SUMMARY OF REC APPROVED ACTIVE TRIAL AMENDMENTS

Amendment Number and date	Type of Amendment	Corresponding revised protocol version No. (if applicable)	Corresponding revised document version No's if applicable	Summary of amendment
1 (March 2006)	substantial	3.2	n/a	Length of time since previous failed procedure at time of randomisation into the trial was changed from 12 months to 6 months.
2 (Jan 2007)	substantial	3.3	n/a	a) This sub-randomisation is now optional - if surgeons prefer not to use periosteum at all then they can choose collagen membrane for patients having ACI. b) A new technique called AMIC was added to the list of non-ACI procedures.(see section 4.4 p6 of the protocol).
3 (Feb 2007)	substantial	n/a	Additional PIL v1.1	This describes the new standard technique called "AMIC" - this has since been replaced by Patient Information Leaflet Version 3.1.
4 (March 2007)	substantial	3.4	Additional PIL v 1	a) The minimum sample size was reduced from 660 to 480, which would provide 80% power instead of 90% power to detect a 30% reduction in the primary outcome of the number of patients ceasing to benefit within 5 years. b) Matrix-assisted ACI (MACI) was added as an allowable option in the ACI arm of the trial so surgeons can select to use MACI or ACI prior to randomisation. Additional PIL describes MACI technique - this has since been replaced by Patient Information Leaflet Version 3.1.
5 (March 2008)	substantial	3.5	PIL v 3.1 (all centres except RNOH Stanmore) and 3.2 (RNOH Stanmore only)	a) Recruitment will continue until the end of 2009. b) Another type of MACI called Chondron to be allowed in the ACI arm, and if selected, will be sub-randomised against MACI. c) To include patients with osteochondral defects. Bone grafting should be used to restore the loss of bone to within 3 mm of the surface alongside treatment to restore cartilage.

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6 (April 2008)	substantial	3.6	n/a	Previously the site of defect had to be on the trochlea or femoral condyle but now patients with a chondral defect on the patella are also eligible.
7/AM09 (April 2010)	substantial	n/a	GP letter 1 (v1.1) GP letter 2 (v1.0) participant newsletter	Amendment of the existing GP letter to include the option of a patient not receiving any surgical intervention. Two new documents were approved: 1) GP letter to advise of withdrawal from the study 2) newsletter to be sent to study participants to inform of study progress and encourage follow-up
AM11 (September 2011)	substantial	3.7	Knee diary v1.1 Continued participation letter v1.0 Postal Qu. Cover letter v1.0	a) Protocol Section 8: A new section on data collection has been added to clarify the data collected at each visit. A paragraph has been added on participant retention to include entry into a prize draw for all questionnaires returned. b) Protocol Section 10. Safety, has been expanded to include definitons of adverse events and assessments of causality and expectedness, and timeframes for reporting. c) A modified knee diary aims to make it more straightforward for the participant to complete d) Two new letters to participants to encourage continued participation

N.B. Please remember to mark all previous versions of controlled documents as 'superseded' and retain in the Investigator Site File.