

and



...working together on CNS studies

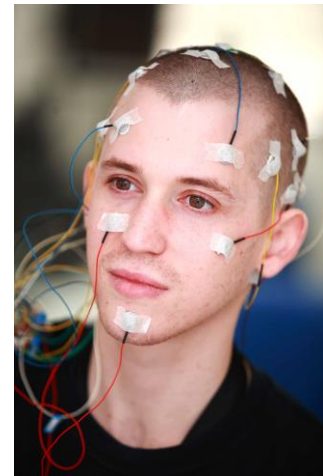
Hammersmith Medicines Research (HMR) and P1vital collaborate on early phase clinical studies. The outstanding phase 1 experience and facilities of HMR together with the unique CNS experimental medicine expertise and capabilities of P1vital provide a comprehensive solution for early assessment of the safety and potential efficacy of novel CNS compounds.

Central nervous system drugs

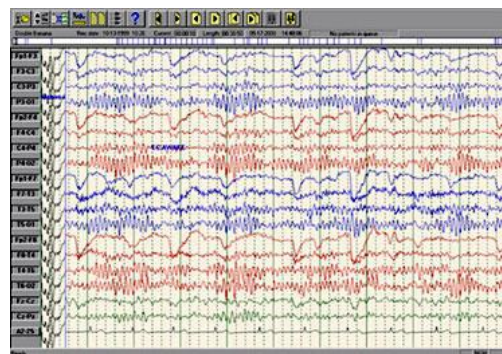
Since 1993, HMR has done over 730 phase 1 studies, over 200 of which involved compounds with central nervous system (CNS) activity. Many of the studies were first-in-man.

We have experience of a wide range of procedures to assess novel CNS compounds, such as:

- psychomotor tests;
- coordination tests;
- sleep and polysomnography
- ataxiometer;
- body sway;
- erythrocyte cholinesterase activity;
- cognitive function assessment, using a computerised system, such as CDR and Cogstate;
- scopolamine model of dementia;
- saliva flow rate;
- pain models;
- saccadic eye movements;
- critical flicker fusion frequency threshold;
- digit span;
- EEG, with interpretation by consultant neurologist;
- PET, with Imanova, Hammersmith Hospital;
- SPECT, with UC Hospital;
- fMRI, with Imanova, Hammersmith Hospital or Institute of Psychiatry, King's College Hospital;
- clinical questionnaires, eg POMS, CSSRS, AIMS, Simpson-Angus, Barnes ARS, TFEQIII, BDI and HRS;



EEG electrodes



EEG



MRI scan

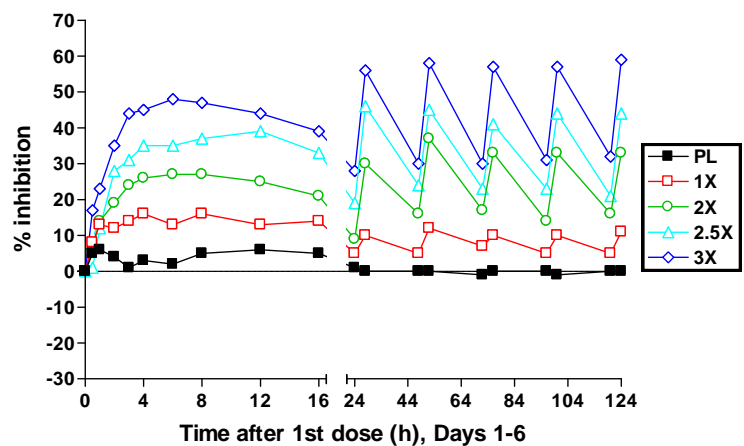
- simple and choice reaction times;
- visual analogue rating scales;
- tyramine challenge tests, to assess MAO-B inhibition; and
- 5-HT_{1A}-receptor mediated function tests.

Types of molecule

Types of molecule that we've studied include:

- dopamine receptor antagonists;
- cannabinoid-1 receptor inverse agonists;
- MAO-B inhibitors;
- anti-convulsants;
- anti-psychotics;
- anti-depressants;
- cholinesterase inhibitors;
- histamine H₃-receptor antagonists;
- histamine H₁-receptor antagonists;
- 5-HT_{1A} receptor agonists;
- benzodiazepine analogues; and
- GABA inverse agonists.

Dose-related inhibition of red-cell cholinesterase in healthy men (reference 4)



Collaboration with P1vital

P1vital provides a unique range of products and services in CNS experimental medicine to enable client companies to more effectively manage their risk and investment in CNS drug development. The P1vital team has extensive expertise in all aspects of CNS drug discovery and development. This enables P1vital to offer their clients customised experimental medicine solutions including:

- Consultancy and study delivery services to enable clients to assess the clinical efficacy of their early phase CNS development compounds;
- P1vital® Oxford Emotional Test Battery (ETB), a product that can be used to assess antidepressant efficacy from Phase 1 MAD studies in healthy volunteers to Phase 2 POC studies in patients.

P1vital has an expanding portfolio of efficacy biomarkers for anxiety, depression, schizophrenia, cognitive disorders and obesity including:

- Depression: P1vital® Oxford ETB;

- Depression: pharmacological fMRI;
- Anxiety: CO₂ inhalation;
- Schizophrenia: pharmacological fMRI;
- Schizophrenia: bi-conditional learning;
- Schizophrenia: eye tracking;
- Cognitive disorders: Arena & Platform fMRI tasks;
- Obesity: universal eating monitor.

P1vital is expanding its portfolio of validated CNS efficacy biomarkers through a pre-competitive consortium agreement with AstraZeneca, GlaxoSmithKline, Lundbeck, Organon (*a subsidiary of Merck*) and Pfizer.

P1vital has established collaborations with internationally renowned opinion leaders in psychiatry, neuroscience and obesity, linked through a network of university hospitals and clinical research facilities within the UK. Through its network of key opinion leaders P1vital provides:

- Translational tools for making more rapid and effective decisions in Phase 1 and Phase 2 clinical development of drugs for CNS disorders and obesity;
- Innovative clinical science in collaboration with its university research teams;
- Synergy through combining CNS drug discovery and development expertise with the strong clinical science base in the UK;
- Expertise in clinical project and quality management to recognised industry and regulatory standards.

To discuss your needs, please contact:

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Some HMR and P1vital publications

1. Addy C, Li S, Warrington S *et al.* Safety, tolerability, pharmacokinetics and pharmacodynamic properties of taranabant, a novel selective cannabinoid-1 receptor inverse agonist, for the treatment of obesity: results from a double-blind, placebo-controlled, single oral dose study in healthy volunteers. *J Clin Pharm* 2008; 48: 418–427.
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3. Clarke A, Johnson ES, Mallard N, Corn TH, Johnston A, Boyce M, Warrington S, MacMahon DG. A new low-dose formulation of selegiline: clinical efficacy, patient preference and selectivity for MAO-B inhibition. *J Neural Transmission* 2003; 110: 1257–1271.
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5. Harmer CJ, Cowen PJ, Goodwin GM. Efficacy markers in depression. *J Psychopharmacol* 2010; Jun 8. [Epub ahead of print].
6. Harmer CJ, de Bodinat C, Dawson GR, Dourish CT, Waldenmaier L, Adams S, Cowen PJ, Goodwin GM. Agomelatine facilitates positive vs negative affective processing in healthy volunteer models. *J Psychopharmacol* 2010; Jul 21. [Epub ahead of print].
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10. Antonova E, Parslow D, Brammer M, Simmons A, Williams S, Dawson GR, Morris RG. Scopolamine disrupts hippocampal activity during allocentric spatial memory in humans: an fMRI study using a virtual reality analogue of the Morris Water Maze. *J Psychopharmacol* 2010; Sep 7. [Epub ahead of print].