Health Research Authority

North West - Greater Manchester South Research Ethics Committee

3rd Floor, Barlow House
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Manchester
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Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval.

06 July 2021

Damien Longson
Greater Manchester Mental Health NHS Foundation Trust
Harrop House, Bury New Road
Prestwich Manchester
M25 3BL

Dear Dr Longson,

Study title:	**A Randomized, Double-Blind, Placebo-Controlled Trial of Adjunctive Troriluzole in Obsessive Compulsive Disorder**
REC reference:	**21/NW/0137**
Protocol number:	**BHV4157-303**
EudraCT number:	**2020-004653-69**
IRAS project ID:	**294656**

Thank you for your letter of 22 June 2021, responding to the Research Ethics Committee's (REC) request for further information on the above research and submitting revised documentation. The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Good practice principles and responsibilities

The UK Policy Framework for Health and Social Care Research sets out principles of good

practice in the management and conduct of health and social care research. It also outlines the responsibilities of individuals and organisations, including those related to the four elements of research transparency:

1. registering research studies
2. reporting results
3. informing participants
4. sharing study data and tissue

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations

Registration of Clinical Trials

All research should be registered in a publicly accessible database and we expect all researchers, research sponsors and others to meet this fundamental best practice standard.

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database within six weeks of recruiting the first research participant. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Failure to register a clinical trial is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

If you have not already included registration details in your IRAS application form, you should notify the REC of the registration details as soon as possible.

For CTIMPs involving both UK and EU sites a record in the EU Clinical Trials Register (other than adult Phase 1 studies) will exist and will satisfy the requirement for registration.

For CTIMPs only taking place in the UK, sponsors must register the trial on an established international registry which is a Primary Registry listed in the WHO Registry Network or the ICMJE list of registries e.g. the ISRCTN registry or ClinicalTrials.gov.

You should notify *both* the REC and the MHRA of the registration details.

Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter.

Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/

N.B. If your study is related to COVID-19 we will aim to publish your research summary within 3 days rather than three months.

During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you haven't already done so, please register your study on a public registry as soon as possible and provide the REC with the registration detail, which will be posted alongside other information relating to your project. We are also asking sponsors not to request deferral of publication of research summary for any projects relating to COVID-19. In addition, to facilitate finding and extracting studies related to COVID-19 from public databases, please enter the WHO official acronym for the coronavirus disease (COVID-19) in the full title of your study. Approved COVID-19 studies can be found at: https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/

Clinical trial authorisation must be obtained from the Medicines and Healthcare products Regulatory Agency (MHRA).

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

After ethical review: Reporting requirements

The attached document “After ethical review – guidance for researchers” gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study, including early termination of the study
- Final report
- Reporting results

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

NHS/HSC sites

The favourable opinion applies to all NHS/HSC sites taking part in the study, subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or management permission (in Scotland) being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS/HSC sites

I am pleased to confirm that the favourable opinion applies to any non-NHS/HSC sites listed in the application, subject to site management permission being obtained prior to the start of the study at the site.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Confirmation of Clinical Trial Authorisation from MHRA and relevant correspondence [MHRA Clinical Trial Acceptance]	n/a	18 March 2021
Copies of materials calling attention of potential participants to the research [Campaign media text]	1.0	31 March 2021
Copies of materials calling attention of potential participants to the research [GP and Consultant invitation letter]	1.0	31 March 2021
Copies of materials calling attention of potential participants to the research [GP]	1.0	31 March 2021
Copies of materials calling attention of potential participants to the research [Study Information Sheet]	1.0	31 March 2021
Copies of materials calling attention of potential participants to the research [Telephone Screen Eligibility]	1.0	31 March 2021

Copies of materials calling attention of potential participants to the research [Telephone Dialogue]	1.0	31 March 2021
Copies of materials calling attention of potential participants to the research [Campaign media text]	version 3.0 (TC)	16 June 2021
Copies of materials calling attention of potential participants to the research [Recruitment material]	n/a	
Covering letter on headed paper [Application lette]	n/a	16 April 2021
Covering letter on headed paper [Application lette]	n/a	17 June 2021
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [UK_Insurance Certificate]	n/a	02 December 2020
GP/consultant information sheets or letters [GP letter]	version 1.1 (TC)	08 June 2021
Investigator's brochure / IMP Dossier [IB]	6.0	24 August 2020
Investigator's brochure / IMP Dossier [Outline of Active trials]	n/a	22 December 2020
Investigator's brochure / IMP Dossier [IMPD]	01	14 December 2020
Investigator's brochure / IMP Dossier [Stability Appendix]	n/a	
Investigator's brochure / IMP Dossier [Stability Appendix]	n/a	
Investigator's brochure / IMP Dossier [IMPD DS Neuland]	01	14 December 2020
Investigator's brochure / IMP Dossier [IMPD Placebo]	01	14 December 2020
Investigator's brochure / IMP Dossier [TSE/BSE DS]		30 August 2020
Investigator's brochure / IMP Dossier [TSE/BSE]		28 March 2020
Investigator's brochure / IMP Dossier [TSE/BSE Catalent]		01 December 2020
Investigator's brochure / IMP Dossier [TSE/BSE Catalent Placebo]		01 December 2020
Investigator's brochure / IMP Dossier [TSE/BSE Catalent 140]		01 December 2020
Investigator's brochure / IMP Dossier [TSE/BSE Catalent Placebo 140]		01 December 2020
IRAS Application Form [IRAS_Form_19042021]		19 April 2021
IRAS Checklist XML [Checklist_19042021]		19 April 2021
Letters of invitation to participant [Invitation letter]	1.0	01 April 2021
Non-NHS/HSC Site Assessment Form [non-NHS form]	1.1	22 March 2021
Non-NHS/HSC Site Assessment Form [non-NHS form]	1.1	22 March 2021
Non-NHS/HSC Site Assessment Form [non-NHS form]	1.1	22 March 2021
Non-NHS/HSC Site Assessment Form [non-NHS form]	1.1	22 March 2021
Other [Confirmation of EudraCT Number]	n/a	25 September 2020
Other [MAC_Insurance Certificate]	n/a	11 June 2020
Other [UK_ACC_Conf Statement]	n/a	23 December 2020
Other [UK_LoA_ACC to Local_Applicant]	n/a	04 February 2021
Other [UK_LoA to ACC]	n/a	18 December 2020
Other [Recruitment Statement]	n/a	24 November 2020
Other [CV_PI_A_Babajide]	n/a	02 March 2021

Other [CV_PI_I_Pampaloni]	n/a	16 March 2021
Other [CV_PI_L_Vivarelli]	n/a	28 September 2020
Other [CV_PI_A_Asher]	n/a	04 January 2021
Other [CV_PI_P_Westhead]	n/a	03 September 2020
Other [CV_PI_V_Lynch]	n/a	20 January 2021
Other [GCP Certificate_A_Babajide]	n/a	21 January 2021
Other [GCP Certificate_PI_I_Pampaloni]	n/a	14 April 2021
Other [GCP Certificate_PI_L_Vivarelli]	n/a	17 January 2020
Other [GCP Certificate_PI_A_Asher]	n/a	26 May 2020
Other [GCP Certificate_PI_P_Westhead]	n/a	21 July 2020
Other [GCP of NCI]	N/A	13 February 2020
Other [List of CAs]	n/a	15 April 2021
Other [Covid-19 Vaccine_Note to File]	n/a	15 April 2021
Other [GCP Certificate_PI_V_Lynch]	n/a	01 September 2020
Participant consent form [ICF genetic]	1.0	01 April 2021
Participant consent form [ICF main]	version 1.1 (TC)	08 June 2021
Participant consent form [ICF pregnancy]	version 1.1 (TC)	08 June 2021
Participant information sheet (PIS) [PIS genetic]	1.0	01 April 2021
Participant information sheet (PIS) [PIS main]	version 1.1 (TC)	08 June 2021
Participant information sheet (PIS) [PIS pregnancy]	version 1.1 (TC)	08 June 2021
Research protocol or project proposal [Protocol]	01.2	15 March 2021
Sample diary card/patient card [Participant ID Card]	1.0	01 April 2021
Summary CV for Chief Investigator (CI) [NCI CV]	NA	03 February 2021
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Protocol Summary]	1.0	05 April 2021
Validated questionnaire [Y-BOCS]		
Validated questionnaire [MGH-TRQ-OCD]		
Validated questionnaire [BABS]		
Validated questionnaire [BAI]		
Validated questionnaire [MINI Standard]		
Validated questionnaire [MINI BDP]		
Validated questionnaire [CGI-I]		
Validated questionnaire [CGI-S]		
Validated questionnaire [C-SSRS Screening]		
Validated questionnaire [C-SSRS Since Last Visit]		
Validated questionnaire [RCRS]		

Validated questionnaire [QIDS-SR16]		
Validated questionnaire [SDS]		
Validated questionnaire [DOCS]		

Statement of compliance

This Committee is recognised by the United Kingdom Ethics Committee Authority under the Medicines for Human Use (Clinical Trials) Regulations 2004, and is authorised to carry out the ethical review of clinical trials of investigational medicinal products.

The Committee is fully compliant with the Regulations as they relate to ethics committees and the conditions and principles of good clinical practice.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS project ID: 294656 Please quote this number on all correspondence

With the Committee's best wishes for the success of this project.

Yours sincerely,

P.P.
Professor Sobhan Vinjamuri
Chair