Funded by NIHR Health Technology Programme (HTA ref: 12/196/08); Protocol Version 1.0 (18Dec2014)

COmmunity based **R**ehabilitation after **K**nee **A**rthroplasty (CORKA). A prospective individually randomised two arm randomised controlled trial.

ISRCTN13517704

HTA - 12/196/08

OCTRU - CTU0013

Trial Steering Committee (TSC) Charter

Version 2.0, 11May2015

(developed using MRC Clinical Trials Unit template TSC Charter version 1.02, 13-Mar-2006)

Authorised by:

Name:	Karen Barker	Role:	Chief Investigator
Signature:		Date:	

Prepared by

Name:	Michael Maia Schlüssel	Role:	Trial Statistician
Signature:		Date:	

CONTENT	DETAILS OF TSC
1. Introduction	
Name (& Sponsor's ID) of trial	CORKA: Community based rehabilitation after knee arthroplasty. A pragmatic multicentre prospective individually two arm randomised controlled trial with blinded outcome assessment at 6 and 12 months. Funder: NIHR HTA - 12/196/08 Sponsor: University of Oxford ISRCTN13517704
Objectives of trial, including interventions being investigated	The primary objective is to determine if a multi-component rehabilitation program improves the outcome of patients who undergo a KR at 12 months after surgery. Secondary objectives includes to assess the impact of the rehabilitation program on physical function and quality of life, as well as the cost effectiveness analysis of the new therapy versus usual care rehabilitation and a qualitative analysis of a subsample of both participants and study staff to obtain in-depth views about the intervention and how it is delivered. The trial aims to recruit a minimum of 632 participants, to be randomly allocated (1:1 ratio) to one of two groups: **Control:** those who will receive the usual care, as the rehabilitation option; **Intervention:** those who will receive a community-based rehabilitation program; the intervention to be tested. Endpoints, to be assessed at 6 and 12 months post-surgery, include the application of Late Life Function and Disability Instrument (LLFDI) and measurements of disease specific function by the Oxford Knee Score (OKS); physical activity by the Physical Activity Scale for the Elderly (PASE) questionnaire; physical function by specific physical performance tasks; pain using the visual analogue score (VAS); health economics using the EQ5D-5L and an estimate of the intervention's cost utility, from both the NHS and a societal perspective. A trial summary diagram is included in Figure 1.
Outline of scope of Charter	The purpose of this document is to describe the membership, terms of reference, roles, responsibilities, authority, decision-making and relationships of the Trial Steering Committee (TSC) for this trial, including the timing of meetings, methods of providing information to and from the TSC, frequency and format of meetings and relationships with other trial committees.

CONTENT	DETAILS OF TSC
Facilitation	The Trial Coordinator in the Critical Care, Trauma and Rehabilitation (CCTR) Trials Group part of the Oxford Clinical Trials Research Unit (OCTRU) at the University of Oxford will be nominated as a Facilitator for the trial. The Facilitator will be responsible for the organisation of meetings and should be copied into all communications with and between the TSC.
2. Roles and responsibilities	
A broad statement of the aims of the TSC	To act as the oversight body for this trial on behalf of the Sponsor and Funder.
Terms of reference	The role of the TSC is to provide oversight for the trial. It should also provide advice through its independent Chair to the Project Management Group (TMG), the funder (HTA) and OCTRU CTU on all aspects of the trial.
Specific roles of TSC	The specific roles include: • provide expert oversight of the trial • maintain confidentiality of all trial information that is not already in the public domain • make decisions as to the future continuation (or otherwise) of the trial • monitor recruitment rates and encourage the TMG to develop strategies to deal with any recruitment problems • approve the protocol • review regular reports of the trial from the clinical trials unit (sent on behalf of the TMG) • receive letters of feedback from the DSMC and consider their recommendations • assess the impact and relevance of any accumulating external evidence • monitor completeness of data and comment on strategies from TMG to encourage satisfactory completion in the future • monitor follow-up rates and review strategies from TMG to deal with problems • censure sites that are deviating from the protocol • approve any amendments to the protocol, where appropriate • approve any proposals by the TMG concerning any change to the design of the trial, including additional sub studies • oversee the timely reporting of trial results • approve / comment on the publication policy

CONTENT	DETAILS OF TSC
	• approve / comment on the main trial manuscript • approve external or early internal requests for release of data or subsets of data or samples including clinical data.
3. Before or early in the trial	
Whether the TSC will have input into the protocol	All potential independent TSC members have had an opportunity to comment on the protocol. Before recruitment begins the trial will have undergone review by the Sponsor and Funder (e.g. peer review for public sector trials), scrutiny by other trial committees and a research ethics committee. Therefore, if a potential independent TSC member has major reservations about the trial (e.g. the protocol, the logistics, ethical concerns) they should report these to OCTRU CTU and may decide not to accept the invitation to join. TSC members should be constructively critical of the ongoing trial, but also supportive of aims and methods of the trial.
Trial specific issues	
Any issues specific to the disease under study	Not applicable
Any specific regulatory issues	Not applicable
Any other issues specific to the treatment under study	Not applicable
Whether members of the TSC will have a contract	TSC members will not be asked to formally sign a contract but should formally register their agreement to join the group by confirming (1) that they agree to be a member of the TSC and (2) that they agree with the contents of this Charter. Any potential competing interests should be declared at the same time. Members should complete and return the form in Annexes 1 or 2. Any observers (attendees who are not members) will sign a confidentiality agreement on the first occasion they attend a meeting (Annexe 3).
4. Composition	
Membership and size of the TSC	The majority of members of the TSC, including the Chair, should be independent 1of the trial (see section 5). Non-independent members will also be part of the TSC. The members of the TSC for this trial are: Prof Anne Forster (Chair) (Independent member)

[1] Independence is defined in Table 1 of Annexe 1

CONTENT	DETAILS OF TSC
	Dr Karen Barker (Chief Investigator, Non-Independent Member) Mrs Elaine Cook (Lay Independent Member) Dr Derek Kyte (Independent Member) Dr Mark Kelson (Independent Member) Dr Mindy Cairns (Independent Member) Ms Rachel Dalton (Independent Member) Prof Jenny Butler (Independent Member) Professor Martin Underwood (Independent Member) Professor Avril Drummond (Independent Member) Jonathan Room (Research Physiotherapist, Non-independent Member) Nicola Kenealy (Trial Coordinator, Observer) Susan Dutton (OCTRU Lead Statistician, Observer) Michael Maia Schlüssel (Trial Statistician, Observer)
The Chair, how they are chosen and the Chair's role.	The Chair has previous experience of serving on trial committees and experience of Chairing meetings, and will be able to facilitate and summarise discussions.
The responsibilities of the Facilitator	The Facilitator will be the Trial Coordinator in the Critical Care, Trauma and Rehabilitation (CCTR) Trials Group part of the Oxford Clinical Trials Research Unit (OCTRU) at the University of Oxford. The Facilitator will be responsible for arranging meetings of the TSC, coordinating reports, producing and circulating minutes and action points. The Facilitator will be the central point for all TSC communications between the TSC and other bodies; will be copied into all correspondence between TSC members; and will be kept aware of trial issues as they arise.
The responsibilities of the trials unit team	The TMG will produce a short report on the trial before each meeting of the TSC.
The responsibilities of the CI and other members of the TMG	The CI (and, if appropriate, other TMG members) is an important member of the TSC and no major decisions should be made without their involvement.
The responsibilities of the observers	Additional observers may be in attendance through (parts of) the TSC meetings in order to provide input on behalf of the trials unit, the trial's Sponsor/Funder or to provide specific relevant expertise.
5. Relationships	

CONTENT	DETAILS OF TSC
Relationships with Chief Investigators, other trial committees (e.g. TMG and DSMC), Sponsor/Funder and regulatory bodies	The responsibilities of each trial committee are detailed in the protocol and in the respective Charters. The relationships between these groups are summarised in Figure 2.
Advisory and executive bodies	The TSC is the oversight body and is delegated the roles in Section 2 by the Sponsor. All substantial issues regarding the trial must go to the TSC for consideration. The DSMC is advisory to the TSC.
Payments to TSC members	Members will be reimbursed for reasonable travel costs (standard rail fares and if travelling by car, mileage up to the amount of the equivalent rail fare). No other payments or rewards would be given to professional members. Honoraria will be paid to lay members.
The need for TSC members to disclose information about any real or potential competing interests	Competing interests should be disclosed. These are not restricted to financial matters – involvement in other trials or intellectual investment could be relevant. Although members may well be able to act objectively despite such connections, complete disclosure enhances credibility. (See Annexe 1) TSC members should not use interim results to inform trading in stock of companies with competing or related products.
6. Organisation of meetings	
Expected frequency of TSC meetings	The TSC will meet in person at least annually. At the request of the TSC, interim meetings, in person or by teleconference, will be organised. Major trial issues may need to be dealt with between meetings, by phone or by email. TSC members should be prepared for such eventualities.
Attendance of TSC members at meetings	Every effort will be made to ensure that all members can attend. The Facilitator will arrange a date that enables this. The CI would be expected to attend all meetings, especially if major actions are expected. Members who cannot attend in person should be encouraged to participate by teleconference. If, at short notice, any TSC members cannot attend then the TSC may still meet if at least four independent members, including the Chair (unless otherwise agreed), will be present, plus also a member of the trial team. If the TSC is considering a major action after such a meeting the TSC Chair should communicate with the absent members, including the CI, as soon after the meeting as possible to check they agree. If they do not, a further teleconference should be arranged with the full TSC.

CONTENT	DETAILS OF TSC
Can TSC members who cannot attend the meeting input	If the report is circulated before the meeting, TSC members who will not be able to attend the meeting may pass comments to the TSC Chair or the Facilitator for consideration during the discussions.
What happens to independent members who do not attend meetings	If an independent member does not attend a meeting or provide comments when requested between meetings, it should be ensured that the independent member is available for the next meeting. If an independent member does not attend the next meeting or provide comments when next requested, they should be asked if they wish to remain part of the TSC. If an independent member does not attend a third meeting, strong consideration should be given to replacing this member
7. Trial documentation and procedures to ensure confidentiality and proper communication	
Intended content of material to be considered during meetings	A short report will be prepared by the Trial Coordinator with assistance from the CI and Trial Statistician. This will report on accrual and any matters affecting the trial. Additionally, the material may include a report from the DSMC, requests from the TMG or draft publications. No trial outcome measure data will be presented by arm unless explicitly authorised by the DSMC. Where relevant, accrual, compliance with follow-up and adherence may be presented by centre.
Whether reports to the TSC be available before the meeting or only at/during the meeting	The TSC should receive the report at least 1 week and preferably 2 weeks before any meetings. Different procedures may apply to teleconference meetings.
The people who will see the accumulating data and interim analysis by randomised group	The accumulating trial data by arm and interim analyses will be confidential. These will be viewed only by the DSMC. The TSC will not be routinely privy to these interim reports. The DSMC will make recommendations to the TSC based on the interim data.
Responsibility for identifying and circulating external evidence (e.g. from other trials/ systematic reviews)	Identification and circulation of external evidence (e.g. from other trials/systematic reviews) is not the responsibility of the TSC members; it is a responsibility of the TMG. However, the TSC should continue to be made aware of other data that may impact on the trial.
To whom the TSC will communicate the decisions that are made	(See Section 9)
What will happen to the papers after the meeting	The TSC members will store their copies of the meeting papers securely after each meeting so they can check future reports against them. After the trial has been reported, TSC members will destroy all copies of interim reports. The trial office team will be responsible for archiving the interim reports.

CONTENT	DETAILS OF TSC
8. Decision making	
What decisions will be open to the TSC	Based on recommendations from the DSMC, possible decisions include:- No action needed, trial continues as planned Early stopping due, for example, to clear benefit or harm of an intervention or external evidence (this should generally involve a recommend from the DSMC to unblind the TSC to these data) Stopping recruitment within a subgroup[2] (this should generally involve a recommendation from the DSMC to unblind the TSC to these data) Modifying target recruitment, or pre-analysis follow-up, based on any change to the assumptions underlying the original trial sample size calculation (but not on any emerging differences) Sanctioning and/or proposing protocol changes Based on other factors, possible decisions include the decisions above and:- Censuring centres for poor recruitment/poor data quality Approving proposed protocol amendments or new trial sub-studies Approving requests for early release of (subsets of) data Approving presentation of results during the trial or soon after closure Approval of strategies to improve recruitment or follow-up

[2] Considerable care should be taken if this is not a pre-specified subgroup

CONTENT	DETAILS OF TSC
The role of formal statistical methods	Formal statistical methods may have been considered by the DSMC in making their recommendations to the TSC. These methods are usually used as guidelines rather than absolute rules. This is because they generally only consider one dimension of the trial. The DSMC will record reasons for disregarding a stopping guideline in the notes of their meetings and may choose to also note this in their report to the TSC if necessary.
How decisions or recommendations will be reached within the TSC	Every effort should be made to achieve consensus. The role of the Chair is to summarise discussions and encourage consensus; therefore, it is usually best for the Chair to give their own opinion last. It is important that all the implications (e.g. ethical, statistical, practical, financial) for the trial are considered before any decision is made.
When the TSC is quorate for decision-making	At least four independent members of the TSC should be present including the Chair, plus a representative of the trials unit and, if major action is to be considered, the CI.
Any specific issues relating to the trial design that might influence the proceedings	(See Section 3)
9. Reporting	
To whom will the TSC report their recommendations/decisions, and in what form	The TSC will report their decisions (via the Facilitator) to the TMG who will be responsible for implementing any actions resulting. The TSC may also provide feedback to the DSMC and, where appropriate, to the Sponsor and Funder. Copies of communications will pass through the Facilitator.
Whether minutes of the meeting be made and, if so, by whom and where they will be kept	Notes of key points and actions will be made by the Facilitator. This will include details of whether potential competing interests have changed for any attendees since the previous meeting. The draft minutes will be initially circulated for comment to those TSC members who were present at the meeting. The TSC Chair will sign off the final version of minutes or notes.
What will be done if there is disagreement between the TSC and other trial committees	The TSC is the oversight body for the trial. However, the TSC should have good reason before deciding not to accept requests from the TMG and recommendations from the DSMC. If there are serious problems or concerns with the TSC decision following a DSMC recommendation, a joint meeting of the TSC and DSMC should be held. The information to be shown would depend upon the action proposed and each committee's concerns. Depending on the reason for the disagreement confidential data may have to be revealed to all or some of those attending such a meeting: this would be minimised where possible. The meeting would be Chaired by a senior member of the Sponsor or an external expert who is not directly involved with the trial, and agreeable to the CI, TSC Chair and DSMC Chair.

CONTENT	DETAILS OF TSC
10. After the trial	
Publication of results	The TSC will oversee the timely analysis, writing up and publication of the main trial results. The independent members of the TSC will have the opportunity to read and comment on the proposed main publications of trial data prior to submission. This review may be concurrent to that of the trial investigators and DSMC.
The information about the TSC that will be included in published trial reports	TSC members will be named and their affiliations listed in the main trial report, unless they explicitly request otherwise.
Any constraints on TSC members divulging information about their deliberations after the trial has been published	Unless permission is agreed with the DSMC, the TSC will not discuss confidential information to what they have been privy to as a result of their involvement in the trial until 12 months after the primary trial results have been published.

Abbreviations and glossary

CI	Chief Investigator
CTA	Clinical Trials Authorisation
CTU	Clinical Trials Unit
DCF	Data Collection Form
DSMC	Data & Safety Monitoring Committee
EUDRACT	European Union Drug Regulatory Agency Clinical Trial
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
ISRCTN	International standard randomised controlled trial number
MDT	Multi-disciplinary team
MHRA	Medicines and Healthcare products Regulatory Authority
MRC	Medical Research Council
NHS	National Health Service
NIHR	National Institute for Health Research
OCTRU	Oxford Clinical Trials Research Unit
PI	Principal Investigator
PIL	Patient Information Leaflet
TMG	Project Management Group
SAE	Serious Adverse Event
TSC	Trial Steering Committee

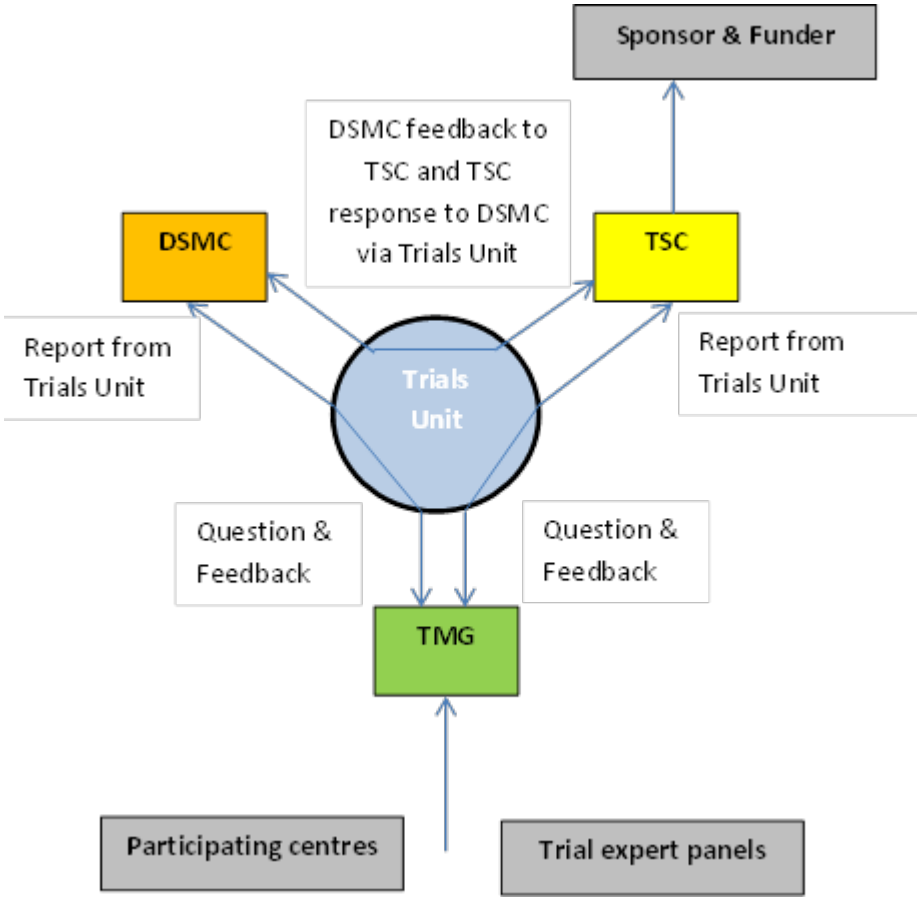
Figures and Annexes

Figure 1: CORKA Summary

Study Title	**CO**mmunity based **R**ehabilitation after **K**nee **A**rthroplasty (CORKA). A prospective, individually randomised, single blinded, two arm, randomised controlled trial
Short title	CORKA Study
HTA Reference	12/196/08
Study Design	A pragmatic multicentre prospective individually randomised single blinded two arm randomised controlled trial
Study Participants	Patients aged 55 years or more, of both sexes, undergoing unilateral knee replacement (KR) and found to be at risk of poor outcome after surgery
Study Treatments	Participants will be randomized to receive either: 'multicomponent community-based rehabilitation' or 'usual care'
Planned Sample Size	600 participants
Randomisation	Randomisation will use a 1:1 allocation ratio, undisclosed permuted block sizes, and considering sites stratification factor. Participants and those delivering rehabilitation will be aware of the treatment allocation due to the nature of the intervention. The Physiotherapists carrying out follow up will remain blind to the participants' allocation.
Data Collection	Data will be collected from participants and the research team onto paper questionnaires/CRFs. Data collected for the two study follow up time points (6 and 12 months) will be via a home visit or an out-patient clinic visit onto paper questionnaire/CRF. The originals will be sent by a member of the local research team to the study coordinating office in Oxford by post; using a Freepost account (keeping a copy at site).
Statistical analysis	The principal comparisons will be performed on an intention-to-treat basis. The primary outcome will be analysed using a linear mixed effects method with repeated measures, on outcome measurements at 6 and 12 months, adjusting for baseline score and stratification/ variables. An interaction between time and randomised group will be fitted to allow estimation of treatment effect at each time point.
Follow-up period	12 months
Planned Study Period	51 months
Primary Objectives	**Endpoints**
To determine if a multi-component rehabilitation programme improves the outcome of patients who undergo a KR.	At 12 months post-surgery: • Late Life Function and Disability Instrument (LLFDI) score
Secondary Objectives	**Endpoints**
To assess the impact of a multi-component rehabilitation programme on physical function and quality of life and cost effectiveness analysis versus usual care rehabilitation.	At 6 months post-surgery: • LLFDI At 6 and 12 months post-surgery: • Measurement of disease specific function by the Oxford Knee Score • Measurement of physical activity by the Physical Activity Scale for the Elderly (PASE) questionnaire • Measurement of quality of life by the subscale of the Knee Osteoarthritis Outcome Score (KOOS) • Measurement of physical function by the physical performance tasks – 30 sec chair stand test, figure of 8 walking test, single leg stance test • Measurement of pain using the visual analogue score (VAS) • Measurement of health economics using the EQ5D-5L and a patient diary • Cost utility analysis from both the NHS and a societal perspective.

Qualitative study embedded in the RCT	Experiences and views of participants
Participants	A subsample of approx. 15 participants and 15 staff members will be interviewed to share their experiences and views about the intervention
Endpoints	Participant interviews using phenomenological analysis approach

Figure 2: Relationship of trial committees



Contact with Trials Unit is via Facilitator

Annexe 1: Agreement and competing interests form for independent members

CORKA Agreement to join the Trial Steering Committee as an independent member and disclosure of potential competing interests

Please complete the following document and return to the CORKA Trial Coordinator. (please initial box to agree)

	I have read and understood the TSC Charter Version 1.0, 24Feb2015
	I agree to join the Trial Steering Committee for this trial as an independent member
	I agree to treat all sensitive trial data and discussions confidentially

The avoidance of any perception that independent members of a TSC may be biased in some fashion is important for the credibility of the decisions made by the TSC and for the integrity of the trial. Potential competing interests should be disclosed via OCTRU CTU. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) independent TSC member should remove the conflict or stop participating in the TSC. **Table 1** lists potential competing interests.

	No, I have no potential competing interests to declare
	Yes, I have potential competing interests to declare (please detail below)

Please provide details of any potential competing interests:

_____

_____

_____

_____

_____

_____

_____

Name: _____

Signed: _____ Date: _____

Table 1: Potential competing interests for independent members

Stock ownership in any commercial companies involved
Stock transaction in any commercial company involved (if previously holding stock)
Consulting arrangements with the Sponsor/Funder
Frequent speaking engagements on behalf of the intervention
Career tied up in a product or technique assessed by trial
Hands-on participation in the trial
Involvement in the running of the trial
Emotional involvement in the trial
Intellectual conflict e.g. strong prior belief in the trial's experimental arm
Involvement in regulatory issues relevant to the trial procedures
Investment (financial or intellectual) or career tied up in competing products
Involvement in the writing up of the main trial results in the form of authorship
Involved as an applicant in a current grant, or one within the last couple of years with any member on the CORKA TSC or DSMC

Note: This TSC charter was developed using MRC CTU template TSC Charter version 1.02, 13-Mar-2006

Annexe 2: Agreement and competing interests form for non-independent members

CORKA Agreement to join the Trial Steering Committee as an non-independent member and disclosure of potential competing interests

Please complete the following document and return to the CORKA Trial Coordinator. (please initial box to agree)

	I have read and understood the TSC Charter Version 1.0, 243Feb2015
	I agree to join the Trial Steering Committee for this trial as an non-independent member
	I agree to treat all sensitive trial data and discussions confidentially

The avoidance of any perception that members of a TSC may be biased in some undisclosed fashion is important for the credibility of the decisions made by the TSC and for the integrity of the trial.

Possible competing interests should be disclosed via OCTRU CTU. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) independent TSC member should remove the conflict or stop participating in the TSC. **Table 1** lists potential competing interests.

	No, I have no competing interests to declare other than involvement in the trial
	Yes, I have competing interests to declare (please detail below)

Please provide details of any competing interests:

_____

_____

_____

_____

_____

_____

_____

Name: _____

Signed: _____ Date: _____

Table 1: Potential competing interests for non-independent members

Stock ownership in any commercial companies involved
Stock transaction in any commercial company involved (if previously holding stock)
Consulting arrangements with the Sponsor/Funder
Ongoing advisory role to a company providing drugs to the trial
Frequent speaking engagements on behalf of the intervention
Intellectual conflict e.g. strong prior belief in the trial's experimental arm
Involvement in regulatory issues relevant to the trial procedures
Investment (financial or intellectual) in competing products
Involved as an applicant in a current grant, or one within the last couple of years with any member on the CORKA TSC or DSMC

Note: This TSC charter was developed using MRC CTU template TSC Charter version 1.02, 13-Mar-2006

Annexe 3: Agreement and confidentiality agreement for observers

CORKA (ISRCTN13517704): Agreement to attend the Trial Steering Committee and treat all information confidentially

Please complete the following document and return to the CORKA Trial Coordinator. (please initial box to agree)

	I have received a copy of the TSC Charter Version 1.0, 23Feb2015
	I agree to attend the Trial Steering Committee meeting on ……
	I agree to treat as confidential any sensitive information gained during this meeting unless explicitly permitted

Name: _____

Signed: _____ Date: _____

Note: This TSC charter was developed using MRC CTU template TSC Charter version 1.02, 13-Mar-2006

Annexe 4: Summary of changes from previous version