommendations provided by reviewers then these will be subject to

further scrutiny and reviewed by the Chair of the ethics committee or Vice Chair in order to provide an appropriate feedback.

If you have any problems or queries, please contact the Ethics Administrator – hcmsethics@bangor.ac.uk. Details of the Ethics Administrator can be found on http://www.bangor.ac.uk/healthcaresciences/ethics.php.en

2.1. Submitting your application

Complete the electronic submission process once you have reviewed the information provided in the policy. Please refer to the information on the submission procedure in section 2.2 below prior to initiating the submission process and additional presentations /*panopto* recordings are included as additional supportive resources. As an applicant a number of pathways exist for the submission of an application. These are as follows:

- ***Educational applications*** - In the case of student applications, these may include either PGT or PGR students - MSc, MSc by Research, MPhil, PhD or Professional Doctorate submissions. As part of such applications please ensure that supervisors are labeled as 'collaborators'. This ensures they have reviewed the application prior to submission. They will need to collaborate in the submission process and the review will only take place once all parties have agreed the submission.
- ***Clinical trial applications*** – The area of clinical trials has a particular pathway relating to sponsorship arrangements (see Appendix 1) as detailed in the policy (Section 2.3). As a consequence there is a dedicated set of reviewers for trials and additional guidance is provided. Please ensure that all relevant Principal Investigators are labeled as 'collaborators'. This ensures they have reviewed the application prior to submission. However care should be exercised in only identifying core team members as they will need to collaborate in the submission process and the review will only take place once all parties have agreed the submission.
- ***Academic Staff applications*** – The application process is required for both educational-focused projects and research-based work that may be undertaken

by academic members of staff. Please ensure that all relevant Principal Investigators are labeled as 'collaborators'. This ensures they have reviewed the application prior to submission. However care should be exercised in only identifying core team members as they will need to collaborate in the submission process and the review will only take place once all parties have agreed the submission.

Please remember that you can only begin your study once approval has been granted. If external approval is also required, your study can only commence once this has been granted. Approval from an Ethics Committee is separate from the Research Governance approval process for undertaking research in the NHS. Further information can be obtained by contacting the R&D department in the NHS Organisation where you are planning to do your research.

2.2. Approval process: Overview

Submitting your application: a summary

1. Access the electronic system using the submission link on the HCMS AEC webpage: https://apps.bangor.ac.uk/ethics/
2. Log on to the online system using your Bangor University username and password in order to access the HCMS AEC ethics page
3. Click on "Start New Ethics Application" or "Submit amendment". Clicking on "Start by Proxy" will allow you to start an application for another researcher using your login.
4. Fill in the title and start and end dates of the project. Note projects are only approved for a three-year period. If you enter an end date that extends beyond three years, you will get an error message.
5. The system will automatically generate an application number and will assign you as PI according to your BU login. In the next widow you will be able to add other researchers. BU researchers are identified by username or surname. External collaborators will need a login.
6. To create a login for an external collaborator click on the line "Add External

Collaborator (Create a login for non BU collaborators). The buttons to the right of the names under the word "Editor", when checked, will grant editorial rights to the application to specific collaborators.

7. At this point you will see a screen with tabs across the top. You can navigate to any part of the application by clicking on the tabs.
8. Complete all the relevant sections of the online form in sequence, using the tabs. You can move between each section by clicking on the relevant tab at the top of the screen, save the document at regular intervals before moving to the next tab.
9. Attach all relevant information by uploading supporting documents(e.g. research proposal, external NHS ethics/governance forms, consent and participants information sheets, questionnaires, interview schedules and so on) in the final tab- called "Supporting Documents"
10. Once you are finished with the form, submit using the "Submit for Review" button.
11. The application is sent to your collaborators for approval. Once each of the collaborators has approved the application it will be sent for review.
12. A framework for reviewers is included in Appendix 1. This provides guidance for all reviewers of applications and also enables applicants to reflect on their application to ensure all relevant information is provided, prior to submission.
13. The Ethics Coordinator will forward your application to TWO Ethics Committee Reviewers for consideration. We aim to send a response regarding your application within 20 working days of the application being made, for all projects.
14. There are several outcomes of the approval process**:**
    - Your application is approved. Research may commence when you receive notification of this from one of the ethics administrators.
    - Your application is approved subject to minor changes. In these cases, you will be contacted by one of the ethics administrators and asked to submit the minor changes but these will not need to be reviewed again.
    - Ethics reviewers may request that some changes or additions to

your proposal are made. In these cases, you will be contacted by one of the ethics administrators and asked to resubmit the amended proposal for further review.

- Your application is not approved.

Please remember that research may only commence your research once approval has been given. Any non-trivial change to the protocol will require an amendment. Also projects lasting more than 3 years will be subject to re-review after 3 years.

It is important to ensure that your proposal is compliant with all relevant legislation, in particular: Data Protection Act, Mental Capacity Act, Child Protection Procedures, Human Tissues Act.

A flow chart indicating the key stages in the HCMS AEC electronic application and review process is shown in Figure 1 below:

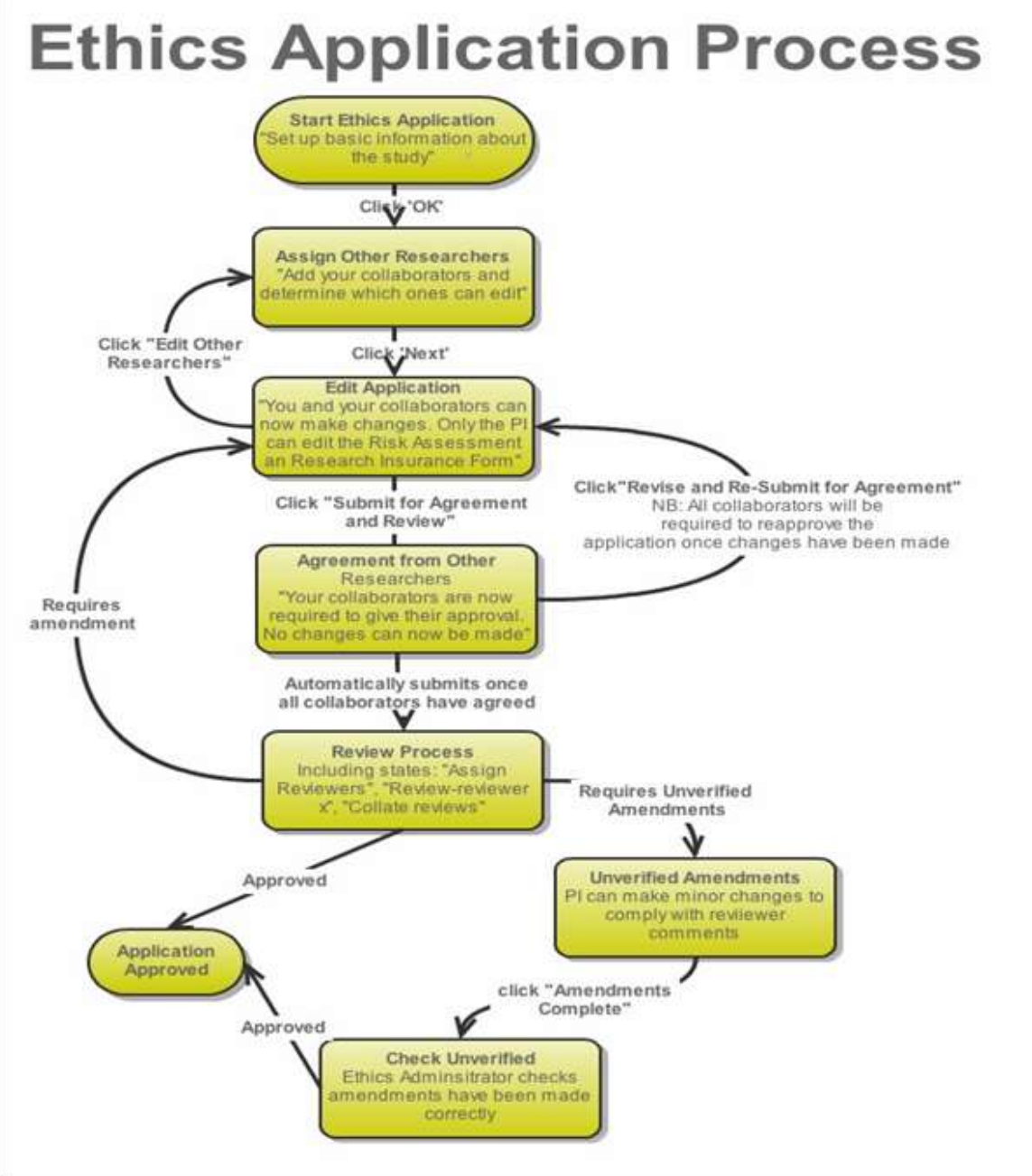


Figure 1 Process map of the HCMS AEC Ethics system

2.3 Amendments To Previously Approved Projects

It is often the case that approved projects undergo a change, or a change becomes necessary. For example, new researchers join or leave the project or where it becomes necessary to change the way in which participants are recruited or consent is gained. Where such modifications to the approved study are *non-trivial*, then they must be submitted for Ethics Committee approval.

- Examples of non-trivial modifications are:
- introduction of a new condition or new measures (such as a change to the inclusion or exclusion criteria to increase/decrease sample size or the use of a different questionnaire)
- change in participant population (e.g., the change from use of students to use of patient representatives or patient group such as a local diabetes group, or the change from only staff participants to also include patients)
- change of investigators, especially where there is a change in the qualifications of the investigators to carry out the study (e.g., a project originally carried out by staff or PhD students will now be carried out by undergraduate students)
- change in ways in which participants are recruited,
- major changes to equipment or research environment or venue (originally planned to interview patients while they attended out-patient appointments to interviewing them in their own homes)
- changes relevant to any of the key questions presented on the tick box sections to the ethics/risk assessment form (i.e. consent, deception, confidentiality, participant payment, potential for distress to participants).

In the case of student projects, please discuss any such changes with your supervisor in the first instance. For clarification or more information you can contact the Ethics Administrator or AEC Chair for advice.

In order to seek approval for an amendment, you should either:

- Complete and submit an *Ethical Approval Substantial Amendment Request Form* (Form 3) to hcmsethics@bangor.ac.uk. We aim to send a response within 14 working days.

OR

- In the case of a number of more substantial changes, submit a **new** proposal on the standard ethical approval form. This second option is generally required where your previous approval was based on there being no significant ethical implications of the study (i.e. you ticked box A on the original ethical approval form), and where you now wish to do one or more of the following:

a. Pay participants;

b. Work with children or other vulnerable populations (i.e. patients, people in custody, physically vulnerable adults, people engaged in illegal activities, people with learning or communication difficulties);

c. Deliberately mislead participants;

d. Utilise procedures that carry a realistic risk of participants experiencing physical or psychological distress or discomfort.

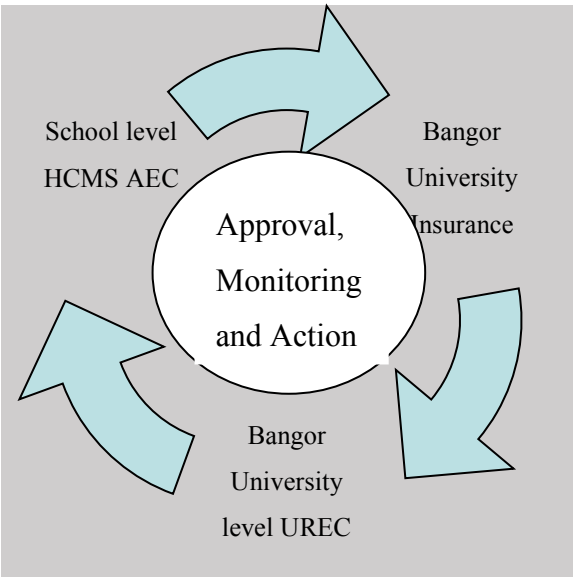
2.4 Clinical Trials And Sponsorship Arrangements

The approval processes for Clinical Trials are positioned within the HCMS AEC as part of a wider approval and governance process, including particular arrangements for sponsorship by the university and governance arrangements. A specified process is detailed for such applications that involves a specific team representing the discrete components of oversight required in managing not only the application but also the ethical conduct of Clinical Trials. This reflects the NHS R&D Forum (V3: 2014) and MHRA principles and guidance. Importantly the application and subsequent oversight is governed by key principles and guidance for sponsorship (Appendix 2 [SOP for Arranging Sponsorship, Contracts Agreements and Indemnity\NWORTH 4.04]; Appendix 3 [Extracts from MHRA GCP Guide]; Appendix 4 [Extracts from DoH]). The stages of approval and oversight represent an integrated process with specific procedures.

2.4.1 Responsibility for approval and monitoring

The approval and subsequent monitoring and oversight processes are focused on close working relationship between three Sponsor's representatives from Bangor University, respectively involved with the Clinical Trials Team (for instance embedded in an applicant team within NWORTH), HCMS AEC and UREC. These processes focus on a continuous and structural set of partnership arrangements (Figure 2). These seek to ensure appropriate ethical and governance standards are evidenced in the development of the application ready for submission to HCMS AEC and following approval external ethics and governance. However these processes are maintained following approval as part of governance arrangements during the duration of the respective Clinical Trial. At its core this partnership seeks to ensure that good governance is established, monitored and any adverse incidents reported and appropriately escalated to maintain approval by Bangor University as sponsor.

Figure 2 Sponsor's representatives (Bangor University) in Clinical Trials approval and monitoring



Continuous cycle of approval, monitoring and oversight, leading to action as appropriate. Sponsorship oversight embedded in HCMS AEC and UREC.

The process of approval by the Sponsor's representatives (Bangor University) as well as ensuring appropriate governance is centered on specific personnel (Table 1). They have responsibility for scrutiny and oversight, including monitoring progress through reports from the Clinical Trials team and maintaining reporting procedures that maintain the integrity of sponsorship arrangements and the protection of participants during a specific Clinical Trial by direct reporting to a Standing Trials Sub-Committee of UREC. This Committee will receive 3- 6 monthly reports of progress.

Table 1 Sponsorship Representatives

Personnel	**Role in relation to process/procedures**
HCMS Chair: Dr Sion Williams	i. Coordination and liaison with Clinical Trials team in developing ethical/governance procedures during study design and application process, as necessary. ii. Conduct and completion of initial approval process by peer review allocated to 2 specialized staff. iii. Ensuring necessary amendments are satisfactorily completed. iv. Monitoring compliance with terms of approval through reports provided by Clinical Trials team that are forwarded by Dr Huw Roberts. v. Expedite any subsequent requests for amendments to study submitted by Clinical Trials team. vi. Initiating any escalation procedures to UREC as necessary.

HCMS AEC Committee member/School Manager/ Sponsor representative liaison with Clinical Trials team: Dr Huw Roberts	i. Coordination and liaison with Clinical Trials team in developing ethical/governance procedures during study design and application process, as necessary. ii. Participate in the initial approval process by peer review allocated to 2 specialized staff. iii. Provide bridging process between sponsor (Bangor University) and the Clinical Trials team by attending team meetings at 3- 6 monthly intervals and provide reports/updates to HCMS AEC. iv. Member of the Standing Trials Sub-Committee of UREC.
Bangor University Governance / UREC Representative : Gwenan Hine	i. Lead Member of the Standing Trials Sub-Committee of UREC with Dr Peter Higson (Chair of UREC). ii. Ensure appropriate safeguards are maintained for governance of Clinical Trials during their conduct. iii. Report any breaches to the terms of approval, risk areas not accounted for in initial approval or actions taken by the Standing Trials Sub-Committee of UREC to Bangor University as Sponsor.
Bangor University Insurance: Chris Benson	i. Provide advice and guidance to Clinical Trials team as part of development of study design relating to risk assessment. ii. Provide approval of initial insurance on behalf of sponsor following detailed assessment and sanction by underwriters.

2.4.2 Approval and monitoring procedures

The process of approval and monitoring is outlined in Figure 3. The process and procedures are embedded in the principles and guidance detailed in Appendix 1. The activity of Clinical Trials team are framed within agreed and current Bangor University SOPs. Risk assessment is completed according the current REC guidelines and the SOP. **All** relevant documentation must be submitted by the Clinical Trials team to the HCMS AEC as outlined in the general guidance, including draft REC and R&D documentation. Following approval the Sponsor's representatives (Bangor University) complete and 'sign off' approval (Appendix 5) and notify UREC and its Standing Trials Sub-Committee.

2.4.3 Adverse Incidents Reporting

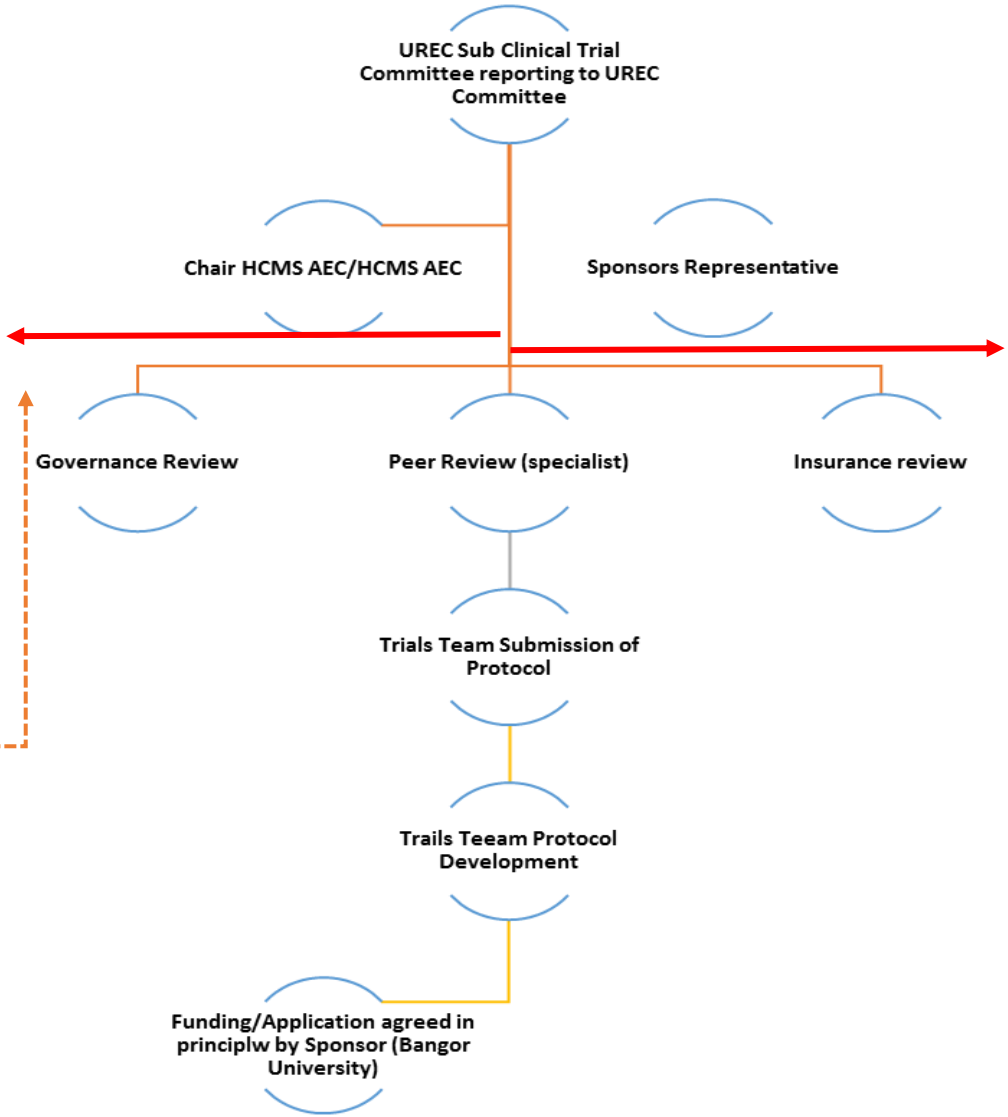
In the event of an adverse incident the Clinical Trials team will immediately inform (1) Dr Huw Roberts or (2) Dr Sion Williams and the information will be immediately provided to (3) Gwenan Hine. An extraordinary meeting of the Standing Trials Sub-Committee of UREC will be held to complete a review and further risk assessment.

Figure 3 HCMS AEC Process of scrutiny, approval and monitoring (Bangor University, 2015 Version 1)

Continuous monitoring/problem solving

- **Amendments as required**
- **critical incident reporting**
- **Sponsor's representative attending Trial Team meeting**

Reporting cycle to UREC



Approval HCMS AEC Following Amendments as required with '3 Sponsor sign off':

- **HCMS AEC chair**
- **University Insurance**
- **University Governance**

Resulting in the Submission Externally to REC/R&D

Development and scrutiny processes for trial based on Policy and procedures (2015 Version 2) [including reference

3. PUBLIC INVOLVEMENT IN RESEARCH

The area of public involvement in research has a number of ethical dimensions and is complex. However the key issue in reflecting on ethical issues as part of discussions by research teams are the need for clarity, in terms of defining the role of public involvement and its application within research projects. Additional material is included in 'Resources' for consideration, for instance *Going the extra mile [Improving the nation's health and wellbeing through public involvement in research NIHR]*, Collins (2009*) Involving People - Guidelines for researchers* as well as NIHR material. **However the position of Bangor University at the UREC level is being currently refined and for discussion regarding public involvement and possible ethical issues please contact the Chair: sionwilliams@bangor.ac.uk for further advice.**

Overall, the term 'members of the public' is usefully defined by Popay & Collins (2014) as part of the *PiiAF -The Public Involvement Impact Assessment Framework* as referring " to users of services (e.g. patients and carers) and members of groups who share a particular interest, for example, residents of particular neighbourhoods. The difficulty for researchers and research teams is that the public are involved in many different ways and not all such 'involvement' requires attention within the ethical approval process. As snoted by Popay & Collins (2014):

> "Distinguishing between the general approach to involvement (e.g. consultation, collaboration, control), the specific methods (e.g. service user researcher, public members of a project advisory group or a consultative panel) and the activities undertaken (e.g. commenting upon a research proposal, peer interviewing) can contribute to a more sophisticated understanding of how the involvement might have an impact".

Within this policy the current benchmarks provided by INVOLVE (2012) [*Briefing notes for researchers: involving the public in NHS, public health and social care research. INVOLVE, Eastleigh*] are utilised. These provide a starting point for discussion by teams regarding the nature of involvement and the implications for study design and ethical approvals:

Involvement

Where members of the public are **actively** involved in research projects and in research organisations.

Examples of public involvement are:

- as joint grant holders or co-applicants on a research project
- identifying research priorities
- as members of a project advisory or steering group

Engagement

Where information and knowledge about research is provided and disseminated.

Examples of engagement are:

- science festivals open to the public with debates and discussions on research
- open day at a research centre where members of the public are invited to find out about research
- raising awareness of research through media such as television programmes,

Participation

Where people take part in a research study.

Examples of participation are:

- people being recruited to a clinical trial or other research study to take part in the research

4. SECONDARY DATA ANALYSIS

HCMS AEC

Guidance for the use of secondary data

Introduction

The purpose of the guidance is to provide a framework for researchers to consider the ethical implications of using secondary data as part of research studies, for educational or other purposes including staff projects. Studies involving further analysis of existing data may require ethical approval depending on whether or not the nature of the data are sensitive or if individuals can be identified from the research. The principles documented in the Research Ethics Framework (www.esrc.ac.uk) indicate that secondary use of some data will be uncontroversial and only require expedited or 'light touch' review, however the guiding principle should be the assessment of risk.

The HCMS AEC guidance on secondary data does not refer to any data that may be considered as a 'secondary' form of data that is governed by the requirements of the HTA (2009).
http://www.hta.gov.uk/legislationpoliciesandcodesofpractice/codesofpractice.cfm

Operational Definition

The guidance is framed within the 6 principles of the Research Ethics Framework and policy guidance, involving the implementation of these principles within research practice (www.esrc.ac.uk) and the Code of Human Research Ethics (British Psychological Society, 2010)
http://www.bps.org.uk/sites/default/files/documents/code_of_human_research_ethics.pdf

Within this HCMS AEC guidance secondary data falls into three categories:

1. Data which is not sensitive and there is a minimal risk of disclosure of the identity of individuals and as such this data may be used without ethical clearance.
2. Data that is protected by legislation such as census data or particular archival restrictions, such as QUALIDATA, ESDS Qualidata so that access to this is controlled and deposits are rigorously anonymized. This data can only be available in certain 'safe' settings where there can be no identification of individuals.
3. Data where information has the potential to identify individuals and as such is ethically sensitive, for instance birth dates or specific personal location are identified.

The focus of ethical considerations regarding secondary analysis centers on data collected from participants during (i) service evaluation that did not receive ethical approval or (ii) data collected from a study that was completed without appropriate ethical approval for later research to engage in secondary analysis. The definition of risk in relation to secondary analysis is based on the criteria of the Research Ethics Framework (www.esrc.ac.uk). The key ethical requirements for secondary analysis are that the data should conform to the following parameters:

- The data is completely anonymous when provided to the researcher;
- It is impossible to identify participants from any resulting reports;
- The use of the data will not result in any damage or distress.

Key issues

- The research ethics framework (www.esrc.ac.uk) suggest that when undertaking secondary analysis of data careful consideration is required by the researcher with regard to **presumed consent** and the potential **risk of disclosure of sensitive information**. This applies to both the user of the data and its original researcher, as there is an expectation that others will also use that data.

- It is advised that consent should be obtained for the original research on this basis with the original researcher taking into account the long-term use of the data.

- The fact that original data research and data collection has been through ethical review does not automatically mean that there are no ethical issues in relation to using this data as part of a secondary analysis.

Framework for consideration of ethical issues

The following might be considered:

- In secondary data analysis the people whose details are recorded in the data are not directly approached for their consent but researchers engaged in secondary analysis still need to think about whether they would object to how data are using an interpreting their data. Consideration should be given to whether they can be contacted and asked for their consent.
- The Data Protection Act (1998) should be considered in relation to the data set. Specifically researchers should check what kind of consent was secured for the original data collection and whether they were asked if they were willing for their data to be archived and made available.
- Are the original participants identifiable or recognizable? As researchers engaged in secondary analysis is there a duty to protect their anonymity or confidentiality? If not can this be justified to the ethics committee?
- Do researchers engaged in secondary analysis need to get the original researchers or data collector's permission to use the data or should they be informed of the secondary analysts purpose?

- A consideration of potentially sensitive personal data may focus on the following:
    - Racial/ethnic origin of the participant
    - His/her political opinions
    - His/her religious or other beliefs

- Membership of a trades union (as defined by the Trade Union and Labour Relations [consolidation] Act, 1992)
- His/her physical or mental condition
- His/her sexual life
- Commission or alleged commission of any offence
- Any proceedings for any offence committed or alleged to have been committed and the disposal of such proceedings or the sentence of any court in such proceedings.

Appendix 1: Ethics Checklist for Reviewers

GUIDANCE FOR REVIEWERS

This guidance is designed to help you think about the points that need to be addressed in an Ethics proposal. However, this is not an exhaustive list, and applications should also be considered on an individual basis.

General considerations The proposal should:	Notes
• be focused on an important question and propose the use of appropriate methodology and methods to address this • provide information about the researcher's skills and experience • provide enough detail for you as the reviewer to make an informed decision	

• demonstrate that the applicant takes into account the potential effects of the study on all involved including participants and researcher(s) • reflect an anti-discriminatory/anti-oppressive approach • have clear inclusion and exclusion criteria which are reasonable and equitable • provide explanation about how identified ethical concerns have been appraised, with detail provided as to how these will be managed in the study • include participant letter, information sheet, project summary, questionnaires and interview schedule (where appropriate) • ensure participant facing documents will be available in Welsh as well as English to reflect the 'active offer' principle • ensure that participant facing documents use short, familiar words and short sentences; and are they written in simple, non-technical terms that a lay person will easily understand • include documents that are aligned (e.g. same project title) and with dates and version numbers	

Participants The proposal should:	Notes
• show how the study is of sufficient importance to warrant the intrusion on the patient population (if the study involves NHS users or those who will be accessed in social care settings) • address issues of respect and dignity • show the process of seeking access to potential participants • show how participants are provided with detail about the study in a way that they will be able to understand • show what provision will be made for participants who have additional needs (where appropriate) • consider issues such of burden on the participants (e.g. time, travel, expense) • acknowledge risk of potential for harm – including distress/upset that might result from participation	

• outline any possibility of coercion or unfair reward from taking part in the study • show that consent is obtained in an acceptable and informed manner • consider, that where deception is necessary in a study, how will participants react (*if the anticipated reaction is negative, then deception is inappropriate) • consider any effect on the participant's mood when they leave the study • indicate if the participant will be able to give feedback on their experience (as participant), and how will this be undertaken (*the responsibility is the researcher's to provide it, not participants to request it) • if the study uses a methodology that involves checking emerging findings with participants, show how will this be undertaken in a way that is meaningful to participants • reflect how participants are made aware of their right to withdraw from the study at any time, including retrospectively, and given clarity about what will happen to any data that relates to them • provide provision for participants to complain if they are not satisfied with the study/researcher conduct (*clearly specified on the consent form and participants' information sheet)	

• indicate if participants will be informed of any evidence of medical/health problems discovered during the study (if relevant), and provide details of counselling services or patient support groups	
Data The proposal should:	Notes
• explain how data will be managed and stored to protect participants' confidentiality, anonymity and personal data (*including how will this be addressed in the use of job title or roles of staff that might make them identifiable) • indicate for participants, use (including future use) of any data • show the measures to be taken to ensure confidentiality and the security of the data (including who has access to data) • indicate data storage and length of time data held https://www.bangor.ac.uk/research/staff/policies/CoP%20Assurance%20of%20Academic%20Integrity%20and%20QA%20in%20RESEARCH.pdf • illustrate how anonymity will be preserved	

• indicate how consent will be properly documented • shows that three copies of the consent form will be required (*one for the participant, one for the researcher and one for the master file for Governance) • indicate that the consent process will be conducted in Welsh or English to reflect the 'active offer' principle • explain how the currency of the consent will be assured if a study involves multiple points of data collection • indicate that, if validated outcome measures are to be used in the study, that participants be provided with Welsh language versions of these measures, where available, in line with the 'active offer' principle (www.micym.org)	
Risk The proposal should:	Notes
• highlight if the study involves any vulnerable groups • include information for participants of any risks incurred by involvement in the study (*participants must not be	

required to take risks greater than those involved in everyday life) • state any anticipated risks and explain measures that will be taken to manage and minimize these (*the appropriate box (es) on the Ethics Application Form should be ticked to identify the particular category of participants to be recruited) • consider if the potential benefits of the research balance any potential risk to the participants/researcher • show the process to be taken if untoward factors are uncovered during the research that require follow-up • indicate the precautions to be taken to ensure researcher(s)' safety	
Researcher The proposal should:	Notes
• indicate how the researcher is involved *as* a researcher, and not as a practitioner, unless appropriate to the study methodology • indicate if the study involves those that might present a risk to the researcher	

Appendix 2 SOP

STANDARD OPERATING PROCEDURE FOR ARRANGING SPONSORSHIP, CONTRACTS/AGREEMENTS AND INDEMNITY (NWORTH 4.04)

Approvals

Principal Author
Name: T.H. Roberts **Signature: T.H. Roberts** **Date: 03-Oct-2011**

Quality Assurance Officer
Name: D. Skelhorn **Signature: D. Skelhorn** **Date: 29-Sep-2011**

NWORTH Director
Name: R.T. Woods **Signature: R.T. Woods** **Date: 13-Dec-2011**

Disclaimer: Printed SOP's are considered uncontrolled. To ensure you are working with current version always refer to the pdf version on the NWORTH website.

DOCUMENT HISTORY

Version number	Effective date	Authorship	Summary of changes
1	04/10/07 *(compiled)*	C. Bray I. Russell	New
2	17/10/07	C. Bray I. Russell	Update
3	06/10/08	C. Bray I. Russell	Update
4	24/05/12	T.H. Roberts D. Skelhorn (based on UKCRC template)	New number and layout, procedure re-written

1. Table of Contents

2. Purpose

The purpose of this document is to describe the procedures required to:

- ensure that appropriate arrangements for sponsorship are in place for trials managed by the NWORTH,
- implement appropriate contracts and model agreements with research sites and third parties,
- ensure activities undertaken by the NWORTH on behalf of the sponsor are appropriately indemnified in order to comply with the necessary regulations including but not limited to, the NHS Research Governance Framework for Health and Social Care (2005), the Medicines for Human Use (Clinical Trials) Regulations 2004 No.1031 and the principles of Good Clinical Practice.

3. Scope

This procedure applies to all research studies and clinical trials carried out by the NWORTH and all NWORTH staff responsible for ensuring that the appropriate sponsorship arrangements are in place, the contracts are implemented and the insurance/indemnity cover is adequate for the relevant research activities, unless the sponsor SOPs are to be followed or the sponsor wishes to conduct this process themselves.

4. Responsibilities

The Sponsor has ultimate responsibility for the management and/or financing of the study. The sponsor may delegate these activities as appropriate to the CI, the NWORTH and/or other organisations. Delegation of responsibilities must be formally documented in the study trial master file (TMF).

Sponsor's main responsibilities under the UK regulations are listed in appendix 1

The Chief Investigator is responsible for ensuring:

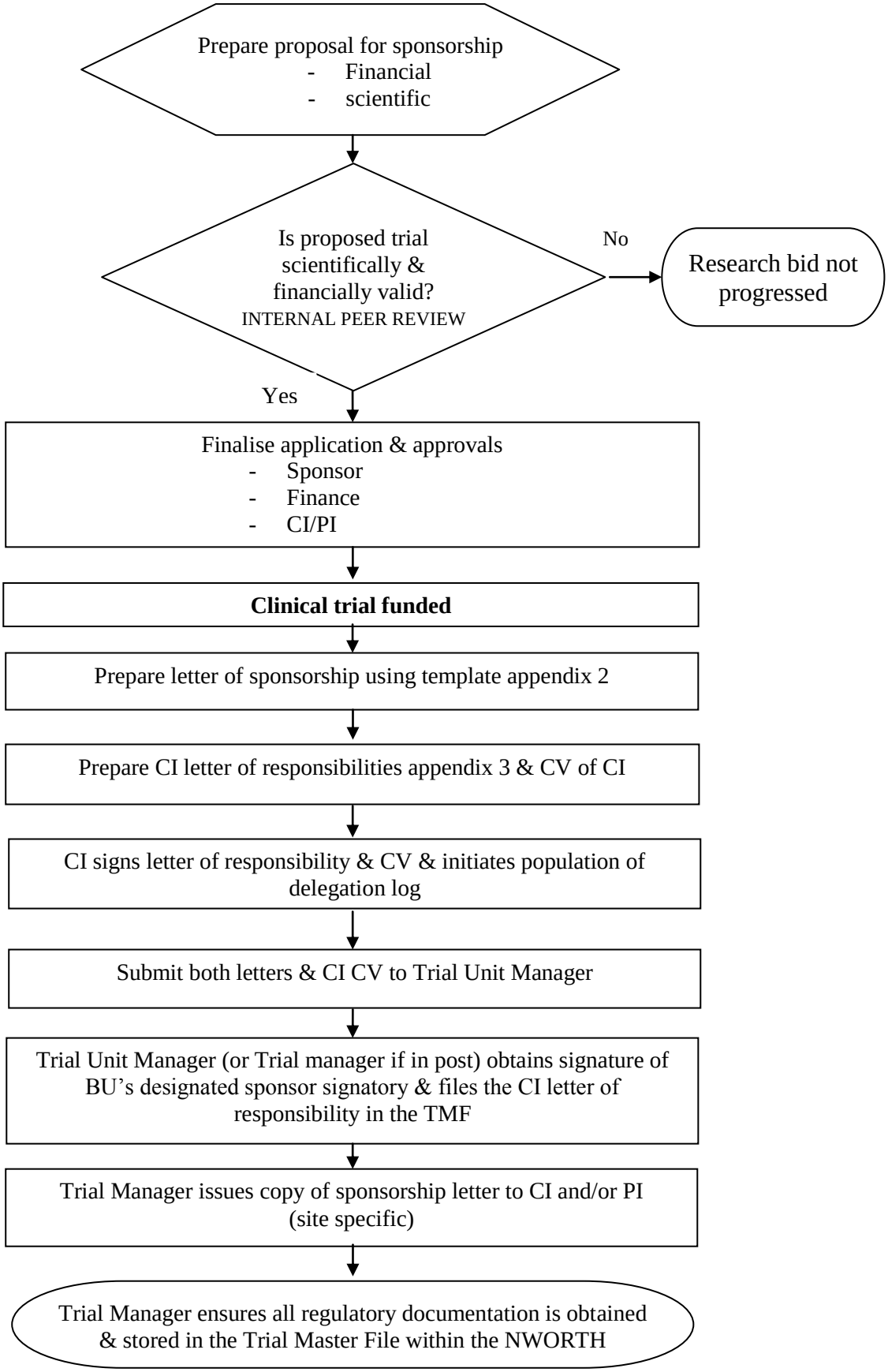
- sponsorship of the trial has been obtained before ethical approval is sought, (for trials where the substantive contract is issued to Bangor University, the sponsor will usually be Bangor University).
- that the appropriate contracts and model agreements with research sites are implemented,
- that the activities undertaken by the NWORTH are appropriately indemnified.
- if sponsorship responsibilities have been delegated, the CI must submit copies of all regulatory and trial documents to the Trial Unit Manager (see appendix 1 for list of documents).

The above responsibilities may be delegated to the Trial Unit Manager or Trial Coordinator/Manager.

The Director of NWORTH has overall responsibility for the integrity of trials managed by NWORTH.

5. Procedure

5.1 Procedure Flow Chart



Note: a sponsorship signature or letter is required for submissions to MREC & to MHRA for CTA and also for R&D approval (see SOP 3.02 Protocol Development, 4.01 Ethical and R&D approval and 4.02 MHRA Approval)

5.2 Arranging sponsorship

5.2.1 The CI should initiate the process of arranging sponsorship at the time of preparation and submission of the Research Grant Application. However, in some cases this may be on receipt of the Grant Award Letter and subsequent approval of funding to ensure that there are no implications with respect to the sponsor's insurance policy, the earlier this is initiated the better.

5.2.2 The CI should contact an appropriate representative (usually within the Research & Development (R&D) office) of the institution/organisation to act as sponsor for the study. Where appropriate, the institution/organisation should be the substantive employer of the CI. N.B: The institution may wish to approach another organisation to act as co-sponsor for the study and assume some of the sponsorship responsibilities. The delegation of responsibilities between the two sponsors should be agreed, documented and authorised by appropriate representatives of both sponsor institutions/organisations. (See delegation log appendix 4)

5.2.3 The sponsor's representative should advise the CI regarding the documentation required to further the sponsorship application (e.g. protocol, ethics application) and current versions should be provided to them promptly. (See SOP 3.02 Protocol Development, 4.01 Ethical and R&D approval and 4.02 MHRA Approval)

5.2.4 The sponsor may wish to institute a risk assessment in order to establish whether their responsibilities will be executed properly by the trial study team before they formally agree to be the sponsor. This may be done by the NWORTH if delegated and as defined in the contract agreement.

5.2.5 The sponsor will usually inform the CI by letter once sponsorship has been agreed.

5.2.6 The CI will usually be asked to sign a letter of sponsorship/Sponsor Registration Form (see appendix 1 & 2), and a copy of this letter should be kept in the TMF.

5.2.7 The CI should ensure that the research team can comply with the sponsors' requirements drawn up in the CI letter of responsibility/contract (see appendix 1). This will include, undertaking to communicate promptly and effectively with the sponsor to satisfy and reassure the sponsor that the sponsor's obligations on the authorisations, the financing and the progress reporting (including emerging safety data) of the study are being met.
NOTE: It is the trial manager's responsibility to identify, at the earliest possible stage, the appropriate sponsor representative who is able to sign off documentation (e.g. protocol amendments, IRAS applications) on behalf of the sponsor.

5.3 Contracts/Agreement

5.3.1 Contracts between the Funder and the CI / Host Institution

- Following receipt of a favourable response from the sponsor, the funder may issue a contract to the Sponsor/Employing organisation of the CI.
- Once the CI or designated team member has reviewed and agreed the contract, it should be signed off by the sponsor i.e. the appropriate contract department of the Host Institution (if the host is Bangor University then it will be the Finance department) and/or by the Director of the NWORTH as applicable to the delegated responsibilities documented in the delegation log. This will highlight the

responsibilities required of the sponsor and set the terms and conditions of the funding agreement along with a timeline for study payments.

- The trial manager is responsible for ensuring that a copy of this contract is retained in the TMF.

5.3.2 Sub-contracts

- Where NWORTH is being sub-contracted as a research partner (e.g. randomisation provision, database provision, trial management), then NWORTH together with the Host Institution (in the main finance department) will produce a contract agreement that outlines the detail of the research service provision.
- This contract will then be sent to the CI for review and sign off.
- The lead trial member is responsible for ensuring that a copy of this contract is retained in the TMF.

5.3.3 Model agreements

- Model agreements for non-commercial research in the Health Service (mNCA) will be issued between the sponsor and the appropriate NHS organisation for the research sites (see section 8 reference number 4).
- The CI or designated NWORTH team member should instruct and monitor contract activity.
- At each site, the PI should ensure that the research team complies with the site-specific delegated responsibilities outlined in the model agreement.
- Delegation of roles and responsibilities may be documented in for example, a Study Delegation Log (see appendix 4) which clearly defines the undertakings of the various parties with a contracted role in the clinical research study. The Study Delegation Log should then be signed by all parties.
- The study should not commence at the sites concerned until all such required contracts are in place.
- A copy of the signed model agreement must be kept in the TMF and study site file.

5.3.4 Other third party agreements

- The sponsor should issue contracts/agreements to third parties (e.g. manufacturers, non-NHS laboratories, commercial research etc), monitor contract activity and ensure that the third parties comply with the study protocol.
- A copy of the signed contracts/agreements must be kept in the TMF.

5.3.5 Financial Disclosure

- The CI or designated team member should ensure that the financial arrangements are transparent and that they follow the terms and conditions of the contract.

5.3.6 Indemnity

- The sponsor must provide indemnity for all investigators taking part in the clinical trial.

- If the sponsor is an NHS organisation they will generally only be able to provide cover in the event that clinical negligence is proven.
- If the sponsor is a University, they may also be able to provide insurance for non-negligent harm.
- The CI or designated NWORTH study team member should check that the sponsor's indemnity arrangements are in place prior to the start of recruitment and are clearly detailed in the protocol and the patient information sheet.
- The CI or trial manager must inform the sponsor of any substantial amendments made to the study protocol in order to ensure that the insurance and indemnity cover is applicable throughout the entire course of the study. Failure to do so could compromise the validity of any insurance and indemnity cover.

6. Training plan for SOP implementation

Training will be carried out in accordance with NWORTH training SOP 2.01

7. Glossary of Terms

For current definitions please refer to Ndrive/researchdata/NWORTH/SOP Glossary of terms

BU **B**angor University

CI **C**hief **I**nvestigator
The investigator with overall responsibility for the research. In a multi-site study, the CI has co-ordinating responsibility for research at all sites. All applications for ethical review should be submitted by the CI.

CTA **C**linical **T**rial **A**uthorisation
the authorisation from the MHRA to conduct a CTIMP. No CTIMP can commence in the UK without both a CTA and a favourable ethical opinion. Applications to the MHRA and the REC may be made in parallel.

CTIMP **C**linical **T**rial of an **I**nvestigational **M**edicinal **P**roduct
Any investigation in human subjects, other than a non-interventional trial, intended:

a. To discover or verify the clinical, pharmacodynamic effects of one or more medicinal products;
b. To identify any adverse reactions to one or more such products;
c. To study absorption, distribution, metabolism and excretion of one or more such products with object of ascertaining the safety or efficacy of those products.

NWORTH **C**linical **T**rial **U**nit

CV **C**urriculum **V**itae

EEA **E**uropean **E**conomic **A**rea (EU plus Iceland Leichenstein and Norway)

EU Directive
European Union Directive 2001/20 EC of the European Parliament and the Council of the European Union relating to the implementation of good clinical practice in the conduct of clinical trials of medicinal products for human use.

GCP **G**ood **C**linical **P**ractice
as defined by the ICH, see www.emea.europa.eu/pdfs/human/ich/013595en.pdf

MHRA **M**edicines and **H**ealthcare products **R**egulatory **A**gency
The competent authority for the UK in relation to the EU Directive and the Clinical Trials Regulations. MHRA (Devices) is the competent authority for the UK in relation to the medical Devices Regulations 2002.

M REC **M**ulticentre **R**esearch **E**thics **C**ommittee
In the case of multi-site studies, the REC undertaking the ethical review of the application.

NCCHTA **N**ational **C**oordinating **C**entre for **H**ealth **T**echnology **A**ssessment

NRES **N**ational **R**esearch **E**thics **Service**
The English body supervising the NHS RECs.

PI **P**rincipal **I**nvestigator
The investigator responsible for the research site where the study involves specific procedures requiring site-specific assessment. There should be one PI for each research site. In the case of a single-site study, the CI and PI will normally be the same person.

SOP **S**tandard **O**perating **P**rocedure.
Written instructions and records of procedures agreed and adopted as standard practice.

Sponsor
an individual, company, institution or organisation which takes responsibility for the initiation, management, financing (or arranging the financing) of a clinical trial.

SUSAR **S**uspected **U**nexpected **S**erious **A**dverse **R**eaction
A suspected serious adverse reaction in a CTIMP which is unexpected, meaning that its nature and severity are not consistent with the information about the medicinal product in question set out:

a. In the case of a product with a marking authorisation, in the summary of product characteristics for that product;
b. In the case of any other investigational medicinal product, in the investigator's brochure relating to the trial in question.

TMF **T**rial **M**aster **F**ile
File kept at NWORTH for each trial containing essential documents for that trial, as defined for CTIMP in section 8 of ICH GCP (www.emea.europa.eu/pdfs/human/ich/013595en.pdf) and following the MRC GCP guidelines for other trials (www.mrc.ac.uk/utilities/Documentrecord/index.htm?d=MRC002416)

Trial Site
A hospital, local government office, GP surgery etc with approval to participate in a trial. The site from which local trial activities are co-ordinated.

8. References

(1) Research Governance Framework for Health and Social care. 2nd Edition, (2005)

http://www.dh.gov.uk/en/Aboutus/Researchanddevelopment/AtoZ/Researchgovernance/DH_4002112

(2) Statutory Instrument 2004 No. 1031 The Medicines for Human Use (Clinical Trials) Regulations 2004

http://www.opsi.gov.uk/si/si2004/20041031.htm

(3) ICH Guidelines for Good Clinical Practice (GCP).

http://www.emea.europa.eu/pdfs/human/ich/013595en.pdf

(4) Model agreements for non-commercial research in the Health Service http://www.ukcrc.org/regulationgovernance/modelagreements/mnca/

(5) Bangor university Finance department web site
http://www.bangor.ac.uk/finance/index.php.en?menu=0&catid=0

9. Referenced SOPs

10. Appendices

Appendix 1 Sponsor's main responsibilities
Appendix 2 Template Letter of Sponsorship
Appendix 3 Template of CI letter of responsibility
Appendix 4 Study Delegation Log template

Appendix 1 Sponsor's main responsibilities

1. For CTIMPs

For CTIMPs the EU Directive defines a sponsor as an individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial. The UK Regulations define legal responsibilities sponsors must arrange to carry out. Sponsor's main responsibilities under the UK regulations are listed below.

Authorisation and ethics committee opinion
Request Clinical Trial Authorisation (CTA), amend the request,
Produce undertaking to allow inspection of premises in third countries (non EEA) if required
Give notice of amendments to CTA, make representations about amendments
Give notice of amendments to the protocol
Give notice a trial has ended

Good Clinical Practice and conduct
Put and keep in place arrangements to adhere to GCP (if no other person is specified)
Ensure Investigational Medicinal Products are available to subjects free of charge
Take appropriate urgent safety measures (with investigator)

Pharmacovigilance
Keep records of all adverse events reported by investigators
Ensure recording and prompt reporting of suspected unexpected serious adverse reactions (SUSARS)
Ensure investigators are informed of SUSARs
Ensure all SUSARs including those in third countries entered into European database
Provide annual list of suspected serious adverse reactions and a safety report

Appendix 1(continued) Sponsor's main responsibilities

2. For non-CTIMPs

In line with Research Governance Framework for Health and Social Care (second edition)
The sponsor is the individual, or organisation (or group of individuals or organisations) that takes on responsibility for confirming there are proper arrangements to initiate, manage and monitor, and finance a study.
For any research study covered by this research governance framework, it is for the sponsor to be satisfied that clear agreements are reached, documented and carried out, providing for proper initiation, management, monitoring and financing. Others will rely on reasonable assurances that the sponsor has taken steps to do this.

- Ensuring before a study begins that arrangements are in place: for the research team to access resources and support to deliver the research as proposed; and to allocate responsibilities for the management, monitoring and reporting of the research.

- To be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, particularly those which put the safety of individuals at risk; and to approve any modifications to the design, obtain any regulatory authority required, implement them, and make them known.

- To be satisfied with the arrangements for management and monitoring.
- Keeps in place arrangements for performance management and audit.
- To be satisfied that:
    - The research proposal respects the dignity, rights, safety and wellbeing of participants and the relationship with care professionals.
    - An appropriate process of independent expert review has demonstrated the research proposal to be worthwhile, of high scientific quality and good value for money.
    - An appropriate research ethics committee or independent ethics reviewer has given a favourable opinion.
    - In the case of a clinical trial involving a medicine, someone acting on behalf of the sponsor obtains a clinical trial authorisation, and the arrangements for the trial comply with the law.
    - Appropriate arrangements are in place for the registration of a trial.
    - The chief investigator, and other key researchers, including those at collaborating sites, have the necessary expertise and experience and have access to the resources needed to conduct the proposed research successfully.
    - The arrangements and resources proposed will allow the collection of high quality, accurate data, and the systems and resources proposed are those required to allow appropriate data analysis and data protection.
    - Arrangements proposed for the work are consistent with this research governance framework.
    - Organisations and individuals involved in the research agree the division of responsibilities between them.
    - There is written agreement about the arrangements for the management and monitoring of the study.
    - Arrangements are in place for the sponsor and other stakeholder organisation to be alerted to significant developments during the study, whether in relation to the safety of individuals or to scientific direction.
    - Agreement has been reached about compensation in the event of harm to research participants.
    - There are arrangements for the conclusion of the study including appropriate plans for disseminating the findings.

Appendix 2 Template Letter of Sponsorship (amend as required)

Sefydliad Ymchwil Gofal
Meddygol A Chymdeithasol
45 College Road
Prifysgol Bangor
Bangor Gwynedd LL57 2AS
Ffon 01248-383719
Ffacs 01248-382229
E-bost b.woods@bangor.ac.uk

Institute for Medical & Social
Care Research
45 College Road
Bangor University
Bangor Gwynedd LL57 2AS
Phone 01248-383719
Fax 01248-382229
Email b.woods@bangor.ac.uk

Insert date

To whom it may concern

Re: insert project title & funder's reference number

This letter is to confirm that Bangor University is to be identified as the sponsor for the above clinical trial. The responsibilities of sponsor accepted by Bangor University are defined in detail under the UK Regulations implementing EU Directive 2001/20/EC and set out in the Research Governance Framework for Health and Social Care (Department of Health 5 April 2004 EU clinical trials directive: sponsorship responsibilities in publicly funded trials).

Responsibilities of sponsorship have been delegated to:

Insert name, address and contact details of CI

Date letter of responsibilities signed:

Signature

Print Name

Post

Appendix 3 Template of CI letter of responsibility(amend as required)

Sefydliad Ymchwil Gofal
Meddygol A Chymdeithasol
45 College Road
Prifysgol Bangor
Bangor Gwynedd LL57 2AS
Ffon 01248-383719
Ffacs 01248-382229
E-bost b.woods@bangor.ac.uk

Institute for Medical & Social
Care Research
45 College Road
Bangor University
Bangor Gwynedd LL57 2AS
Phone 01248-383719
Fax 01248-382229
Email b.woods@bangor.ac.uk

Confirmation that the undersigned accepts the responsibilities of Chief Investigator for the project *insert project title* sponsored by Bangor University.

I confirm that:

1. I have the education, training and experience needed to conduct this trial (See attached CI CV).

2. I have access to the resources and support necessary to conduct this trial accurately, efficiently and expeditiously.

3. I accept the responsibilities of Chief Investigator:
   A. To protect the dignity, rights, safety and well-being of participants in this trial.
   B. To secure all necessary approvals, including clinical trial authorisation, contracts with research partners, and approvals relating to ethics, funding, insurance, NHS research governance, scientific peer review and sponsorship.
   C. To ensure that the proposed sample size is feasible and gives enough statistical power to test plausible hypotheses.
   D. Through the trial manager or coordinator, to maintain an auditable record of these approvals and all other essential documents.
   E. To ensure that all Principal Investigators (Pls) have access to the resources and support needed to complete the trial accurately, efficiently and expeditiously.
   F. Through the trial manager or coordinator, to ensure that all PIs, and staff employed to work on this trial whether by Bangor University or by its formal collaborators ("trial staff"), are qualified and trained to fulfil the duties assigned to them.
   G. To ensure that all PIs and trial staff, receive copies of, and agree to adhere to, the currently approved protocol (including the approved list of participating sites, the currently approved Research Ethics Committee documents, and where applicable the Clinical Trial Authorisation (CTA).
   H. Through the trial manager or coordinator, to maintain an auditable record of the duties assigned to all PIs and trial staff, qualifications they hold, and the training they receive, including training in the currently approved protocol, GCP and relevant legislation,
   I. to ensure that all PIs and trial staff conduct the trial in accordance with the currently approved protocol;
      i. the principles of Good Clinical Practice in clinical trials (GCP);
      ii. relevant legislation, including the Data Protection Act 1998;
      iii. the research funder's terms and conditions; and
      iv. the Standard Operating Procedures (SOPs) developed by NWORTH or site/trial specific procedures
   J. To store the trial drug in a safe and secure fashion (where applicable)
   K. To inform trial participants' general practitioners, through the PIs, about their participation and progress in the trial, if they give extra consent according to the currently approved protocol.

L. To implement quality assurance procedures designed to ensure and record that, inter alia, trial participants give informed consent to participate and receive rigorous randomisation & accurate administration of the trial drug (all in accordance with the currently approved protocol); and that all trial data are as accurate, complete and verifiable as the trial resources permit.

M. To report every *six* months through the trial manager or coordinator to the Chair of the trial Data Monitoring & Ethics Committee, and if necessary to PIs and the responsible Research Ethics Committee, on all adverse events defined in the trial protocol.

N. To report every *six* months through the trial manager or coordinator to the Chair of the Trial Steering Committee, and if necessary to PIs, staff and the responsible Research Ethics Committee, on newly published findings, relating to the trial drug (or other procedures defined in the protocol) and identified through an agreed search strategy, that could adversely affect the safety or wellbeing of trial participants.

O. To report trial data as accurately, completely & expeditiously, and as consistently with the principles of statistical inference, as the trial resources permit.

P. To develop and implement an explicit publication plan for the trial, including an authorship policy and summaries of all currently proposed publications.

Q. To provide the Medicines & Health products Regulatory Authority, the University as sponsor, and any other authorised auditor with access on request to the documents required by clauses D, L, M, N , O and P (where applicable).

Name of Chief Investigator: ***insert name***

Signature of Chief Investigator:

Insert Date:

Note: section 3 to be amended for specific trial requirements

Appendix 4 Study Delegation Log template

Delegation Log

Name of trial:	**Protocol No:**
Name of Principal Investigator:	**Centre:**

Full Name & Title	Signature	Initials	Role in trial *	Duration		PIs Signature
				From	To	

*The responsibilities associated with each role are listed in the following table

TRIAL RESPONSIBILIES

*(*remove sections that are not relevant to specific trials add any additional roles and responsibilities*)*

Role	Responsibilities
Chief Investigator	A. To protect the dignity, rights, safety and well-being of participants in this trial. B. To secure all necessary approvals, including clinical trial authorisation, contracts with research partners, and approvals relating to ethics, funding, insurance, NHS research governance, scientific peer review and sponsorship. C. To ensure that the proposed sample size is feasible and gives enough statistical power to test plausible hypotheses. D. Through the trial manager or coordinator, to maintain an auditable record of these approvals and all other essential documents. E. To ensure that all Principal Investigators (PIs) have access to the resources and support needed to complete the trial accurately, efficiently and expeditiously. F. Through the trial manager or coordinator, to ensure that all PIs, and staff employed to work on this trial whether by Bangor University or by its formal collaborators ("trial staff"), are qualified and trained to fulfil the duties assigned to them. G. To ensure that all PIs and trial staff, receive copies of, and agree to adhere to, the currently approved protocol (including the approved list of participating sites, the currently approved Research Ethics Committee documents, and where applicable the Clinical Trial Authorisation (CTA). H. Through the trial manager or coordinator, to maintain an auditable record of the duties assigned to all PIs and trial staff, qualifications they hold, and the training they receive, including training in the currently approved protocol, GCP and relevant legislation, I. to ensure that all PIs and trial staff conduct the trial in accordance with the currently approved protocol; I. the principles of Good Clinical Practice in clinical trials (GCP); II. relevant legislation, including the Data Protection Act 1998; III. the research funder's terms and conditions; and IV. the Standard Operating Procedures (SOPs) developed by NWORTH or site/trial specific procedures J. To store the trial drug in a safe and secure fashion (where applicable) K. To inform trial participants' general practitioners, through the PIs, about their participation and progress in the trial, if they give extra consent according to the currently approved protocol. L. To implement quality assurance procedures designed to ensure and record that, inter alia, trial participants give informed consent to participate and receive rigorous randomisation & accurate administration of the trial drug (all in accordance with the currently approved protocol); and that all trial

	data are as accurate, complete and verifiable as the trial resources permit. M. To report every *six* months through the trial manager or coordinator to the Chair of the trial Data Monitoring & Ethics Committee, and if necessary to PIs and the responsible Research Ethics Committee, on all adverse events defined in the trial protocol. N. To report every *six* months through the trial manager or coordinator to the Chair of the Trial Steering Committee, and if necessary to PIs, staff and the responsible Research Ethics Committee, on newly published findings, relating to the trial drug (or other procedures defined in the protocol) and identified through an agreed search strategy, that could adversely affect the safety or wellbeing of trial participants. O. To report trial data as accurately, completely & expeditiously, and as consistently with the principles of statistical inference, as the trial resources permit. P. To develop and implement an explicit publication plan for the trial, including an authorship policy and summaries of all currently proposed publications. Q. To provide the Medicines & Health products Regulatory Authority, the University as sponsor, and any other authorised auditor with access on request to the documents required by clauses D, L, M, N , O and P (where applicable).
Principal Investigator	A. To protect the dignity, rights, safety and well-being of participants in this trial. B. To ensure the necessary local approvals such as approvals relating to ethics, funding, insurance, NHS research governance, scientific peer review and sponsorship are in place. C. To complete the trial accurately, efficiently and expeditiously in accordance to the currently approved protocol and the resources and support available. D. To ensure they and their trial staff are qualified and trained to fulfil the duties assigned to them. E. To ensure that they and their trial staff, receive copies of, and agree to adhere to, the currently approved protocol and where applicable the summary of product characteristics F. To maintain an auditable record of the duties assigned to their trial staff, qualifications they hold, and the training they receive, including training in the currently approved protocol, GCP and relevant legislation. G. To ensure that they and their trial staff conduct the trial in accordance with – i. the currently approved protocol; ii. the principles of Good Clinical Practice in clinical trials (GCP); iii. relevant legislation, including the Data Protection Act 1998; iv. the research funder's terms and conditions; and v. the Standard Operating Procedures (SOPs) developed by NWORTH (where applicable). H. To store the trial drug in a safe and secure fashion (where applicable). I. To inform trial participants' general practitioners about their participation and progress in the trial, if they give extra consent according to the currently approved protocol. J. To implement quality assurance procedures designed to ensure and record that, inter alia, trial

	participants give informed consent to participate and receive rigorous randomisation & accurate administration of the trial (all in accordance with the currently approved protocol); and that all trial data are as accurate, complete and verifiable as the trial resources permit. K. To ensure local trial data is recorded accurately, completely & expeditiously in participants' Case Report Form in the trial database. L. To delegate trial related tasks to appropriately qualified trial staff M. To ensure that all patients are screened in accordance to the currently approved protocol N. To ensure that all trial participants have given informed consent O. To ensure adequate supervision and monitoring of trial participants P. To ensure adverse events occurring locally are documented and followed up in accordance with the currently approved protocol Q. To provide regular progress reports to the trial co-ordinating centre and Trial Management Group (TMG).
Researcher	A. To manage the daily running of the research centre B. To be responsible for and to undertake all the research duties within the centre in accordance with the currently approved protocol, GCP and trial regulations C. To engage with local GPs and other care professionals to recruit patients into the trial (where applicable) D. To organise, arrange and assist local trial care professionals in conducting the initial screening interview with potential participants E. To collect, record and maintain local trial data accurately, completely & expeditiously in participants' Case Report Form in the trial database. F. To maintain and appropriately file all local trial documents G. To ensure timely recruitment of trial participants at the local centre H. To carryout the duties in accordance to available resources and to manage the centre's budget I. To organise and plan all local trial appointments J. To take blood samples in accordance with the currently approved protocol (where applicable) K. To document the supply, handling and accountability of all local trial drugs L. To comply with the randomisation procedures for participants allocation

	M. To comply with the SOP for dispense trial N. To report any Serious Adverse Events to PI immediately in accordance with the currently approved protocol O. To regularly report progress to the trial co-ordinating centre and Research Group (RG).
Co-ordinator/Manager	A. To ensure the overall day-to-day co-ordination and management of the trial B. To establish procedures that ensure adherence to trial protocols and administrative requirements. C. To ensure that all PIs, and staff employed to work on this trial whether by Bangor University or by its formal collaborators ("trial staff"), are qualified and trained to fulfil the duties assigned to them and to maintain an up-to-date record of staff training and CVs. D. To ensure that all PIs and trial staff, receive copies of, and agree to adhere to, the currently approved protocol (including the approved list of participating sites, the currently approved Research Ethics Committee documents, and where applicable the Clinical Trial Authorisation (CTA). E. To maintain an auditable record of the duties assigned to all PIs and trial staff, qualifications they hold, and the training they receive, including training in the currently approved protocol, GCP and relevant legislation. F. To ensure that all PIs and trial staff conduct the trial in accordance with – i. the currently approved protocol; ii. the principles of Good Clinical Practice in clinical trials (GCP); iii. relevant legislation, including the Data Protection Act 1998; iv. the research funder's terms and conditions; and v. any applicable Standard Operating Procedures (SOPs) developed by NWORTH. G. To ensure that the trial drugs are stored in a safe and secure fashion and that an auditable log of trial drug deliveries and dispensing are maintained (where applicable) H. To implement quality assurance procedures designed to ensure and record that, inter alia, trial participants give informed consent to participate and receive rigorous randomisation & where applicable accurate administration of the trial drug (all in accordance with the currently approved protocol); and that all trial data are as accurate, complete and verifiable as the trial resources permit I. To ensure timely recruitment of trial participants with secure randomisation processes and subsequent efficient and effective data management J. To monitor trial progress to ensure compliance with and adherence to the project plan and to identify, evaluate and rectify problems K. Management of the trial budget(s) and maintenance of the accounts L. Act as the point of contact for all external and internal agencies M. To liaise with the Trials Steering Committee and Data Monitoring and Ethics Committee with a

	particular view on compliance with Research Governance, Good Clinical Practice, Data Protection and Ethical Requirements N. To report every six months to the Chair of the trial Data Monitoring & Ethics Committee, and if necessary to PIs and the responsible Research Ethics Committee, on all adverse events defined in the trial protocol O. To report every six months to the Chair of the Trial Steering Committee, and if necessary to PIs, staff and the responsible Research Ethics Committee, on newly published findings, relating to the trial drug or other procedures defined in the protocol and identified through an agreed search strategy, that could adversely affect the safety or wellbeing of trial participants P. To report trial data as accurately, completely & expeditiously, and as consistently with the principles of statistical inference, as the trial resources permit. Q. To provide the Medicines & Health products Regulatory Authority (where applicable), the University as sponsor, and any other authorised auditor with access on request to the documents required by clauses D, L, M, N , O and P R. To co-ordinate the preparation and publication of data, reports and information, ensuring that these meet legislative, contractual and ethical requirements S. Understand the requirements of the various controlling bodies, agencies and frameworks, guiding the project in conforming to those requirements and co-ordinating any necessary audit processes T. To provide regular and ad hoc information, both written and verbal, to all the trial participants and sponsors, to include reports, updates, guidance and proformed commitments U. To work with the CI to ensure that the trial is meeting its targets, is producing meaningful output and to predict and plan any changes that warrant requests to changes in protocol, funding or time V. To ensure inclusion of consumer group representatives at the appropriate levels and times. W. To plan and support meetings and work of various groups and bodies associated with the trial X. To create and maintain of all trial files, including the trial master file, and oversight of site files Y. To provide assurance that personal and confidential information is restricted to those entitled to know Z. To maintain an auditable record of all approvals and all other essential documents. AA. To maintain an auditable record of the duties assigned to all PIs and trial staff, qualifications they hold, and the training they receive, including training in the currently approved protocol, GCP and relevant legislation
Trial Secretary	A. To support the trial co-ordinator/manager in the daily running of the trial B. To support the needs of the Trial Management Group and Research Group C. To organise face-to-face meetings and audio conferences on behalf of the Trial coordinating team

	D. To prepare agendas for meetings, take minutes and ensure all actions are carried out E. To support the local researchers where necessary and where resources allow F. To set up and maintain a filing system for trial G. To liaise with the Universities support services H. To maintain the trial web page through regular updates I. To support trial team in publicising the trial J. To assist with the production of reports ,summaries and publications K. To undertake other as yet unspecified clerical duties necessary for the smooth running of the trial
Statistician	A. To contribute statistical expertise during the conduct of the trial B. To devise the data analysis plan C. To analyse trial data D. To report trial results to the DMEC E. To ensure the randomisation process is secure and working efficiently F. To contribute to production of reports, summaries and publications G. To advise the trial team on the development of the database
IT	A. To design, develop and maintain the trial databases in accordance with trial specification B. To ensure that the data collection databases are installed at each of the recruiting centres C. To develop a mechanism for transferring anonymised trial data to the master database at the coordinating centre D. To advise on technical issues related to the database E. To provide remote IT support F. Training research staff in the use of the database
Pharmacy Department	A. To take delivery of the trial drugs. B. To check the shipment details. C. To attach the pharmacy address details to each trial package.

	D. To give researchers trial drug packages and to sign the drug accountability log E. To keep the unblinding procedure for the trial drugs in a safe place in and out of hours. F. To break the code of a trial drug package if required to do so in an emergency. G. To destroy unused trial drugs once a participant has completed the trial and maintain a record of destruction.
Laboratory	A. to carry out analysis in accordance with agreed contract. B ensure procedures are established and followed for: i. sample receipt and chain of custody ii. method validation iii. repeat analysis iv. data recording v. reporting vi. equipment maintenance and calibration vii. computer systems have the appropriate level of validation C to send results to.....
List any other trial specific roles and responsibilities	

Appendix 3: MHRA GCP Guide

28/01/2015

Responsibilities of Sponsor for Clinical Trial of Investigational Medicinal Product

From the MHRA GCP guide:

The sponsor has specific legal responsibilities as defined in the SI 2004/1031. These relate to obtaining and maintain the authorisation for clinical trials and research ethics committee (REC) opinion, GCP and trial conduct, pharmacovigilance and IMP manufacture and labelling. These responsibilities are summarised in tables 1.1. (*this is in the attached download from the NHS R&D forum)*

The sponsor can formally delegate one or more of the functions of sponsorship; for example, a commercial pharmaceutical company may employ a contract research organisation (CRO) to perform monitoring activities or an NHS trust may delegate curtain functions to the chief investigator of a clinical trial……

Ultimately the sponsor remains accountable for all functions of sponsorship whether delegated or not. This is stated in Regulation 3(12) of SI 2004/1031

From the CT Toolkit

Sponsorship is required for studies under the Research Governance Framework(s) including trials that that fall within the scope of the Clinical Trial Regulations. It may take some time to secure a sponsor(s), so identification of the sponsor must be considered early in the planning process.

For Clinical Trials of Investigational Medicinal Products (CTIMPs), the European Commission Directive 2001/20/EC define the sponsor as: *An individual, company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial.*

The sponsor therefore is not simply responsible for ensuring there are adequate funds for the trial and for CTIMPs; the Clinical Trials Regulations define legal responsibilities that the sponsor **must** arrange to carry out. These legal responsibilities should not be confused with liability for the harm of a subject. In 2004, the

Department of Health and Universities UK published Responsibilities, Liabilities and Risk Management in Clinical Trials (PDF, 160 KB) to clarify the implications of the Clinical Trials Regulations.

Before initiating a trial, the sponsor should define, establish and allocate all trial-related duties and functions. The NHS R&D Forum Sponsorship Principles document (pdf, 101.04 KB) provides a comprehensive summary of the legal responsibilities that an organisation sponsoring a CTIMP must arrange to carry out. This document also describes various models of sponsorship that are possible under the Clinical Trials Regulations and the allocation of responsibilities, duties or functions.

For CTIMPs, the person(s) responsible for the sponsor's functions must be named on the Clinical Trial Authorisation (CTA). If the sponsor of a CTIMP with sites in the European Economic Area (EEA) does not reside within the EEA, a legal representative should be appointed. Further guidance can be found in the Sponsorship Principles document (pdf, 101.04 KB) which also includes advice and future developments for UK sponsors of international CTIMPs.

As of 21 July 2014, sponsors are also responsible for the mandatory posting of clinical trial summary results within EudraCT. Results should be submitted within six or twelve months following the end of a trial, depending on the type of trial.

Further reading:

- In England, NHS organisations that sponsor trials, conduct these activities in line with The Research support Services Framework. Please see Annex 5 of the Support Services Framework Documents
- Resources relation to Indemnity and Insurance:
- Insurance and compensation in the event of injury in Phase I clinical trials : Guidance developed by the Association for the British Pharmaceutical Industry, the BioIndustry Association and the Clinical Contract Research Association, in consultation with the Department of Health and the National Research Ethics Service.
- EudraCT trial results: modalities and timing of posting document.

Appendix 4: Extracts from: Department of Health Research Governance Framework for Health and Social Care

Second edition, 2005

Sponsor

Individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study. (A group of individuals and/or organisations may take on sponsorship responsibilities and distribute them by agreement among the members of the group, provided that, collectively, they make arrangements to allocate all the responsibilities in this research governance framework that are relevant to the study.)

1. Confirming that everything is ready for the research to begin:

- taking on responsibility for putting and keeping in place arrangements to initiate, manage and fund the study;
- satisfying itself the research protocol, research team and research environment have passed appropriate scientific quality assurance;
- satisfying itself the study has ethical approval before it begins;
- for clinical trials involving medicines , seeking a clinical trial authorisation and taking arrangements for investigational medicinal products.

2. Satisfying itself that arrangements are kept in place for good practice in conducting the study, and for monitoring and reporting, including prompt reporting of suspected unexpected serious adverse events or reactions.

3.8 RESPONSIBILITIES OF THE SPONSOR

3.8.1 The sponsor is the individual, or organisation (or group of individuals or organisations) that takes on responsibility for confirming there are proper arrangements to initiate, manage and monitor, and finance a study. For any research that takes place in the context of the NHS or social care services in England there must be a sponsor. Normally, the sponsor will be one of the organisations taking the lead for particular aspects of the arrangements for the study. It may be the Chief Investigator's employing organisation, or the lead organisation providing health or social care, or the main funder. If the sponsor is outside the United Kingdom, it must

have a legal representative in the United Kingdom.[21] For any research study covered by this research governance framework, it is for the sponsor to be satisfied that clear agreements are reached, documented and carried out, providing for proper initiation, management, monitoring and financing. Others will rely on reasonable assurances that the sponsor has taken steps to do this.

3.8.2 The sponsor is responsible for ensuring before a study begins that arrangements are in place:

- for the research team to access resources and support to deliver the research as proposed; and
- to allocate responsibilities for the management, monitoring and reporting of the research.

The sponsor also has to be satisfied there is agreement on appropriate arrangements to

- record, report and review significant developments as the research proceeds, particularly those which put the safety of individuals at risk; and to
- approve any modifications to the design, obtain any regulatory authority required, implement them, and make them known.

3.8.3 It is the sponsor's responsibility to be satisfied with the arrangements for management and monitoring. Normally, if the Chief Investigator's employer takes on the sponsor's responsibilities (alone or as a member of a group), it will assume responsibility for operating the management and monitoring systems in collaboration with the employers of other members of the research team.

Exceptionally, it may be inappropriate for the Chief Investigator's employer to take responsibility for the management and monitoring of a study. In that case, the sponsor should make arrangements with one or more other organisations that will operate the management and monitoring systems.

3.8.4 Provided the sponsor keeps in place arrangements for performance management and audit, the responsibility for design and management may be delegated to the research team. The extent of delegation should be specified, even for a research team with proven expertise and track record. Commercial sponsors may arrange for their own audit processes.

3.8.5 When no external sponsor takes on responsibility for it, a study may proceed only if a health or social care organisation takes on sponsorship. For example, an NHS trust or a Council with Social Services Responsibilities (CSSR) may be willing and able to act as the sponsor for research that does not have an external sponsor (sometimes called "own account" research).

3.8.6 When research is for research training purposes, research supervisors normally carry out the sponsorship responsibilities on behalf of their employers. Exceptionally, a university may authorise a suitably experienced postgraduate student to carry out these responsibilities on its behalf.

3.8.7 It is the sponsor's responsibility to be satisfied that:

- The research proposal respects the dignity, rights, safety and wellbeing of participants and the relationship with care professionals.
- An appropriate process of independent expert review has demonstrated the research proposal to be worthwhile, of high scientific quality and good valuefor money.
- An appropriate research ethics committee or independent ethics r eviewer[22] has given a favourable opinion.
- In the case of a clinical trial involving a medicine, someone acting on behalf of the sponsor obtains a clinical trial authorisation, and the arrangements for the trial comply with the law.
- Appropriate arrangements are in place for the registration of a trial.
- The chief investigator, and other key researchers, including those at collaborating sites, have the necessary expertise and experience and have access to the resources needed to conduct the proposed research successfully.
- The arrangements and resources proposed will allow the collection of high quality, accurate data, and the systems and resources proposed are those required to allow appropriate data analysis and data protection.
- Arrangements proposed for the work are consistent with this research governance framework.
- Organisations and individuals involved in the research agree the division of responsibilities between them.
- There is written agreement about the arrangements for the management and monitoring of the study.

• Arrangements are in place for the sponsor and other stakeholder organisations to be alerted to significant developments[23] during the study, whether in relation to the safety of individuals or to scientific direction.

• Agreement has been reached about compensation in the event of harm to research participants[25]; and if any organisation, or the sponsor itself offers compensation without proof of negligence, it has made the necessary financial arrangements.

• There are arrangements for the conclusion of the study including appropriate plans for disseminating the findings. Scientific judgements made by the sponsor in relation to these responsibilities should be based on independent and expert advice. The sponsor is expected to assist any enquiry, audit or investigation related to the funded work.

3.9 RESPONSIBILITIES OF UNIVERSITIES AND OTHERS EMPLOYING RESEARCHERS

3.9.1 Employers of staff undertaking health and social care research have responsibility for developing and promoting a high quality research culture in their organisation and for ensuring that their staff are supported in, and held to account for, the professional conduct of research. This involves careful attention to training, career planning and development, and the use of clear codes of practice and systems for monitoring compliance, dealing with noncompliance or misconduct, and learning from errors and complaints. These responsibilities apply to both private and public sector employers.

3.9.2 Organisations that employ chief investigators and other researchers have responsibility for ensuring that those researchers understand and discharge the responsibilities set out for them in this frame work, and under the law. They may do this, for example, through terms of employment, staff handbooks, and training. They will normally take on some or all of the responsibility for ensuring that a study is properly managed and for monitoring its pr ogress. When the employing organisation is not the sponsor, it should agree its responsibilities with the sponsor and the organisation(s) providing care. The sponsor has to be satisfied with the

arrangements for the management of a study; and that there is agreement on appropriate arrangements for monitoring and reporting.

3.9.3 Employers should ensure there are agreements between them and their staff and between them and research funders and care organisations about ownership, exploitation and income from any intellectual property that may arise from research conducted by their employees. They have a responsibility for ensuring that employees identify and protect intellectual property.

3.9.4 Universities and other employers of staff engaged in research are responsible for:

- compliance with all current employment and health and safety legislation;
- demonstrating the existence of clear codes of practice in other areas for their staff, and mechanisms to monitor and assess compliance;
- ensuring that investigators and other research staff are aware of, understand and comply with this framework;
- discharging their agreed role in the management and monitoring of work undertaken by their organisation;
- demonstrating systems for continuous professional development of staff at all levels;
- having agreements and systems to identify, protect and exploit intellectual property;
- ensuring that they are able to compensate anyone harmed as a result of negligence on the part of staff, students and others for whom they have liability; and, if they have agreed to do so, to compensate participants for non-negligent harm arising from the research;
- Having systems to detect and address fraud, and other scientific or professional misconduct by their staff.
- Having systems to process, address and learn lessons from any errors or complaints brought against their employees.
- Permitting and assisting in any statutory inspection, audit, or investigation arising from errors or complaints associated with

Appendix 5: HCMS SPONSORSHIP STANDARD APPROVAL 'SIGN OFF' LETTER AND FORM- NWORTH STUDIES, BANGOR UNIVERSITY

Prifysgol Bangor 

Etc.

9.3.2015

To whom it may concern

Study title: .
REC reference:
Protocol number:
EudraCT number:
IRAS project ID:

This letter is to confirm that Bangor University is to be identified as the sponsor for the above clinical trial. The responsibilities of sponsor accepted by Bangor University are defined in detail under the UK Regulations implementing EU Directive 2001/20/EC and set out in the Research Governance Framework for Health and Social Care (Department of Health 5 April 2004 EU clinical trials directive: sponsorship responsibilities in publicly funded trials).

Responsibilities of sponsorship have been delegated to the following team as part of the operational procedures documented in the HCMS AEC Policy and Procedures (V2/2015), accordingly completing the necessary review, approval and monitoring processes:

Dr Sion Williams (HCMS AEC Chair/ UREC & Trial Standing Group Representative)
Dr Huw Roberts (Sponsor Representative/ HCMS AEC)
Gwenan Hine (UREC & Trial Standing Group Representative/ Head of Compliance, Planning & Governance)
Chris Benson (Bangor University Insurance)

Details of Chief Investigator:

Date letter of responsibilities signed:

Signature:

Print Name: Dr Sion Williams

Post: Chair HCMS AEC

Signature:

Print Name: Professor Jo Rycroft-Mallone

Post: Head of School

HCMS AEC Clinical Trial Sponsorship approval Checklist

HCMS AEC and UREC Bangor University
Proposal Title/number:

Study title:	A randomised controlled trial of adalimumab injection compared with placebo for patients receiving physiotherapy treatment for sciatica.
REC reference:	15/WA/0105
Protocol number:	12/201/02
EudraCT number:	2015-000636-15
IRAS project ID:	171596

Review completed and approved	*Delegated role & Area of responsibility*	*Post holder*	*Checked*
1. Application reviewed and comments addressed	**UREC & Trial Standing Group Representative/ Head of Compliance, Planning & Governance**	Gwenan Hine	Signature
2. Application reviewed and comments addressed	**Sponsor Representative/ HCMS AEC**	Dr Huw Roberts	Signature
3. Application reviewed and comments addressed	**Bangor university Insurance**	Chris Benson	Signature
4. Application reviewed and comments addressed	**HCMS AEC Chair/ UREC & Trial Standing Group Representative**	Dr Sion Williams	Signature

Agreement to proceed and monitor completed and approved:

Signed:

Post: Chair HCMS AEC

Date**:**

Appendix 6: Human Tissue Act

Ethical approval must be given by an NHS REC either where a study involves collection, storage or use of tissue samples from NHS patients, or in any case where a legal requirement for ethical review applies under the Human Tissue Act.

A legal requirement would apply in any of the following cases:

1. "Relevant material" (i.e. material consisting of or including cells) will be stored/used for the purpose of the study other than under the terms of a Licence from the Human Tissue Authority for scheduled purposes (including research). In such circumstances, ethical approval from a "research ethics authority" provides exemption from licensing for the duration of the project. A research ethics authority is defined in Regulations in a way that means it must be an NHS REC. This applies equally in England, Wales and Northern Ireland.
2. The study involves storage/use of relevant material from the living without specific consent for research. In such circumstances, the material must be non-identifiable to the researcher and ethical approval is required from a research ethics authority (i.e. an NHS REC).
3. The study involves analysis of DNA in tissue from the living without specific consent for this. In such circumstances, the material must be non-identifiable to the researcher and ethical approval is required from a research ethics authority (i.e. an NHS REC).

Where legal requirements apply, the fact that the donors are not NHS patients does not affect the need for ethical approval from a NHS REC. A university ethics committee could not give approval for the purposes of the Act.

Where no legal requirement applies and the donors are not NHS patients, ethical approval from an NHS REC is not required.

For guidance on the standards to apply to storage, disposal and consent we would suggest you look at the HTA Codes of Practice, which cover these areas in detail and are available at www.hta.gov.uk and

www.bangor.ac.uk/ar/ro/recordsmanagement/HTALicence.php. It is good practice for donors to be informed about who will store the tissue, who will have access, what purposes it will be used for and how their confidentiality will be protected.