NHS
Health Research Authority

**North West - Greater Manchester South Research Ethics Committee**

3rd Floor, Barlow House
4 Minshull Street
Manchester
M1 3DZ

**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**

11 January 2019

Dr Shruti Garg
Clinical Senior Lecturer in Translational Child Psychiatry
University of Manchester
Room 3.310 Jean McFarlane Building
Oxford Road
M13 9PT

Dear Dr Garg

| | |
|---|---|
| **Study title:** | **Mechanism of action of transcranial direct current stimulation in Neurofibromatosis type 1** |
| **REC reference:** | **18/NW/0762** |
| **Protocol number:** | **Version 1** |
| **IRAS project ID:** | **254686** |

Thank you for your letter of 28 November 2018, responding to the Committee's 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 and the Lead Reviewer.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

**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.

**Conditions of the favourable opinion**

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

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

*Management permission 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, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.*

*Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.*

*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 clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be

registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

**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).**

**Ethical review of research sites**

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission 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 sites

**Approved documents**

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

| *Document* | *Version* | *Date* |
|---|---|---|
| Copies of advertisement materials for research participants | 1.0 | 01 October 2018 |
| GP/consultant information sheets or letters | 1.0 | 01 October 2018 |
| IRAS Application Form [IRAS_Form_12102018] | | 12 October 2018 |
| IRAS Checklist XML [Checklist_04122018] | | 04 December 2018 |
| Letter from funder | | 27 July 2018 |
| Letter from sponsor | | 11 October 2018 |
| Letters of invitation to participant | 1.0 | 01 October 2018 |
| Other [Transfer of Data Consent Form] | 1.0 | 01 October 2018 |
| Other [NF1 Child Assent Form] | 1.0 | 01 October 2018 |
| Other [Indication of Interest Form] | 1.0 | 01 October 2018 |
| Other [Acceptability Questionnaire for Parents] | 1.0 | 01 October 2018 |
| Other [Control Group Children Information Sheet] | 1.0 | 01 October 2018 |
| Other [Control Group Parent Consent Form] | 1.0 | 01 October 2018 |
| Other [Control Group School Invitation Letter] | 1.0 | 01 October 2018 |
| Other [Control Group Advert] | 1.0 | 01 October 2018 |
| Other [Working memory n-back task] | 1.0 | 01 October 2018 |
| Other [Aberrant Behavior Checklist] | | |
| Other [TEA-Ch: Test of Everyday Attention for Children] | | |
| Other [Adaptive Behavior Scales] | | |
| Other [Safety Declaration] | 1.0 | 01 October 2018 |
| Other [Side Effects Questionnaire ] | | 01 October 2018 |
| Other [Insurance Certificate] | | 07 May 2018 |
| Other [Employers' Liability Certificate] | | |
| Other [UoM Insurance Confirmation] | | 11 October 2018 |
| Other [reviewer comments from funder] | | |

| | | |
|---|---|---|
| Other [Computerised Working Memory Corsi Block Test] | | |
| Other [Control Group Assent Form] | 1.0 | 01 October 2018 |
| Other [Digit Span] | | |
| Other [Control Group Adolescent Consent Form] | 1.0 | 01 October 2018 |
| Other [Control Group Parent Information Sheet] | 1 | 01 October 2018 |
| Other [Validation Queries] | | 22 October 2018 |
| Other [PIS parent control group] | v2.0 | 28 November 2018 |
| Other [PIS adolescent control group] | v2.0 | 28 November 2018 |
| Other [PIS children] | v2.0 | 28 November 2018 |
| Other [NF1 parent invitation letter] | v2.0 | 28 November 2018 |
| Other [PIS NF1 parent group] | v2.0 | 28 November 2018 |
| Other [PIS NF1 adolescent group] | v2.0 | 28 November 2018 |
| Other [NF1 adolescent consent form] | v2.0 | 28 November 2018 |
| Other [Eligibility questionnaire] | v2.0 | 28 November 2018 |
| Other [response letter to ethics committee] | | |
| Other [Social story] | v1.0 | 28 November 2018 |
| Participant consent form [NF1 Parent Consent Form] | 1.0 | 01 October 2018 |
| Research protocol or project proposal [Research protocol] | V1.0 | 01 October 2018 |
| Summary CV for Chief Investigator (CI) [Summary CV] | V1.0 | 01 October 2018 |
| Validated questionnaire [Conners] | | |

**Statement of compliance**

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.

**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

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

**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 Training**

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

| **18/NW/0762** | **Please quote this number on all correspondence** |
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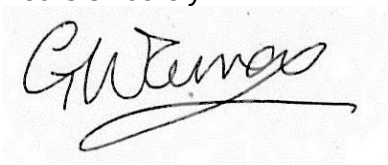
With the Committee's best wishes for the success of this project.

Yours sincerely



pp
**Professor Sobhan Vinjamuri**
**Chair**

Email:nrescommittee.northwest-gmsouth@nhs.net

*Enclosures:* "After ethical review – guidance for researchers"

*Copy to:* *Ms Lynne Macrae*
*Ms Elizabeth Mainwaring, Manchester University NHS Foundation Trust*