SUPPLEMENTARY FILE 1: Study Protocol for Fish oil in knee osteoarthritis: A randomised clinical trial of low dose versus high dose (also known as the FOSTAR study).

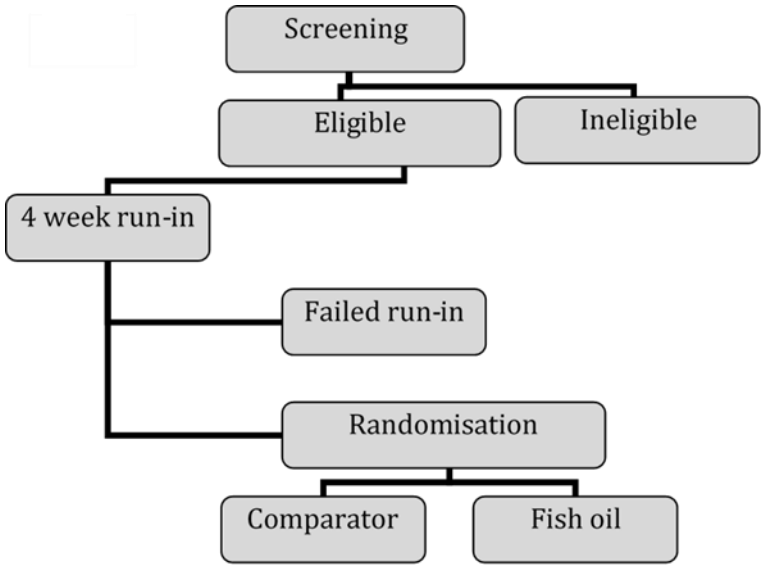
STUDY DESIGN

The FOSTAR study is a randomised double-blind controlled clinical trial of 200 subjects with symptomatic knee osteoarthritis from three Australian centres (The Queen Elizabeth Hospital, Adelaide, South Australia; Menzies Research Institute, Hobart, Tasmania and Royal North Shore Hospital, Sydney, New South Wales). Participants will be recruited and randomly allocated to either high or low dose fish oil, following completion of a one month run-in period.

All participants will provide written informed consent. The study has been approved by The Queen Elizabeth Hospital, Royal North Shore Hospital and Tasmanian Human Research Ethics Committees. The trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN 12607000415404) on 19th August 2007.

The proposed flow of subjects through the study is shown in Figure 1.

Figure 1. Flow of subjects through the FOSTAR study



RECRUITMENT

Subjects will be recruited at three centres through patient databases currently held by study

Investigators and direct advertising in local newspapers and Arthritis Australia newsletters.

INCLUSION CRITERIA

The inclusion criteria required (i) age greater than 40 years (ii) clinical knee OA defined using American College of Rheumatology criteria [1] and (iii) VAS knee specific pain score greater than 20mm (0-100mm scale). The knee which is most symptomatic knee, as determined by the participant, will represent the 'index' knee for the remainder of the study.

EXCLUSION CRITERIA

Exclusion criteria included (i) dementia or inability to give informed consent, (ii) pregnancy or lactation, (iii) severe knee OA (Grade 3 radiographic joint space narrowing using the Osteoarthritis Research Society International atlas), (iv) planned knee replacement surgery, (v) long-term use ($\geq$6 months) of anti-inflammatory dose of fish oil (15mL of oil or $\geq$9 capsules), (vi) presence of inflammatory arthritis and (vii) contra-indications to MRI.

RUN-IN PERIOD

Once volunteers have been screened, they will enter a 4-week pre-randomisation run-in period to exclude participants intolerant to taking liquid oil. All subjects will be instructed to take 15 ml daily of a similarly flavoured oil (citrus flavoured Sunola oil). While the exact contents of this preparation will not be revealed, it will be explained to participants that this preparation is designed to test common aspects of the interventions, but differs from the actual test oil preparations. A standardized instructional video demonstrating a method of taking liquid oil that enhanced tolerability by 'layering' on juice will be shown to all participants prior to run-in. Participants will be instructed to take the test oil on juice using the two glass technique [2]. Briefly, one of two shot glasses is filled with fruit juice and the other half filled with juice. The required dose of oil is then measured and layered onto the juice in the half filled glass. Without stirring, the contents are then swallowed in a single gulp. Immediately thereafter, the glass of juice alone is sipped slowly over a period of about 15 seconds. The oil and juice is taken with a meal and not on an empty stomach. Carbonated drinks are avoided. The oil can be taken in divided doses. This method has generally been effective in avoiding a 'repeating' fish oil taste.

Patients will be reviewed in the 3rd week after commencing the run-in oil. Subjects who do not attend the appointments or are non-compliant (who consume less than 75% of the oil as assessed by volume) or are intolerant of the oil will not be randomised. The requirements

for the run-in test (and the consequences of failing) will be disclosed to the subjects prior to screening. During this run-in period, subjects will be asked to cease fish oil and glucosamine but will be permitted to take paracetamol for first line analgesia and NSAID (ibuprofen up to 400mg QID if required) for second line analgesia. In our experience about 20% of subjects recommended fish oil fail to establish a pattern of daily ingestion. This period will establish the patient's ability to take a test oil preparation using the recommended oil on juice technique as well as tolerance to and adequacy of rescue analgesia, including, if required, the selected NSAIDs. None of these medications, including the 'run-in' oil will be taken in the week prior to the baseline assessment, when randomisation and commencement of the allocated test preparation will take place. The use of a run-in has been used to improve compliance and retention in RCTs [3]

RANDOMIZATION BY CENTRE

Subjects who satisfy compliance criteria and VAS pain score criteria during the run-in period will be randomised (1:1) to one of the two arms of the RCT. The randomisation will be done centrally at The Queen Elizabeth Hospital in Adelaide by computer generated random numbers and will be stratified by centre.

INTERVENTION

Participants will be randomly allocated to one of two treatment arms:

1. Anti-inflammatory dose of fish oil, 15 ml/day (high dose fish oil)
2. Comparator oil comprising 10% fish oil in sunola oil, 15 ml/day (low dose fish oil)

High dose fish oil contains EPA 18% and DHA 12%, supplying 4.5g EPA+DHA per day. The low dose comparator oil, a blend of fish oil and high oleic sunola oil in a ratio of 1:9, supplies 0.45g EPA + DHA per day, which is equivalent to 1.5 standard 1g fish oil capsule daily. Both oils are flavoured with citrus oils and will be provided in identical dark 500mL bottles. Fish oil is sourced from Berg LipidTech Aalesund, Norway. The oils, blending, masking and bottling is performed by Melrose Health, Victoria, Australia. Study oil bottles will be returned at each study visit and volume of unconsumed oil measured to assess compliance. The presence of fish oil in the comparator will obviate the ethical problem of denying patients n-3 fatty acids that are recommended for cardiovascular health and will also add 'fishy' sensate properties that will militate against unmasking. We have previously shown addition of citrus flavouring to fish oils and vegetable oils achieves masking. The EPA and

DHA dose in the undiluted test fish oil has been shown to have anti-inflammatory effects in a variety of clinical settings, whereas the comparator oil will deliver a dose of fish oil that is well below the minimum amount (10ml/d) that has been associated with anti-inflammatory effects in RCTs. Participants will be provided with paracetamol (500mg) tablets with instructions that they could safely use up to 8 per day.

Participants will undergo assessments at baseline, 6 weeks, 3, 6, 9, 12, 18 and 24 months with interim phone calls to participants to encourage continuing compliance and participation

Dietary and general advice:

Subjects will be instructed to use olive oil based products (spreads, cooking oils, dressings etc), where possible, to minimise variation in consumption of n6 polyunsaturated fatty acids which compete with dietary n3 fatty acids. Written instructions regarding technique for taking the oil and directions for the background diet will be provided. All participants will also be given written information on knee osteoarthritis and generic instructions regarding exercises appropriate for maintaining knee function in OA and general fitness. The package of informed consent and written advice will include information regarding potential unwanted effects of fish oil and paracetamol.

COMPLIANCE

The degree of compliance with test oils will be measured in two ways: (i) calculation of consumed fish oil by count of bottles provided and measurement of oil remaining in returned partly used bottles and (ii) fasting plasma omega-3 fatty acid analysis. These assessments will be undertaken at 3, 6, 12, 18 and 24 months. The plasma fatty acid analysis results will not be available to subjects or investigators till the completion of the study.

OUTCOME MEASURES

Primary outcomes:

1. Pain (WOMAC NRS 3.1 index [4], 10 point numerical scale) at 3, 6, 9, 12 and 24 months (knee specific)
2. Change in knee MRI cartilage volume at 2 yrs.

Secondary outcomes:

1. Disability (WOMAC NRS 3.1 index [4], 10 point numerical scale) at 3,6, 9,12 and 24 months (knee specific)

2. Quality of life (AQOL) [5]
3. Analgesic use, measured using a daily diary (NSAID) and paracetamol (pill count at each visit)
4. Change in MRI scores of bone marrow lesions at 2 years
5. Safety assessments/adverse events

In addition to the designated outcome measures, blood pressure, full blood count and electrolytes and liver function testing, presence of comorbidities (eg renal disease, cardiovascular disease, peptic ulcer disease) and a diet questionnaire, DQES V2[6], used to assess n-3 and n-6 fatty acid intake in usual diet, will be assessed at baseline.

As the study will extend over two years in a population at an age at risk for cardiovascular disease and declining bone density, routine investigations will be undertaken at baseline and two years to monitor collateral health effects and risks including:

1. fasting blood lipids
2. low titre c-reactive protein
3. bone mineral density of hip and spine
4. lung spirometry (The Queen Elizabeth Hospital participants only)

The assessment schedule is summarized in Table 1, and data collection forms are presented in Appendix 1.

Table 1. Schedule of assessment for primary and secondary outcome measures

FOSTAR STUDY ASSESSMENTS								
	Enrolment	Ransomisation	Treatment					Completion
	Visit 1 (-4 weeks)	Visit 2 (0 weeks)	Visit 3 (3 month)	Visit 4 (6 month)	Visit 5 (9 month)	Visit 6 (12 month)	Visit 7 (18 month)	Visit 8 (24 month)
Informed Consent for FOSTAR	X							
Medical History	X							
Surgical History	X	X	X	X	X	X	X	X
OA History		X						
Inclusion/Exclusion Criteria	X	X						
Concomitant medications	X	X	X	X	X	X	X	X
Physical Exam/Vital Signs	X	X	X	X	X	X	X	X
Fish Oil Dosing DVD	X	X						
Run-In Fish Oil	X							
Diet information sheet		X						
Exercise information sheet		X						
Osteoarthritis Information sheet		X						
Laboratory testing								
Blood sampling for FBC, CRP, LFT electrolytes and fasting lipids		X				X		X
Blood sampling for serum fatty acids		X	X	X	X	X	X	X
Imaging								
Knee X-ray	X							
MRI scan		X						X
DEXA scan		X						X
Questionnaires								
WOMAC Questionnaire	X	X	X	X	X	X	X	X
NRS pain Questionnaire	X	X	X	X	X	X	X	X
MAPT Questionnaire		X				X		X
AQoL Questionnaire		X	X	X	X	X	X	X
Diet Questionnaire		X						X
Analgesic Medication		X	X	X	X	X	X	
Take-Home Diary	X	X	X	X	X	X	X	
Randomisation		X						
Study Fish Oil		X	X	X	X	X	X	
Pedometer Readings		X						X

MRI scanning and scoring:

MRI scans will be performed at each of the study centres. MRI will be performed on the most symptomatic knee as determined by the participant, and will represent the 'index'

knee for the remainder of the study. Each participant will have an MRI performed on their 'index' knee at baseline and after 2 years. The 'index' knee will be imaged in the sagittal plane on the same model 1.5T whole-body MR unit using a commercial receive-only extremity coil. The following sequence and parameters will be used: a T1-weighted, fat-suppressed, 3-dimensional gradient recall acquisition in the steady state; flip angle 55 degrees; repetition time 58 msec; echo time 12 msec; field of view 16 cm; 60 partitions; 512 × 192 matrix; one acquisition time 11 minutes, 56 seconds. Sagittal images will be obtained at a partition thickness of 1.5 mm and an in-plane resolution of 0.31 × 0.83 mm (512 × 192 pixels).

The MRI scans will be assessed by a single trained observer. Each participant's baseline and follow-up MRI scans will be scored unpaired with blinding to subject identification and timing of MRI. The volumes of individual cartilage plates (medial tibia, lateral tibia and patella) will be isolated from the total volume by manually drawing disarticulation contours around the cartilage boundaries on a section by section basis. These data will then be resampled by means of bilinear and cubic interpolation (area of 312 mm and 1.5 mm thickness, continuous sections) for the final 3D rendering. The coefficient of variation for this method in our hands is 2.1% to 2.6% [7].

Bone marrow lesions (BMLs) will be assessed on a proton density-weighted fat saturation 2D fast spin echo sequence in the sagittal plane. They will be defined as areas of increased signal adjacent to the subcortical bone at the medial tibial, medial femoral, lateral tibial, lateral femoral, superior patella and inferior patella sites. One trained and blinded observer will score BMLs by measuring the maximum area of the lesion (mm^2) at baseline and follow-up, as previously described [8]. The intraclass correlation coefficient (ICC) in our hands for this method of measurement is 0.97 [8].

Radiographic assessment:

Radiographs will only be used as a screening tool at participant recruitment, and not as an outcome measure. Radiographs of the index knee in the Buckland-Wright view will be taken at baseline, to allow comparison with MRI assessments and as this is putatively the most reproducible technique with regard to non-fluoroscopic positioning [9].

Radiographs will scored independently by 2 trained observers at each site using a published atlas to classify disease in the tibiofemoral joint. The radiographic features of tibiofemoral

OA will be graded in each compartment on a 4-point scale (0-3) for individual features of osteophytes and joint space narrowing [10]. We have shown previously high degrees of intra-observer and inter-observer reproducibility for agreement on features of OA in the knee with regard to both osteophytes and joint space narrowing [11].

Success of Blinding:

Success of blinding will be assessed by asking the participants the following question:
"If you were asked which oil you were taking during the FOSTAR study would you say? Possible responses: Low dose, comparison oil OR high dose fish oil OR I am not sure which oil I may have been taking". This will be asked at final visit.

ANALYSIS PLAN

Both intention-to-treat and per protocol analyses will be undertaken. Multiple imputation will be used for missing data. Analyses will be performed using longitudinal mixed model regression. The primary interpretation will be the comparison between the two treatment groups at the end of study.

SAMPLE SIZE CONSIDERATION

Sample sizes of 100 per treatment group were selected based on power calculations for longitudinal (ie repeated data) data with 6 treatment visits, $\alpha = 0.05$, $\beta = 0.2$, an attrition rate of 5% per visit, and a standardised treatment effect at the end of the study of 0.4 (i.e. a medium effect).

WITHDRAWALS

All participants will be followed for the duration of the two year study, irrespective of whether they discontinue the study oil (unless they decide to withdraw consent).

REFERENCES

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4. Bellamy N. WOMAC Osteoarthritis Index User Guide. Version VIII. Brisbane, Australia, 2007.
5. Whitfield K, Buchbinder R, Segal L, Osborne RH. Parsimonious and efficient assessment of health-related quality of life in osteoarthritis research: validation of the Assessment of Quality of Life (AQoL) instrument. Health Qual Life Outcomes. 2006; 4:19.
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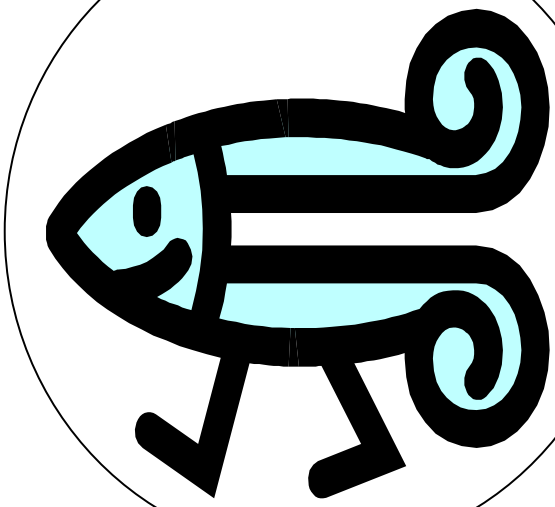
APPENDIX 1: FOSTAR STUDY DATA COLLECTION FORMS

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

FOSTAR



STUDY

A two year, multi-centre, double-blinded, randomised, controlled clinical trial to assess the benefits of high-dose oral fish oil in patients experiencing symptomatic knee osteoarthritis.

Site Number: ☐

Randomisation Number: ☐☐☐☐

Subject Initials: ☐☐☐

Study Selected Knee:

☐☐☐☐☐

FOSTAR STUDY ASSESSMENTS

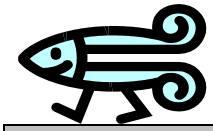
Shaded areas are specific to TQEH site ONLY	Enrolment	Randomisation	Treatment					Completion
	Visit 1 (-4weeks)	Visit 2 (0weeks)	Visit 3 (3month)	Visit 4 (6month)	Visit 5 (9month)	Visit 6 (12month)	Visit 7 (18month)	Visit 8 (24month)
Informed Consent for FOSTAR	X							
Informed Consent for PFT sub-study	X							
Informed Consent for DNA sub-study	X							
Medical History	X							
Surgical History	X	X	X	X	X	X	X	X
OA History		X						
Inclusion/Exclusion Criteria	X	X						
Concomitant medications	X	X	X	X	X	X	X	X
Physical Exam/Vital Signs	X	X	X	X	X	X	X	X
Serum Pregnancy Test		X						X
Blood sampling for FBC, CRP, LFT electrolytes and fasting lipids		X				X		X
Blood sampling for serum fatty acids		X	X	X	X	X	X	X
Blood sampling for DNA sub-study		X						
Lung Function sub-study test		X				X		X
Knee X-ray (if required)	X							X
MRI scan		X						X
DEXA scan		X						X
WOMAC Questionnaire	X	X	X	X	X	X	X	X
NRS pain Questionnaire	X	X	X	X	X	X	X	X
MAPT Questionnaire		X				X		X
AQoL Questionnaire		X	X	X	X	X	X	X
Diet Questionnaire		X						X
CES-D Questionnaire (Depression)		X				X		X
Fish Oil Dosing DVD	X	X						
Run-In Fish Oil	X							
Analgesic Medication		X	X	X	X	X	X	
Take-Home Diary	X	X	X	X	X	X	X	
Randomisation		X						
Study Fish Oil		X	X	X	X	X	X	
Diet information sheet		X						

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

Exercise information sheet		X						
Osteoarthritis Information sheet		X						
Pedometer Readings		X						X



FOSTAR STUDY

Visit 1 – ENROLMENT

Visit Date …… ☐☐/☐☐/☐☐☐☐
DD/MM/YYYY

INFORMED CONSENT

Date Written Informed Consent Obtained …… ☐☐/☐☐/☐☐☐☐
DD/MM/YYYY

	Yes	No
Has a copy been provided to the subject for their records	☐	☐
Has a copy been added to the subjects hospital records ☐	☐	
Has the original been filed in the subjects CRF	☐	☐

DEMOGRAPHICS

Date of Birth …….. ☐☐/☐☐/☐☐☐☐
DD/MM/YYYY

Gender ☐ Female ☐ Male

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

Ethnic Origin	☐ Caucasian ☐ Asian ☐ Hispanic ☐ Other (specify below) ☐

SURGICAL HISTORY	
Previous Surgical Procedures	Date of Procedure (DD/MM/YYYY)
If the subject is currently taking any medications for any of the above procedures, ensure that details are recorded in the Concomitant Medications record.	

CO-MORBIDITIES				
Have you ever been told by a Dr or a nurse that you have any of the following conditions?			If yes, Do you currently have these conditions?	
	YES	NO	YES	NO
Diabetes	☐	☐	☐	☐
Osteoporosis	☐	☐	☐	☐
High Blood Pressure	☐	☐	☐	☐
Asthma	☐	☐	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

Bronchitis	☐ ☐	☐ ☐
Emphysema/Chronic bronchitis	☐ ☐	☐ ☐
Stroke	☐ ☐	☐ ☐
Heart Attack	☐ ☐	☐ ☐
Angina	☐ ☐	☐ ☐
High Cholesterol	☐ ☐	☐ ☐
None of the above	☐ ☐	

MEDICAL HISTORY		
CURRENT MEDICAL CONDITIONS	Date of Onset (DD/MM/YYYY)	Date Resolved Or √ Ongoing (DD/MM/YYYY)
		☐
		☐
		☐
		☐
		☐
		☐
		☐
		☐
If the subject is currently taking any medications for any of the above procedures, ensure that details are recorded in the Concomitant Medications record.		

QUESTIONNAIRES		
	YES	NO
Has analgesic and anti-inflammatory medications been with-held today	☐	☐
Questionnaires supplied: YES NO	Questionnaires Completed	YES NO

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

WOMAC	☐	☐	☐	☐
NRS PAIN	☐	☐	☐	☐

INCLUSION CRITERIA	YES	NO
Is the subject aged 40 or over?	☐	☐
Does the subject experience symptomatic knee osteoarthritis (ACR criteria) a) Knee pain (at least 20mm on NRS pain scale) b) An osteophyte on x-ray c) At least one of the following: - knee age greater than 50 years - stiffness lasting less than 30 minutes - crepitus	☐	☐
Is the subject able to read, speak and understand English, capable of understanding the study requirements and willing to co-operate with the study instructions?	☐	☐
Is the subject able and willing to give informed consent?	☐	☐
Has the subject used an investigational drug within 30 days of the screening visit?	☐	☐
Is the subject willing and able to give blood samples	☐	☐
Is the subject willing and able to have MRIs performed	☐	☐
Is the subject willing and able to have DEXA scans performed?	☐	☐
A tick recorded in any of the shaded boxes above signifies that the subject is ineligible and should be excluded from entering the study		

EXCLUSION CRITERIA	YES	NO

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

	☐	☐
Does the subject suffer from dementia or be unable to give informed consent?		
Is the subject pregnant or breastfeeding, or is she unable or unwilling to use an adequate method of contraception?	☐	☐
Does the subject have Grade – 4 changes in their knee which is to be investigated	☐	☐
Has the subject ingested ≥10mL or ≥ 9 standard capsules of fish oil daily for the proceeding 3 months	☐	☐
Does the subject have any contra-indications for having MRIs or DEXA scans performed?	☐	☐
Does the subject have any clinically significant condition(s) such as (but not limited to) cancer, rheumatoid arthritis, psoratic arthritis, lupus or fibromyalgia? that in the opinion of the investigator may compromise their safety or compliance, interfere with evaluation or preclude completion of the study	☐	☐
A tick recorded in any of the shaded boxes above signifies that the subject is ineligible and should be excluded from entering the study		

ENROLMENT CODE
If ALL inclusion and NO exclusion criteria have been met, the study subject may be assigned an enrolment code: **E** ☐☐☐☐☐☐☐

PHYSICAL EXAMINATION/VITAL SIGNS	
Height	cms
Weight	kgs
Blood Pressure	mmHG

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

RUN-IN FISH OIL		
	YES	NO
Has the run-in fish oil been supplied and explained?	☐	☐
Has the dosing DVD been shown to the subject?	☐	☐
Has the first dose of fish oil been taken under supervision in the clinic?	☐	☐

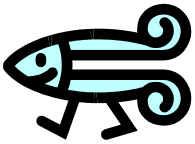
PREVIOUS FISH OIL USE		
	YES	NO
Have you ever used fish oil prior to your involvement in this study?	☐	☐
If yes, what was your average daily consumption of fish oil? Where 1 capsule OR 1 mL of liquid fish oil = 1g	……g/day	

PREPARATION FOR NEXT APPOINTMENT		
	YES	NO
	☐	☐
Has a baseline/randomisation appointment been made?	☐	☐
Has the subject been booked in for fasting blood tests prior to randomisation visit?	☐	☐
Has the take home diary been supplied and explained?	☐	☐
Has the subject been supplied with analgesic medication for pain relief? Make sure the details of this are recorded on the Paracetamol Accountability Sheet	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐



FOSTAR STUDY

Visit 2 (0 months) - RANDOMISATION

Visit Date…… ☐☐/☐☐/☐☐☐☐
DD / MM / YYYY

KNEE X-RAY

	YES	NO
If not available at Visit 1,has an x-ray (no older than 12 months) of the study selected knee been assessed by the PI	☐	☐
Does the subject meet knee inclusion criteria	☐	☐

1. Less than Grade – 4 changes in their study selected knee
2. An osteophyte on x-ray
   And at least one of the following:

- knee age greater than 50 years
- stiffness lasting less than 30 minutes
- crepitus

STUDY SELECTED KNEE

	LEFT	RIGHT
This subject's Study Selected knee is their	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

RUN-IN FISH OIL		
	YES	NO
Was the run-in oil well tolerated? If not, describe the symptoms below: …… ……	☐	☐
Any adverse events recorded here or in take-home diary to be transcribed to Adverse Events Record		
Has the run-in oil been returned Volume of the returned bottle ……mL % of returned oil ……% (% = amount returned/amount supplied x 100)	☐	☐
Was at least 75 % of expected run-in fish oil consumption confirmed?	☐	☐
Was tolerance and compliance adequate? If no, withdraw subject If yes, continue with visit……..	☐	☐

ANALGESIC USE		
	YES	NO
Has subject withheld taking anti-inflammatory and analgesic medications prior to appointment If YES, continue with questionnaires. If NO, ask subject to withhold analgesic and inflammatory	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

medications from today and complete questionnaires at home. The questionnaires are then to be returned in pre-paid envelopes.	

QUESTIONNAIRES				
	Supplied		Completed	
	YES	NO	YES	NO
NRS pain / PGA Does the subject still meet pain inclusion criteria (≥ score of 4 on NRS pain scale) If NO, withdraw the subject. If YES, continue……..	☐	☐	☐ ☐	☐ ☐
WOMAC	☐	☐	☐	☐
AQoL I	☐	☐	☐	☐
MAPT	☐	☐	☐	☐
Diet Diet Questionnaire Barcode …….	☐	☐	☐	☐
Physical Activity (PASE)	☐	☐	☐	☐

BLOOD TESTS		
	YES	NO
Has a fasting blood sample been taken for FBC, MBA, CRP, fasting lipids (HDL, TGC, LDL)	☐	☐
Has a serum pregnancy test been taken (if subject male, tick No box)	☐	☐
Has a fasting blood sample been taken to measure serum fatty acids?	☐	☐
Has a blood sample been taken for DNA sub-study?	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

INCLUSION CRITERIA		
	YES	NO
Did the subject consume at least 75% of the expected volume of run-in fish oil	☐	☐
Did the subject record a measurement of at least 20mm on the NRS pain scale for their study selected knee	☐	☐
Does the subject still consent to taking part in the FOSTAR study	☐	☐
Have knee x-rays, no older than 12 months old been reviewed	☐	☐
Does the subject meet inclusion criteria of: 1. Less than Grade – 4 changes in their study selected knee 2. .An osteophyte on x-ray 3. At least one of the following: - knee age greater than 50 years - stiffness lasting less than 30 minutes 4. crepitus	☐	☐
A tick recorded in any of the shaded boxes above signifies that the subject is ineligible and should be excluded from entering the study		

RANDOMISATION CODE
If ALL inclusion criteria have been met, the study subject may be assigned a randomisation code**:** **R** ☐☐☐☐☐☐☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

MEDICAL CHANGES		
Has the subject been diagnosed with any **NEW** medical conditions since their last visit?		
NEW MEDICAL CONDITION	Date of Onset (DD/MM/YYYY)	Date Resolved Or √ Ongoing (DD/MM/YYYY)
		☐
		☐
		☐
If the subject is currently taking any medications for any of the above conditions, ensure that details are recorded in the **Concomitant Medications record**.		

CONCOMITANT MEDICATIONS					
Has the subject started, stopped or changed the doses of any medications since their last visit? (Ask to see all medications used)					
Brand Name	Dose (4)	Units (mg)	Route (po)	Start/Stop Dates (DD/MM/YYYY)	Ongoing
				Start…../…../…… Stop…../…/……..	☐
				Start…../…../…… Stop…../…/……	☐
				Start…../…../…… Stop…../…/……	☐
				Start…../…../…… Stop…../…/……	☐
Please remember to transfer any details here to concomitant medications page					

HOSPITALISATIONS/DAY PROCEDURES			
Has the subject been to hospital for any medical procedures since their last visit? ☐YES ☐NO			
If Yes, please provide details below			
Date Admitted DD/MM/YYYY	Date Discharged DD/MM/YYYY	Doctor's Details	Purpose

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

Total Number of Hospitalisations since last visit: …….			

KNEE OSTEOARTHRITIS HISTORY	
With regard to the pain in your **study-selected knee**;	
How long have you experienced pain in that knee?	…….years
Have you had previous surgery to this knee	YES / NO
If yes, what type of surgery?	☐ YES ☐ NO ☐ Arthroscope ☐ Meniscal Surgery ☐ Cartilage Surgery ☐ Tendon Surgery ☐ Ligament Surgery ☐ Other .....
If yes, when did you have surgery?	Date:…../…../……

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

Have you had a previous injury to **this** knee, requiring use of walking stick, frame or wheelchair? If so, what year	☐ Yes ☐ No Year: ……

JOINT OSTEOARTHRITIS HISTORY	
Over the past month have you had pain on most days in any of the following joints?	☐ Other knee. **Not** the one being investigated in this study ☐ Lower Back ☐ Neck ☐ Shoulder ☐ Hands ☐ Other (details)……. ☐ No others

EDUCATION	
What is highest level of education?	☐ Didn't finish high school ☐ Finished high school

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

	☐ Trade/Apprenticeship ☐ Certificate/Diploma ☐ Bachelor degree or higher ☐ Didn't answer

EMPLOYMENT HISTORY	
What is your current work status?	☐ Full-time employed ☐ Part-time/casual employment ☐ Unemployed ☐ Home Duties ☐ Retired ☐ Student ☐ Other Please specify ……..……...

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

What kind of work have you done for most of your life? **(Study coordinator: please code into:-**	…… ☐ Manual ☐ Office/Professional ☐ Not Applicable

STUDY FISH OIL		
	YES	NO
Has the study fish oil been supplied and explained	☐	☐
Has the dosing DVD been shown to the subject (only if necessary)	☐	☐
Has the take home diary been supplied and explained	☐	☐

PHYSICAL EXAMINATION/VITAL SIGNS	
Height (without shoes)	cms
Weight (without shoes, with clothes)	kgs
Blood Pressure (sitting, after resting for 5 minutes)	mmHG

ANALGESIC MEDICATION	
Number of Paracetamol tablets supplied at previous visit	
Number of Paracetamol tablets returned	
Number of paracetamol tablets accounted for in diary	
Difference between number of tablets recorded taken and actual number of tablets removed from package.	

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

Remember to remind Subject the importance of returning the empty foil strips. Remember to record these details in the Analgesic Medication Record

PREPARATION FOR NEXT APPOINTMENT		
	YES ☐	NO ☐
Has an appointment been made for the subjects DEXA scan Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has an appointment been made for the subjects MRI Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has the subject been supplied an IMVS form for fasting bloods prior to next visit	☐	☐
Has the subject been supplied with a FOSTAR fridge magnet	☐	☐
Has the subject been supplied with a FOSTAR business card	☐	☐
Has the subject been issued with a pedometer, had it's use explained and been asked to use it over a 7 day consecutive period? Please record details in Pedometer Record	☐	☐
Has the subject been issued with analgesic medication for pain relief? Please ensure all details are recorded on the Analgesic medication Form	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

FOSTAR STUDY

Visit 3 (3 months) - TREATMENT

Visit Date……

☐☐/☐☐/☐☐☐☐

DD / MM / YYYY

	ANALGESIC USE	
	YES	NO
Has subject withheld taking anti-inflammatory and analgesic medications prior to appointment If YES, continue with questionnaires. If NO, ask subject to withhold analgesic and inflammatory medications from today and complete questionnaires at home. The questionnaires are then to be returned in pre-paid envelopes.	☐	☐

	QUESTIONNAIRES			
	Supplied		Completed	
	YES	NO	YES	NO
WOMAC	☐	☐	☐	☐
AQol I	☐	☐	☐	☐
NRS pain	☐	☐	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

MEDICAL CHANGES		
Has the subject been diagnosed with any NEW medical conditions since their last visit?		
NEW MEDICAL CONDITION	Date of Onset (DD/MM/YYYY)	Date Resolved Or √ Ongoing (DD/MM/YYYY)
		☐
		☐
		☐
If the subject is currently taking any medications for any of the above procedures, ensure that details are recorded in the Concomitant Medications record.		

CONCOMITANT MEDICATIONS					
Has the subject started, stopped or changed the doses of any medications since their last visit? (Ask to see all medications used)					
Brand Name	Dose	Units	Route	Start/Stop Dates (DD/MM/YYYY)	Ongoing
				Start…../…../…… Stop…../…/……..	☐
				Start…../…../…… Stop…../…/……	☐
Please remember to transfer any details here to concomitant medications page					

ANALGESIC MEDICATION	
Number of Paracetamol tablets supplied at previous visit	
Number of Paracetamol tablets returned	
Number of paracetamol tablets accounted for in diary	
Difference between number of tablets recorded taken and actual	

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

number of tablets removed from package.	
Remember to remind Subject the importance of returning the empty foil strips. Remember to record these details in the Analgesic Medication Record	

HOSPITALISATIONS/DAY PROCEDURES			
Has the subject been to hospital for any medical procedures since their last visit? ☐YES ☐NO If Yes, please provide details below			
Date Admitted DD/MM/YYYY	Date Discharged DD/MM/YYYY	Doctor's Details	Purpose
Total Number of Hospitalisations since last Appointment: …….			

BLOOD TESTS		
	YES	NO
Has a fasting blood sample been taken to measure serum fatty acids?	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

PHYSICAL EXAMINATION/VITAL SIGNS	
Height (without shoes)	cms
Weight (without shoes, with clothes)	kgs
Blood Pressure(sitting, after resting for 5 minutes)	mmHG

STUDY FISH OIL		
	YES	NO
Has the Visit 2 fish oil been returned (inc. any empty bottles) How many mLs are remaining? ……..mL What percentage of expected was taken? ……..% (=amount actually taken/amount expected to be taken x 100) We want at least 75% compliance so if necessary, encourage subject to keep taking the fish oil on a daily basis	☐	☐
Has Visit 3 fish oil been explained and supplied	☐	☐

VISIT 2 DIARY		
	YES	NO
Has the subject's Visit 2 diary been collected and reviewed	☐	☐
Have all diary concomitant medication records been transcribed into the CRFs Concomitant Medication Section	☐	☐
Have all diary adverse event records been transcribed into the CRFs Adverse Events Section	☐	☐

PREPARATION FOR NEXT APPOINTMENT		
	YES	NO
Has an appointment been made for the subjects next appointment in	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

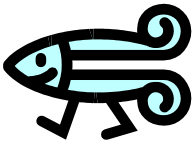
☐☐☐☐☐

3 months time Details: ……/……/……. ..……am/pm DD/MM/YYYY	
Has the subject been supplied an IMVS form for fasting bloods prior to next visit	☐ ☐
Has a Visit 3 take home diary been supplied and explained	☐ ☐
Has the pedometer issued at Visit 2 been collected and the information recorded in the Pedometer Record section	☐ ☐
Has the subject been issued with Analgesic medication to use for pain relief Please record this information on the Analgesic Medication Form	☐ ☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐



FOSTAR STUDY

Visit 4 (6 months) - TREATMENT

Visit Date…….…… ☐☐/☐☐/☐☐☐☐ DD / MM / YYYY

ANALGESIC USE		
	YES	NO
Has subject withheld taking anti-inflammatory and analgesic medications prior to appointment If YES, continue with questionnaires. If NO, ask subject to withhold analgesic and inflammatory medications from today and complete questionnaires at home. The questionnaires are then to be returned in pre-paid envelopes.	☐	☐

QUESTIONNAIRES				
	Supplied		Completed	
	YES	NO	YES	NO
WOMAC	☐	☐	☐	☐
AQol I	☐	☐	☐	☐
NRS pain	☐	☐	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

MEDICAL CHANGES		
Has the subject been diagnosed with any NEW medical conditions since their last visit?		
NEW MEDICAL CONDITION	Date of Onset (DD/MM/YYYY)	Date Resolved Or √ Ongoing (DD/MM/YYYY)
		☐
		☐
		☐
If the subject is currently taking any medications for any of the above procedures, ensure that details are recorded in the Concomitant Medications record.		

CONCOMITANT MEDICATIONS					
Has the subject started, stopped or changed the doses of any medications since their last visit? (Ask to see all medications used)					
Brand Name	Dose (4)	Units (mg)	Route (po)	Start/Stop Dates (DD/MM/YYYY)	Ongoing
				Start…../…../….. Stop…../…/……	☐
				Start…../…../…. Stop…../…/……	☐
Please remember to transfer any details here to concomitant medications page					

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

HOSPITALISATIONS/DAY PROCEDURES			
Has the subject been to hospital for any medical procedures since their last visit? ☐YES ☐NO If Yes, please provide details below			
Date Admitted DD/MM/YYYY	Date Discharged DD/MM/YYYY	Doctor's Details	Purpose
Total Number of Hospitalisations since last visit:……..			

BLOOD TESTS		
	YES	NO
Has a fasting blood sample been taken to measure serum fatty acids?	☐	☐

PHYSICAL EXAMINATION/VITAL SIGNS	
Height (without shoes)	cms

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

Weight (without shoes, with clothes)	kgs
Blood Pressure (sitting, after resting for 5 minutes)	mmHG

	STUDY FISH OIL	
	YES	NO
Has the Visit 3 fish oil been returned (inc. any empty bottles) How many mLs are remaining? ……..mL What percentage of expected was taken? ……..% (=amount actually taken/amount expected to be taken x 100) We want at least 75% compliance so if necessary, encourage subject to keep taking the fish oil on a daily basis	☐	☐
Has Visit 4 fish oil been explained and supplied	☐	☐

ANALGESIC MEDICATION	
Number of Paracetamol tablets supplied at previous visit	
Number of Paracetamol tablets returned	
Number of paracetamol tablets accounted for in diary	
Difference between number of tablets recorded taken and actual number of tablets removed from package.	
Remember to remind Subject the importance of returning the empty foil strips. Remember to record these details in the Analgesic Medication Record	

	VISIT 3 DIARY	
	YES	NO

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

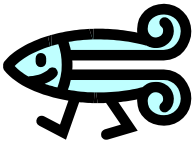
Has the subject's Visit 3 diary been collected and reviewed	☐ ☐
Have all diary concomitant medication records been transcribed into the CRFs Concomitant Medication Section	☐ ☐
Have all diary adverse event records been transcribed into the CRFs Adverse Events Section	☐ ☐

PREPARATION FOR NEXT APPOINTMENT		
	YES	NO
Has an appointment been made for the subjects next appointment in 3 months time? Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has the subject been supplied an IMVS form for fasting bloods prior to next visit?	☐	☐
Has a Visit 4 take home diary been supplied and explained?	☐	☐
Has the subject been supplied with analgesic medication for pain relief? Please record all details on the Analgesic Medication Form	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐



FOSTAR STUDY

Visit 5 (9 months) - TREATMENT

Visit Date…… ☐☐/☐☐/☐☐☐☐ DD / MM / YYYY

ANALGESIC USE		
	YES	NO
Has subject withheld taking anti-inflammatory and analgesic medications prior to appointment If YES, continue with questionnaires. If NO, ask subject to withhold analgesic and inflammatory medications from today and complete questionnaires at home. The questionnaires are then to be returned in pre-paid envelopes.	☐	☐

QUESTIONNAIRES				
	Supplied		Completed	
	YES	NO	YES	NO
WOMAC	☐	☐	☐	☐
AQol I	☐	☐	☐	☐
NRS pain	☐	☐	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

MEDICAL CHANGES		
Has the subject been diagnosed with any NEW medical conditions since their last visit?		
NEW MEDICAL CONDITION	Date of Onset (DD/MM/YYYY)	Date Resolved Or √ Ongoing (DD/MM/YYYY)
		☐
		☐
		☐
If the subject is currently taking any medications for any of the above procedures, ensure that details are recorded in the Concomitant Medications record.		

CONCOMITANT MEDICATIONS					
Has the subject started, stopped or changed the doses of any medications since their last visit? (Ask to see all medications used)					
Brand Name	Dose (4)	Units (mg)	Route (po)	Start/Stop Dates (DD/MM/YYYY)	Ongoing
				Start…../…../…. Stop…../…./….	☐
				Start…../…../…. Stop…../…./….	☐
Please remember to transfer any details here to concomitant medications page					

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

HOSPITALISATIONS/DAY PROCEDURES			
Has the subject been to hospital for any medical procedures since their last visit? ☐YES ☐NO If Yes, please provide details below			
Date Admitted DD/MM/YYYY	Date Discharged DD/MM/YYYY	Doctor's Details	Purpose
Total Number of Hospitalisations since last Appointment: ……			

BLOOD TESTS		
	YES	NO
Has a fasting blood sample been taken to measure serum fatty acids?	☐	☐

PHYSICAL EXAMINATION/VITAL SIGNS	
Height (without shoes)	cms

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

Weight (without shoes, with clothes)	kgs
Blood Pressure (sitting, after resting for 5 minutes)	mmHG

STUDY FISH OIL		
	YES	NO
Has the Visit 4 fish oil been returned (inc. any empty bottles) How many mLs are remaining? ……..mL What percentage of expected was taken? ……..% (=amount actually taken/amount expected to be taken x 100) We want at least 75% compliance so if necessary, encourage subject to keep taking the fish oil on a daily basis	☐	☐
Has Visit 5 fish oil been explained and supplied	☐	☐

ANALGESIC MEDICATION	
Number of Paracetamol tablets supplied at previous visit	
Number of Paracetamol tablets returned	
Number of paracetamol tablets accounted for in diary	
Difference between number of tablets recorded taken and actual number of tablets removed from package.	
Remember to remind Subject the importance of returning the empty foil strips. Remember to record these details in the Analgesic Medication Record	

VISIT 4 DIARY		
	YES	NO
Has the subject's Visit 4 diary been collected and reviewed		

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:**

☐☐☐☐☐

	☐	☐
Have all diary concomitant medication records been transcribed into the CRFs Concomitant Medication Section	☐	☐
Have all diary adverse event records been transcribed into the CRFs Adverse Events Section	☐	☐

PREPARATION FOR NEXT APPOINTMENT		
	YES ☐	NO ☐
Has an appointment been made for the subjects next appointment in 3 months time Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has the subject been supplied an IMVS form for fasting bloods prior to next visit	☐	☐
Has a Visit 5 take home diary been supplied and explained	☐	☐
Has the subject been issued with analgesic medication for pain relief Please record all details on the Analgesic Medication Form	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

FOSTAR STUDY

Visit 6 (12 months) - TREATMENT

Visit Date……..…… ☐☐/☐☐/☐☐☐☐ DD / MM / YYYY

	ANALGESIC USE	
	YES	NO
Has subject withheld taking anti-inflammatory and analgesic medications prior to appointment If YES, continue with questionnaires. If NO, ask subject to withhold analgesic and inflammatory medications from today and complete questionnaires at home. The questionnaires are then to be returned in pre-paid envelopes.	☐	☐

	QUESTIONNAIRES			
	Supplied		Completed	
	YES	NO	YES	NO
WOMAC ☐	☐		☐	☐
AQol I ☐	☐		☐	☐
NRS pain	☐	☐	☐	☐
MAPT	☐	☐	☐	☐
Diet **Diet Barcode ……..**	☐	☐	☐	☐
Physical Activity (PASE)	☐	☐	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

MEDICAL CHANGES		
Has the subject been diagnosed with any NEW medical conditions since their last visit?		
NEW MEDICAL CONDITION	Date of Onset (DD/MM/YYYY)	Date Resolved Or √ Ongoing (DD/MM/YYYY)
		☐
		☐
		☐
If the subject is currently taking any medications for any of the above procedures, ensure that details are recorded in the Concomitant Medications record.		

CONCOMITANT MEDICATIONS					
Has the subject started, stopped or changed the doses of any medications since their last visit? (Ask to see all medications used)					
Brand Name	Dose (4)	Units (mg)	Route (po)	Start/Stop Dates (DD/MM/YYYY)	Ongoing
				Start…../…../…… Stop…../…./……..	☐
				Start…../…../…… Stop…../…./……	☐
Please remember to transfer any details here to concomitant medications page					

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

HOSPITALISATIONS/DAY PROCEDURES			
Has the subject been to hospital for any medical procedures since their last visit? ☐YES ☐NO If Yes, please provide details below			
Date Admitted DD/MM/YYYY	Date Discharged DD/MM/YYYY	Doctor's Details	Purpose
Total number of hospital admissions since last visit:……..			

CURRENT EMPLOYMENT	
What is your current work status?	☐Full-time employed ☐Part-time/casual employment ☐Unemployed ☐Home Duties ☐Retired ☐Student ☐Other Please specify …….....

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

JOINT OSTEOARTHRITIS HISTORY	
Over the past month have you had pain on most days in any of the following joints?	☐ Other knee. **Not** the one being investigated in this study ☐ Lower Back ☐ Neck ☐ Shoulder ☐ Hands ☐ Other (details)……. ☐ No others

BLOOD TESTS		
	YES	NO
Has a fasting blood sample been taken to measure serum fatty acids?	☐	☐

PHYSICAL EXAMINATION/VITAL SIGNS	
Height (without shoes)	cms
Weight (without shoes, with clothes)	kgs
Blood Pressure (sitting, after resting for 5 minutes)	mmHG

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

STUDY FISH OIL		
	YES	NO
Has the Visit 4 fish oil been returned (inc. any empty bottles) How many mLs are remaining? ……..mL What percentage of expected was taken? ……..% (=amount actually taken/amount expected to be taken x 100) We want at least 75% compliance so if necessary, encourage subject to keep taking the fish oil on a daily basis	☐	☐
Has Visit 5 fish oil been explained and supplied	☐	☐

ANALGESIC MEDICATION	
Number of Paracetamol tablets supplied at previous visit	
Number of Paracetamol tablets returned	
Number of paracetamol tablets accounted for in diary	
Difference between number of tablets recorded taken and actual number of tablets removed from package.	
Remember to remind Subject the importance of returning the empty foil strips. Remember to record these details in the Analgesic Medication Record	

VISIT 5 DIARY		
	YES	NO
Has the subject's Visit 5 diary been collected and reviewed	☐	☐
Have all diary concomitant medication records been transcribed into the CRFs Concomitant Medication Section	☐	☐
Have all diary adverse event records been transcribed into the CRFs Adverse Events Section	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

PREPARATION FOR NEXT APPOINTMENT		
	YES ☐	NO ☐
Has an appointment been made for the subjects next appointment in 6 months time Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has the subject been supplied an IMVS form for fasting bloods prior to next visit	☐	☐
Has a Visit 6 take home diary been supplied and explained	☐	☐
Has the subject been issued with a pedometer, had its use explained and been asked to use it for seven consecutive days. Please record details in Pedometer Record	☐	☐
Has the subject been supplied with analgesic medication for pain relief? Please ensure all details are recorded on the Analgesic Medication Form	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

FOSTAR STUDY

Visit 7 (18 months) - TREATMENT

Visit Date…… ☐☐/☐☐/☐☐☐☐ DD / MM / YYYY

ANALGESIC USE		
	YES	NO
Has subject withheld taking anti-inflammatory and analgesic medications prior to appointment If YES, continue with questionnaires. If NO, ask subject to withhold analgesic and inflammatory medications from today and complete questionnaires at home. The questionnaires are then to be returned in pre-paid envelopes.	☐	☐

QUESTIONNAIRES				
	Supplied		Completed	
	YES	NO	YES	NO
WOMAC ☐	☐		☐	☐
AQol I ☐	☐		☐	☐
NRS pain	☐	☐	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

MEDICAL CHANGES		
Has the subject been diagnosed with any NEW medical conditions since their last visit?		
NEW MEDICAL CONDITION	Date of Onset (DD/MM/YYYY)	Date Resolved Or √ Ongoing (DD/MM/YYYY)
		☐
		☐
		☐
If the subject is currently taking any medications for any of the above procedures, ensure that details are recorded in the Concomitant Medications record.		

CONCOMITANT MEDICATIONS					
Has the subject started, stopped or changed the doses of any medications since their last visit? (Ask to see all medications used)					
Brand Name	Dose (4)	Units (mg)	Route (po)	Start/Stop Dates (DD/MM/YYYY)	Ongoing (tick)
				Start…../…../…… Stop…../…./……..	☐
				Start…../…../…… Stop…../…./……	☐
Please remember to transfer any details here to concomitant medications page					

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

HOSPITALISATIONS/DAY PROCEDURES			
Has the subject been to hospital for any medical procedures since their last visit? ☐YES ☐NO If Yes, please provide details below			
Date Admitted DD/MM/YYYY	Date Discharged DD/MM/YYYY	Doctor's Details	Purpose
Total number of hospitalisations since last visit:…….			

BLOOD TESTS		
	YES	NO
Has a fasting blood sample been taken to measure serum fatty acids?	☐	☐

PHYSICAL EXAMINATION/VITAL SIGNS	
Height (without shoes)	cms
Weight (without shoes, with clothes)	kgs
Blood Pressure (sitting, after resting for 5 minutes)	mmHG

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

STUDY FISH OIL		
	YES	NO
Has the Visit 6 fish oil been returned (inc. any empty bottles) How many mLs are remaining? ……..mL What percentage of expected was taken? ……..% (=amount actually taken/amount expected to be taken x 100) We want at least 75% compliance so if necessary, encourage subject to keep taking the fish oil on a daily basis	☐	☐
Has Visit 7 fish oil been explained and supplied	☐	☐

ANALGESIC MEDICATION	
Number of Paracetamol tablets supplied at previous visit	
Number of Paracetamol tablets returned	
Number of paracetamol tablets accounted for in diary	
Difference between number of tablets recorded taken and actual number of tablets removed from package.	
Remember to remind Subject the importance of returning the empty foil strips. Remember to record these details in the Analgesic Medication Record	

VISIT 6 DIARY		
	YES	NO
Has the subject's Visit 6 diary been collected and reviewed	☐	☐
Have all diary concomitant medication records been transcribed into the CRFs Concomitant Medication Section	☐	☐
Have all diary adverse event records been transcribed into the CRFs Adverse Events Section	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

PREPARATION FOR NEXT APPOINTMENT		
	YES ☐	NO ☐
Has an appointment been made for the subjects next appointment in 6 months time Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has the subject been supplied an IMVS form for fasting bloods prior to next visit	☐	☐
Has a Visit 7 take home diary been supplied and explained	☐	☐
Has the pedometer that was issued to the subject at Visit 6 been returned and the details transcribed to the Pedometer record Section	☐	☐
Has the subject had a pedometer issued, had its use explained and been asked to use the pedometer over 7 consecutive days. Please record details in Pedometer Record Section of CRF	☐	☐
Has the subject been issued with analgesic medication for pain relief? Please ensure all details are recorded on the Analgesic Medication Form	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

FOSTAR STUDY

Visit 8 (24 months) – Completion/Withdrawal

Visit Date…… ☐☐/☐☐/☐☐☐☐ DD / MM / YYYY

	ANALGESIC USE	
	YES	NO
Has subject withheld taking anti-inflammatory and analgesic medications prior to appointment If YES, continue with questionnaires. If NO, ask subject to withhold analgesic and inflammatory medications from today and complete questionnaires at home. The questionnaires are then to be returned in pre-paid envelopes.	☐	☐

	QUESTIONNAIRES			
	Supplied		Completed	
	YES	NO	YES	NO
WOMAC ☐	☐		☐	☐
AQol I	☐	☐	☐	☐
NRS pain	☐	☐	☐	☐
MAPT ☐	☐		☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

Diet ☐ ☐ ☐ ☐ **Diet Barcode ……**	
Physical Activity (PASE) ☐ ☐	☐ ☐

MEDICAL CHANGES		
Has the subject been diagnosed with any NEW medical conditions since their last visit?		
NEW MEDICAL CONDITION	Date of Onset (DD/MM/YYYY)	Date Resolved Or √ Ongoing (DD/MM/YYYY)
		☐
		☐
		☐
If the subject is currently taking any medications for any of the above procedures, ensure that details are recorded in the Concomitant Medications record.		

CONCOMITANT MEDICATIONS					
Has the subject started, stopped or changed the doses of any medications since their last visit? (Ask to see all medications used)					
Brand Name	Dose (4)	Units (mg)	Route (po)	Start/Stop Dates (DD/MM/YYYY)	Ongoing
				Start…../…../…… Stop…../…./……..	☐
				Start…../…../…… Stop…../…./……	☐
Please remember to transfer any details here to concomitant medications page					

Site Number: ☐

Randomisation Number: ☐☐☐☐

Subject Initials: ☐☐☐

Study Selected Knee: ☐☐☐☐☐

HOSPITALISATIONS/DAY PROCEDURES			
Has the subject been to hospital for any medical procedures since their last visit? ☐YES ☐NO If Yes, please provide details below			
Date Admitted DD/MM/YYYY	Date Discharged DD/MM/YYYY	Doctor's Details	Purpose
Total Number of Hospitalisations since last visit: ……			

JOINT OSTEOARTHRITIS HISTORY	
Over the past month have you had pain on most days in any of the following joints?	☐ Other knee. **Not** the one being investigated in this study ☐ Lower Back ☐ Neck ☐ Shoulder ☐ Hands

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

	☐ Other (details)…….. ☐ No others

CURRENT EMPLOYMENT	
What is your current work status?	☐ Full-time employed ☐ Part-time/casual employment ☐ Unemployed ☐ Home Duties ☐ Retired ☐ Student ☐ Other Please specify …….....

BLOOD TESTS		
	YES	NO
Has a fasting blood sample been taken to measure serum fatty acids?	☐	☐
Has a fasting blood sample been taken for FBC, MBA, CRP, fasting lipids (HDL, TGC, LDL)	☐	☐
Has a serum pregnancy test been taken (if subject male, tick No box)	☐	☐

PHYSICAL EXAMINATION/VITAL SIGNS	
Height (without shoes)	cms
Weight (without shoes, with clothes)	kgs
Blood Pressure (sitting, after resting for 5 minutes)	mmHG

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

STUDY FISH OIL		
	YES	NO
Has the Visit 7 fish oil been returned (inc. all empty bottles) How many mLs are remaining? ……..mL What percentage of expected was taken? ……..% (=amount actually taken/amount expected to be taken x 100) We want at least 75% compliance so if necessary, encourage subject to keep taking the fish oil on a daily basis	☐	☐

ANALGESIC MEDICATION	
Number of Paracetamol tablets supplied at previous visit	
Number of Paracetamol tablets returned	
Number of paracetamol tablets accounted for in diary	
Difference between number of tablets recorded taken and actual number of tablets removed from package.	
Remember to remind Subject the importance of returning the empty foil strips. Remember to record these details in the Analgesic Medication Record	

VISIT 7 DIARY		
	YES	NO
Has the subject's Visit 7 diary been collected and reviewed	☐	☐
Have all diary concomitant medication records been transcribed into the CRFs Concomitant Medication Section	☐	☐
Have all diary adverse event records been transcribed into the CRFs Adverse Events Section	☐	☐

Site Number: ☐ **Randomisation Number:** ☐☐☐☐

Subject Initials: ☐☐☐ **Study Selected Knee:** ☐☐☐☐☐

FINALISING THE STUDY		
	YES	NO
Has an appointment been made for the subjects final DEXA scan on their study selected knee? Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has an appointment been made for the subjects final MRI on their study selected knee? Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has an appointment been made for the subjects x-ray on their study selected knee? Details: ……/……/……. ..……am/pm DD/MM/YYYY	☐	☐
Has the subject been sincerely thanked for their time, effort and cooperation during the study?	☐	☐
Has the pedometer that was issued to the subject at their last visit been returned? Please record all details in the Pedometer Record Section of the CRF	☐	☐
Has the subject's Hospital records been updated to show that they have completed/withdrawn from the study?	☐	☐
Has a letter been sent to the subject's GP to notify their Dr of their completion/withdrawal from the study?	☐	☐