

Efficacy and Mechanism Evaluation Programme

Public minutes of the Third Meeting

Date	Tuesday 10 th March & Wednesday 11 th March 2009
Place	Grange Holborn Hotel, 50-60 Southampton Row, London WC1B 4AR
Present Members	Professor Rajesh Thakker (Chair) Professor Tom Walley (Programme Director) Professor Martin Brown Professor David Cameron (11 th March) Professor Rona Campbell Professor Graham Dunn Professor Diana Elbourne Professor Kim Fox Professor Jayne Franklyn (10 th March) Professor Ian Goodyer Professor Ian Harvey Professor David Jones Professor Paul Little Professor Jane Norman Professor Munir Pirmohamed (10 th March & afternoon 11 th March) Professor Judith Stephenson Professor Moira Whyte (Deputy Chair) Professor John Williams Professor Bryan Williams (10 th March)
NCCEME Secretariat	Ian Cree (Director) Dani Preedy (Senior Programme Manager) Fabia Ward (Assistant Programme Manager) James Preston (Assistant Programme Manager) (10 th March) Rumyana Voutchkova (Administrator) (11 th March) Tracey Waterhouse (Administrator) (11 th March) Maria Chorooglou (Programme Manager Finance) (11 th March)
Observers	Dr Morven Roberts (MRC) Professor GJ Van Der Wilt (Department of Epidemiology, Biostatistics & HTA , Netherlands)
Apologies	Professor David Cameron (10 th March) Professor Andrew Carr Professor Jayne Franklyn (11 th March) Professor Graham Russell Professor Stephen Senn Professor Pierre Guillou Professor Bryan Williams (11 th March)

DISCUSSION OF FULL PROPOSALS – Tuesday 10TH March 2009
<i>Professor Thakker Chaired</i>
08/43/03 Parent-determined oral montelukast therapy for preschool wheeze with stratification for arachidonate-5-lipoxygenase (ALOX5) promoter genotype
<i>Professors Whyte, Pirmohamed and Campbell presented the proposal</i>
The Board recommended the proposal for funding subject to changes. 08/43/03: Grigg
08/43/08 Randomised placebo control trial of a multi species probiotic to prevent bowel dysfunction after campylobacter gastroenteritis.
<i>Professors J Williams, Pirmohamed and Dunn presented the proposal</i>
The Board did not recommend the proposal for funding. 08/43/08: Spiller
08/43/12 Therapeutic potential of Vitamin D Immunomodulation of Subclinical Hypothyroidism (DISH)
<i>Professor Thakker left the room. Professor Whyte chaired. Professors Norman, Harvey and Goodyer presented the proposal</i>
The Board did not recommend the proposal for funding. 08/43/12: Pearce
08/43/41 Simvastatin Treatment for Onset-Prevention of Dementia. Double-blind, randomised controlled trial with older adults with Down syndrome (The STOP Dementia Study)
<i>Professor Goodyer left the room. Professors Dunn and Fox presented the proposal</i>
The Board did not recommend the proposal for funding. 08/43/41: Cooper
08/43/27 Reduction of Abdominal Fat in Teenagers (RAFT): Randomised controlled trial of metformin in obese insulin resistant pubertal adolescents
<i>Professor Goodyer left the room. Professors Franklyn and Campbell presented the proposal</i>
The Board did not recommend the proposal for funding. 08/43/27: Viner
08/43/55 Examination of the Role of Inflammation in Herpes Simplex Virus Encephalitis through a Randomised Double-Blind Placebo Controlled Trial of Adjunct Corticosteroids, a UK arm of a European Phase III study
<i>Professors Walley and Pirmohamed left the room. Professors B Williams, Brown and Elbourne presented the proposal.</i>
The Board invited the applicants to resubmit a full proposal in response to feedback provided. 08/43/55: Solomon
08/43/50 Randomised controlled trial to investigate whether increased intake of Prebiotic carbohydrate will reduce appetite resulting in increased weight loss.
<i>Professor Fox left the room. Professors J Williams, Franklyn and B Williams presented the proposal.</i>
The Board did not recommend the proposal for funding. 08/43/50: Frost
<i>Professor Bryan Williams left the meeting</i>
08/43/38 A multi-centre randomised controlled trial to study the efficacy of bicarbonate supplementation on renal graft function and polypeptide proximal tubular catabolism in patients with transplanted kidneys. BICARBGRAFT
<i>Professors Walley, Pirmohamed and Dunn left the room. Professors Jones and Franklyn presented the proposal</i>
The Board deferred the discussion of the proposal to the next meeting. 08/43/38: Rustom
08/43/29 The diagnostic efficacy of circulating C-reactive Protein-Very Low Density Lipoprotein (CRP-VLDL) complexes in sepsis and an evaluation of its underlying mechanism.
<i>Professors Walley and Pirmohamed left the room. Professors Elbourne, Little and Whyte presented the proposal.</i>
The Board did not recommend the proposal for funding. 08/43/29: Toh
08/43/39 Antiglucocorticoid augmentation of antidepressants in Depression (The ADD study)
<i>Professor Dunn left the room. Professors Goodyer, Harvey and Little presented the proposal.</i>
The Board recommended the proposal for funding subject to changes. 08/43/39:

Ferrier
08/43/61 Does Levodopa (3,4-dihydroxy-L-phenylalanine) drug treatment in combination with routine NHS occupational and physical therapy, delivered early after stroke within a stroke service, improve functional recovery including walking and arm function
<i>Professors Little, Stephenson and Harvey presented the proposal.</i>
The Board recommended the proposal for funding subject to changes. 08/43/61: Bhakta
08/43/56 Randomised controlled trial on the efficacy, safety and mechanisms of pregabalin preventing post-thoracotomy neuropathic pain (PPP trail)
<i>Professor Franklyn left the room. Professor Whyte presented the proposal.</i>
The Board did not recommend the proposal for funding. 08/43/56: Gao-Smith
08/43/52 Imaging perfusion deficits and thrombolysis safety and efficacy in acute ischaemic stroke. The Third International Stroke Trial (IST-3).
<i>Professors Brown and Fox presented the proposal.</i>
The Board recommended the proposal for funding subject to changes. 08/43/52: Wardlaw
08/43/25 Neural and biomechanical correlates of response to the use of an ankle-foot cast provided to improve walking recovery early after stroke. A Phase II trial.
<i>Professors Harvey and Goodyer left the room. Professors Jones and Brown presented the proposal.</i>
The Board agreed that the proposal was fundable depending on overall Board spend and requested further clarification on a number of specific issues before agreeing to fund. 08/43/25: Pomeroy
<i>Professor Brown left the meeting</i>
08/43/57 Effect of Sodium Nitrite Injection on Infarct Size in Patients with Myocardial Infarction undergoing Primary Angioplasty
<i>Professor Fox presented the proposal.</i>
The Board did not recommend the proposal for funding however invited the applicant to resubmit a revised preliminary application in response to feed back. 08/43/57: Webb
<i>Professor Stephenson left the meeting</i>
08/43/15 A randomised controlled trial of losartan as an anti-fibrotic agent in non-alcoholic steatohepatitis
<i>Professors Pirmohamed, Norman and Jones presented the proposal.</i>
The Board recommended the proposal for funding subject to changes. 08/43/15: Day

DISCUSSION OF FULL PROPOSALS – Wednesday 11TH March 2009

Professor Thakker Chaired

08/43/19 A phase II multicentre, randomised controlled trial of intravenous recombinant human interleukin-1 receptor antagonist (rhIL-1RA) therapy in acute ischaemic Stroke: effect on cerebral infarct expansion in patients with at-risk brain tissue.

Professors Dunn, Fox, Goodyer and Thakker left the room. Professor Whyte chaired. Professors Brown, Elbourne and Norman presented the proposal.

The Board did not recommend the proposal for funding. 08/43/19: Tyrell

08/43/42 A phase II cluster randomised controlled trial comparing the effectiveness and cost effectiveness of a nurse-led psychological self-help approach plus medical therapy with standard paediatric care of children referred with constipation

Professors Stephenson and Campbell presented the proposal.

The Board did not recommend the proposal for funding. 08/43/42: Tappin

08/43/44 A feasibility study comparing cryotherapy versus conservative management in men with radiation relapsed localised prostate cancer.

Professors Cameron and Dunn presented the proposal.

The Board did not recommend the proposal for funding. 08/43/44: Leung

DISCUSSION OF PRELIMINARY APPLICATIONS – Wednesday 11TH

March 2009
08/246/01 Cognitive Behaviour Therapy for aggressive men with antisocial personality disorder: MASCOT 2. *MASCOT: Men with Antisocial personality disorder treated with Cognitive Therapy
<i>Professor Dunn left the room. Professors Goodyer, Brown and Jones presented the proposal.</i>
The Board shortlisted 08/246/01: Davidson
08/246/07 Efficacy and safety of the peri-operative Methylprednisolone on outcome from cardiopulmonary bypass in children undergoing surgery for congenital heart disease (PUMP study).
<i>Professors Fox and Elbourne left the room. Professors Guillou, Carr and Senn provided comments on the proposal which Professor Thakker presented to the Board.</i>
The Board rejected 08/246/07: Pathan
08/246/08 The effect of Dexmedetomidine Sedation on Post-Operative Cognitive Dysfunction induced by Orthopaedic Surgery in Elderly Patients
<i>Professor Walley left the room Professors Little and Franklyn presented the proposal.</i>
The Board rejected 08/246/08: Maze
08/246/02 Peroxisome Proliferator-Activated Receptor-gamma: a novel therapeutic target for asthma?
<i>Professors Little and Whyte presented the proposal.</i>
The Board shortlisted 08/246/02: Knox
08/246/03 Investigation Of Optimal Reduction In Dialysate Temperature On Systemic Haemodynamics And Regional Left Ventricular Dysfunction In Paediatric Haemodialysis
<i>Professors J.Williams and Elbourne presented the proposal.</i>
The Board shortlisted 08/246/03: Rees
08/246/05 A randomised controlled trial of a pedometer-based intervention combined with primary care physical activity consultations, with or without accelerometer feedback, in patients aged 60-75 years.
<i>Professor Goodyear left the room. Professors Stephenson and Harvey presented the Proposal.</i>
The Board shortlisted 08/246/05: Harris
08/246/09 Does metformin reduce excess birthweight in offspring of obese pregnant women? A randomised controlled trial of efficacy, exploration of mechanisms and evaluation of other pregnancy complications.
<i>Professors Walley and Norman left the room. Professors Campbell, Stephenson and Elbourne presented the proposal.</i>
The Board shortlisted 08/246/09: Norman
08/246/24 Multi-centre Randomised Controlled Trial of the Optimisation of Cardiovascular Health with Growth Hormone Therapy in the Transition Phase
<i>Professors Walley, Whyte, Goodyer and Norman left the room. Professors Jones and Fox presented the proposal.</i>
The Board shortlisted 08/246/24: Kelnar
08/246/16 Investigation of the efficacy of pregnenolone in the treatment of rheumatoid arthritis (RA) patients and characterisation of the underlying biological mechanisms
<i>Professor Elbourne presented the proposal</i>
The Board shortlisted 08/246/16: Emery
<i>Professor Pirmohamed joined the meeting.</i>
08/246/13 The first prospective biomarker-selected phase III randomised controlled trial of cyclo-oxygenase 2 inhibitor, celecoxib, in the adjuvant treatment of colorectal cancer.
<i>Professor Thakker left the room. Professor Whyte chaired. Professors J.Williams, Cameron and Dunn presented the proposal.</i>
The Board rejected 08/246/13: Midgley
08/246/14 Enhanced recovery after hip fracture with rapid repletion of vitamin D: double blind randomized clinical trial of efficacy and safety [OXID- HIP: Oxford

Vitamin D intervention after hip fracture]
<i>Professors Thakker and Little left the room. Professor Whyte chaired. Professors Dunn and Pirmohamed presented the proposal.</i>
The Board rejected 08/246/14: Javaid
08/246/12 A prospective study of gonadal toxicity and ovarian tissue cryostorage for fertility preservation in young women with Hodgkin's Lymphoma.
<i>Professors Norman, Little, Cameron and Cree left the room. Professors Stephenson and Pirmohamed presented the proposal.</i>
The Board rejected 08/246/12: Anderson
08/246/17 A pilot randomised trial to show that arterial stiffness is likely to be a more effective and efficient target than routine cardiovascular risk factor control and is amenable to treatment with intensive vascular therapy and vitamin D.
<i>Professors Dunn and J Williams left the room. Professors Fox and Campbell presented the proposal.</i>
The Board rejected 08/246/17: Cruickshank
08/246/15 A Phase I/II dose escalation to determine the optimal dose fractionation for High Dose Rate (HDR) Brachytherapy used as monotherapy for the treatment of localised carcinoma of the prostate
<i>Professors Cameron and Norman presented the proposal.</i>
The Board rejected 08/246/15: Hoskin. The Board invited the applicants to resubmit a revised preliminary application in response to feedback from the Board
08/246/18 Activity Management and Exercise Therapy for chronic fatigue Syndrome Trial (AMETHYST)
<i>Professors Dunn, Goodyer and Fox presented the proposal.</i>
The Board rejected 08/246/18: Chalder
08/246/20 Neuroendocrine functions regulating cortisol and child health/mental health outcomes: an RCT on exposure to FAST, an evidence based parenting programme which manipulates social capital, empowers parents, and strengthens parent-child
<i>Professors Goodyer and Campbell presented the proposal.</i>
The Board rejected 08/246/20: McDonald
08/246/21 Effect of dietary nitrate ingestion on coronary restenosis
<i>Professors Fox and Whyte presented the proposal.</i>
The Board rejected 08/246/21: Ahluwalia
08/246/22 Combination of anti-interleukin 4 with allergen immunotherapy restores tolerance and promotes remission in severe hayfever
<i>Professors Fox left the room. Professors Whyte, Norman and Harvey presented the proposal.</i>
The Board rejected 08/246/22: Schmidt-Weber
08/246/28 Randomised Controlled Early Phase Trial of Dopamine and Dobutamine in Preterm Infants - analysis of biological effect using Cardiac Magnetic Resonance Imaging
<i>Professors Norman, Elbourne and Little presented the proposal.</i>
The Board rejected 08/246/28: Edwards
08/246/27 A randomised controlled trial of exercise to preserve beta cell function in patients with latent autoimmune diabetes of adults (LADA).
<i>Professors Harvey, Brown and Dunn presented the proposal.</i>
The Board rejected 08/246/27: Narendran
08/246/25 CRASH-2 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage) sub study: The effect of tranexamic acid on intracranial bleeding among CRASH-2 trial participants
<i>Professors Elbourne and Goodyer left the room. Professors Jones, Brown and J. Williams presented the proposal.</i>
The Board rejected 08/246/25: Perel
08/246/06 Cocoa flavonoids and stroke risk: a pilot randomised controlled trial to explore potential mechanisms

Professor Harvey left the room. Professors Brown and Cameron presented the proposal.

The Board rejected 08/246/06: Myint

SUMMARY

- *7 preliminary applications were shortlisted to submit a full proposal for consideration at the June 2009 EME Board*
- *6 full proposals were funded, subject to changes in response to Board feedback and further clarification on specific issues raised by the Board*
- *1 full proposal was invited to resubmit, in response to Board feedback*
- *1 full proposal was deferred until the next EME Board Meeting*
- *1 full proposal was invited to submit a revised preliminary application*
- *10 full proposals were not recommended for funding*