

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)

MSBase Registry

1. Is your project research?

☒ Yes ☐ No

2. Select one category from the list below:

- ☐ Clinical trial of an investigational medicinal product
- ☐ Clinical investigation or other study of a medical device
- ☐ Combined trial of an investigational medicinal product and an investigational medical device
- ☐ Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
- ☐ Basic science study involving procedures with human participants
- ☐ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ☐ Study involving qualitative methods only
- ☐ Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- ☒ Study limited to working with data (specific project only)
- ☐ Research tissue bank
- ☐ Research database

If your work does not fit any of these categories, select the option below:

☐ Other study

2a. Please answer the following question(s):

a) Will you be processing identifiable data at any stage of the research (including in the identification of participants)?

☒ Yes ☐ No

3. In which countries of the UK will the research sites be located?(Tick all that apply)

- ☒ England
- ☒ Scotland
- ☒ Wales
- ☒ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- ☐ England
- ☐ Scotland
- ☐ Wales
- ☒ Northern Ireland
- ☐ This study does not involve the NHS

4. Which applications do you require?

- ☒ IRAS Form
- ☐ Confidentiality Advisory Group (CAG)
- ☐ Her Majesty's Prison and Probation Service (HMPPS)

Most research projects require review by a REC within the UK Health Departments' Research Ethics Service. Is your study exempt from REC review?

- ☐ Yes ☒ No

5. Will any research sites in this study be NHS organisations?

- ☒ Yes ☐ No

5c. You have indicated that your study has sites located in England. For the research sites located in England, do you wish for the study to be considered for NIHR Clinical Research Network (CRN) support and inclusion in the NIHR Clinical Research Network (CRN) Portfolio? Please see information button for further details

- ☒ Yes ☐ No

6. Do you plan to include any participants who are children?

- ☐ Yes ☒ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

- ☐ Yes ☒ No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

- ☐ Yes ☒ No

9. Is the study or any part of it being undertaken as an educational project?

☐ Yes ☒ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

☐ Yes ☒ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

☐ Yes ☒ No

Integrated Research Application System

Application Form for Study limited to working with data (specific project only)

IRAS Form (project information)

Please refer to the E-Submission and Checklist tabs for instructions on submitting this application.

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting [Help](#).

Please define any terms or acronyms that might not be familiar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
MSBase Registry

Please complete these details after you have booked the REC application for review.

REC Name:
PR Committee

REC Reference Number:
20/PR/0837

Submission date:
23/11/2020

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

MSBase Registry Global Cohort Study of Multiple Sclerosis (MS) and other Neuroimmunological Diseases (NIDs)

A3-1. Chief Investigator:

	Title Forename/Initials Surname
	Dr Orla Gray
Post	Consultant Neurologist
Qualifications	MD FRCP
ORCID ID	
Employer	South Eastern Health and Social Care Trust
Work Address	Ulster Hospital Dundonald
Post Code	BT161RH
Work E-mail	Orla.Gray@setrust.hscni.net
* Personal E-mail	
Work Telephone	02890553101
* Personal Telephone/Mobile	

Fax

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*

A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?

This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.

	Title Forename/Initials Surname
	Research Governance Administrator
Address	Home 3 Ulster Hospital Dundonald
Post Code	BT161RH
E-mail	Research.Development@setrust.hscni.net
Telephone	02890553101
Fax	

A5-1. Research reference numbers. Please give any relevant references for your study:

Applicant's/organisation's own reference number, e.g. R & D (if available):	N/A
Sponsor's/protocol number:	N/A
Protocol Version:	2.0
Protocol Date:	09/06/2020
Funder's reference number (enter the reference number or state not applicable):	N/A
Project website:	https://www.msbase.org/

Additional reference number(s):

Ref.Number	Description	Reference Number
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Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

A5-2. Is this application linked to a previous study or another current application?

☒ Yes ☐ No

Please give brief details and reference numbers.

REC Ref: 10/H1010/12

MSBase Registry was given REC Favourable Opinion for 5 years in June 2010. This application was made by another Organisation.

SEHSCT (who are acting as Lead site for MSBase in UK) are now advised by HRA that MSBase cannot be re-reviewed as a registry as it is not hosted within the UK.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of

specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments' Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.*

The MSBase Registry is a longitudinal, observational Multiple Sclerosis database open to all practicing Neurologists and their team, worldwide. In collaboration with participating Neurologists, the MSBase Registry has established a unique, web-based platform dedicated to sharing, tracking and evaluating outcomes data in Multiple Sclerosis (MS) and other Central Nervous System (CNS) demyelinating diseases.

In particular, MSBase aims to advance multi-centre, multi-national epidemiological and outcomes research by providing a freely accessible resource to compile, combine, compare and analyse large datasets.

The Principal Investigators (Neurologists) at participating centres submit coded clinical information using compatible data collection software. To date, the most commonly used software is the freely available iMed software. MSBase has recently developed its own electronic data entry software, MDS. Data can be collected using either iMed or MDS. The data to be collected comprises key parameters relating to demographic data, diagnosis, serial neurological examinations (Kurtzke Functional Systems Score and Expanded Disability Status Score, EDSS), relapse information, specific safety related data and treatment exposures. All aspects of patient management are entirely at the discretion of the site's managing neurologist and the patient.

The MSBase Scientific Leadership Group (SLG) acts as the Scientific Advisory Board to the MSBase Foundation Ltd. The SLG has been delegated the role of custodian of the composite data, while individual datasets (which contain identifiable data) at all times remain the property of the participating centre, under management of the Principal Investigator (PI). The MSBase SLG will ensure data integrity and monitor all MSBase activities including core study designs, promotion and implementation, and perform composite data analyses.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, HRA, or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

MSBase is a research database but it is not eligible for voluntary REC review in the UK as a research database as the database is hosted outside of the UK in Australia. HRA have advised that, instead, a project specific application solely for the collection of data from participants in the UK may be submitted as patients are being recruited into the registry via the NHS.

MSBase is Sponsored by MSBase Foundation, as not-for-profit organisation based in Australia. The Chief Investigator for the study is not an employee of MSBase but is the UK representative for the MSBase Scientific Leadership Group and a Director of the MSBase Board.

Fully informed consent will be sought from each patient before inclusion in the registry. This consent will be collected either in person or by post (due to the COVID-19 related changes in clinic attendances). This informed consent includes for non-identifiable data to be transferred outside of the UK and for use by a variety of organisations (including drug companies) for research purposes.

There are two types of studies - investigator-initiated analysis and investigator-initiated sub-studies.

1. Investigator - initiated analysis

Centres, through its PIs, and the SLG, can request to receive MSBase Registry data and perform analyses on the entire Registry dataset or Registry data subsets. The procedures for proposing and conducting scientific analyses are outlined in detail in the MSBase Participation Agreement.

2. Investigator-initiated sub-studies

Investigator-initiated prospective sub-studies can be created and managed on the Registry website. Sub-studies capture specific sub-cohort information (e.g. national, regional, thematic). Centres exclusively decide if they wish to participate and share their Centre data, in any proposed sub-studies.

Governance and data use frameworks of sub-studies are defined by the sub-study lead PI, and are described in the MSBase Registry Participation Agreement. MSBase request permission for involvement in any sub-study that uses observational data only. A sub-study involving any other type of additional non-routine data or any non-routine

intervention, would require a separate, individual ethics opinion.

At times the MSBase registry SLG may perform global analyses on the entire dataset. The global analyses work on an "opt out" system whereby a two stage process of permission will be sought from centre PIs. Analyses occur for research publication and for contract reports requested by Pharmaceutical companies. Analyses for contract reports are conducted by the MSBase Foundation team and only the reports are released to the company, with a copy to the PIs.

Investigator-initiated analysis and investigator-initiated sub-studies that use observational data only, will be run from the UK utilising the global registry data. However as this data will be anonymous to the researchers and the person from whom the data originated will not be able to be identified alone or in combination with other linked data these analysis or sub-studies will be exempt from NHS or REC review.

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. Please tick all that apply:

- ☐ Case series/ case note review
- ☐ Case control
- ☒ Cohort observation
- ☐ Controlled trial without randomisation
- ☐ Cross-sectional study
- ☒ Database analysis
- ☐ Epidemiology
- ☐ Feasibility/ pilot study
- ☐ Laboratory study
- ☐ Metanalysis
- ☐ Qualitative research
- ☐ Questionnaire, interview or observation study
- ☐ Randomised controlled trial
- ☒ Other (please specify)

Research Registry

A10. What is the principal research question/objective? Please put this in language comprehensible to a lay person.

MSBase is an ongoing, longitudinal, strictly observational registry that tracks outcomes of routine clinical practice for patients with MS and other neuroinflammatory diseases. The primary rationale for MSBase Registry is the creation of a web-based platform to facilitate the conduct of large, multi-centre, multi-national clinical studies.

MSBase is an ongoing, longitudinal, strictly observational registry that tracks outcomes of routine clinical practice for patients with MS and other neuroinflammatory diseases . No experimental intervention is involved.

The MSBase observational registry aims to:

- collect clinical information from a large number of patients with diagnosed neuroimmunological diseases and people who have had symptoms that are suggestive of MS,
- enable researchers to observe the effects and safety of current and future treatments,
- enable researchers to document disease outcomes in different parts of the world.

The major challenges for investigator initiated clinical research of this nature include the identification of collaborators, ongoing communication between study sites, data quality assurance, and all aspects of data management. The MSBase platform is dedicated to providing investigators with the best possible independent logistic solution to these challenges at no cost.

A11. What are the secondary research questions/objectives if applicable? Please put this in language comprehensible to

a lay person.

N/A

A12. What is the scientific justification for the research? Please put this in language comprehensible to a lay person.

Multiple Sclerosis is a chronic, inflammatory, demyelinating disease of the Central Nervous System (CNS) and is one of the most common causes of neurological disability in young adults. It is characterized by multi-focal recurrent attacks of neurological symptoms and signs with variable recovery. The exact cause of multiple sclerosis is unknown, although an autoimmune process has been implicated. The clinical course of MS is highly variable, ranging from sub-clinical disease to rapidly progressive MS. During the past seven years, several clinical trials and cohort studies have shown efficacy of disease-modifying drug therapies in reduction of MS relapses and disability progression. Similarly, in NMO and anti-MOG antibody disease, small cohort studies have revealed probable disease-modifying drug effects. In myasthenia gravis, a mixture of clinical trial and cohort data have revealed disease-modifying effects of several drugs. In other neuroimmunological diseases, definitive evidence for treatment effectiveness evidence is often lacking. Many areas of uncertainty remain in the management of all these diseases, which can only be answered with prospective cohort studies.

For instance, long-term treatment outcomes are poorly understood, personalised medicine (the right drug for the right patient) is virtually non-existent, and the early and even pre-clinical course of the diseases is uncertain.

The long-term benefit-risk profiles for different therapies and different therapy sequences remain unknown.

The risks versus benefits of drug exposure during early pregnancy, throughout pregnancy and during breast-feeding are virtually unknown, as all studies to date are under-powered.

Disease and treatment outcomes in patients that fall outside the standard trial populations, e.g. children, older patients, and patients with significant comorbid diseases are poorly understood.

Differences in disease outcomes in different ethnic groups or different regions of the world are largely unknown, as individual cohort studies typically do not collect the same outcome data.

Treatment failure is poorly and arbitrarily defined, and the impact of monitoring tests (e.g. serial MRI changes) for prognostication and to guide treatment change are substantially unknown.

For all of the above themes, large, prospectively databased cohorts have major advantages over clinical trials, primarily because the focus is on long-term effectiveness and safety in an entire population rather than short-term outcomes defined in highly selected populations.

Wherever possible, it is important that data collection is embedded into routine standard neurological clinical care.

The Study aims to assess real-world long-term disease outcomes; in particular relapse rates and functional/disability change over time. The relationship between demographics, comorbid diseases, relapses, diagnostic and monitoring test results, drug exposures, and outcomes will be assessed using various statistical techniques to minimise indication bias and other biases.

The major rationale for the MSBase project is the creation of a web-based platform to facilitate the conduct of large, multi-centre, multi-national clinical studies. The major challenges for investigator-initiated clinical research of this nature include the identification of collaborators, ongoing communication between study sites, data quality assurance, and all aspects of data management. The MSBase platform is dedicated to providing investigators with the best possible independent logistic solution to these challenges at no cost.

A13. Please summarise your design and methodology. It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.

The direct care team at participating Trusts will identify eligible patients and make the initial approach (either by phone or face-to-face) to establish willingness to consider participation in MSBase Registry.

The direct care team will supply Participant information sheets either by post or face-to-face to those patients willing to consider participation. Potential participants will be asked to confirm that they are happy to be contacted by the research team at site (who, dependent on particular site arrangements, may be either be members of the Direct Care Team or the research team) to discuss the study following an agreed period of time and at a time that is suitable to the patient. Due to the observational nature of the study, patients may consent on the day if willing or those who wish to take more time to consider participation, may do so, before being contacted by a member of the site's MSBase team to answer any further questions about Registry participation.

Those willing to consent will complete the ICF and return to the MSBase team at site (via post in a pre-paid envelope if consenting remotely).

Routine /standard care will not alter for any participant by virtue of participation in MSBase. The only thing that will change is that the normal information collected at appointments will become part of the MSBase Registry.

4. RISKS AND ETHICAL ISSUES**RESEARCH PARTICIPANTS****A15. What is the sample group or cohort to be studied in this research?**

Select all that apply:

- ☐ Blood
- ☐ Cancer
- ☐ Cardiovascular
- ☐ Congenital Disorders
- ☐ Dementias and Neurodegenerative Diseases
- ☐ Diabetes
- ☐ Ear
- ☐ Eye
- ☐ Generic Health Relevance
- ☐ Infection
- ☐ Inflammatory and Immune System
- ☐ Injuries and Accidents
- ☐ Mental Health
- ☐ Metabolic and Endocrine
- ☐ Musculoskeletal
- ☒ Neurological
- ☐ Oral and Gastrointestinal
- ☐ Paediatrics
- ☐ Renal and Urogenital
- ☐ Reproductive Health and Childbirth
- ☐ Respiratory
- ☐ Skin
- ☐ Stroke

Gender: Male and female participants

Lower age limit: 18 Years

Upper age limit: No upper age limit

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

1. Over 18 years of age
2. Diagnosis of MS or other neuroinflammatory disease, or have experienced an episode of symptoms suggestive of MS or other neuroinflammatory disease
3. Able and willing to provide informed consent

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

1. Under 18 years of age
2. Unable/unwilling to provide informed consent

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used? *For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

Potential participants will be identified by the P.I. and direct care team who are directly responsible for providing routine care and treatment to individual patients. Potential participants will be identified through new referral lists and existing clinic lists.

Eligibility criteria is extremely broad for this study and so it is expected that most patients will be eligible for approach by the direct care team.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

☒ Yes ☐ No

Please give details below:

Members of the direct care team who are directly responsible for providing routine care and treatment to individual patients will access clinic records and referrals to review for eligibility and to make the initial approach/invitation to participate.

A27-3. Describe what measures will be taken to ensure there is no breach of any duty of confidentiality owed to patients, service users or any other person in the process of identifying potential participants. *Indicate what steps have been or will be taken to inform patients and service users of the potential use of their records for this purpose. Describe the arrangements to ensure that the wishes of patients and service users regarding access to their records are respected. Please consult the guidance notes on this topic.*

Only the direct care team who are directly responsible for providing routine care and treatment to individual patients, and who would normally have contact with the patient, will access clinic records and referrals to review for eligibility and make the initial approach.

Patient name, address, phone number or day of birth will not be transmitted to MSBase in order to preserve confidentiality. Patients are identified by an assigned "globally unique identification number" (GUID) incorporating encoded site and PI number. Data is encrypted before transmission and uploaded via a secure connection to the MSBase Registry website complying with local and international law.

Association of patient identifying information and their GUID is only possible within the participating sites data collection program. The Extract file generated by iMed or MDS does not contain any identifying information specified above, which is therefore never uploaded into MSBase.

Transparency information has been provided within the PIS.

A27-4. Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?

☒ Yes ☐ No

A27-5. Has prior consent been obtained or will it be obtained for access to identifiable personal information?

☒ Yes ☐ No

If Yes, please give details below.

Following identification of eligible participants by the direct care team, research nurses (or other site research team members) may be involved in the Registry consent process at some sites. This will only occur where the direct care team have recorded consent of the patient for this to occur.

Research team members may also be involved in data entry into imed but this will only occur following consent of the patient to participation in MSBase Registry via the ICF form.

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

☐ Yes ☒ No

A29. How and by whom will potential participants first be approached?

Potential participants will be identified through new referral lists and existing clinic lists. Eligible potential participants will be identified by the direct care team who are directly responsible for providing routine care and treatment to individual patients. The direct care team will make the initial approach either at a face-to-face clinic visit or at phone visit before providing a copy of the MSBase Registry information sheets to those willing to consider involvement.

A30-1. Will you obtain informed consent from or on behalf of research participants?

☒ Yes ☐ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

If you are not obtaining consent, please explain why not.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

☒ Yes ☐ No

A31. How long will you allow potential participants to decide whether or not to take part?

Due to the observational nature of the study a defined period of time to consider participation has not been specified.

Patients may consent on the day they receive a PIS or may wish to review it and discuss participation with others before being followed up by the local research team.

If the approach for the research is made remotely, following post/email of the information sheet, potential participants will be given at least three days to consider involvement. Patients will be asked to provide a date and time suitable for a call from the research team at site to discuss participation and to have any questions answered.

Willingness to continue participation will be established in an ongoing manner at routine calls and clinics.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?(e.g. translation, use of interpreters)

While MSBase is a global registry the UK document set has been specifically designed to align with UK governance requirements and there are not any plans to provide translated versions.

As site participation in MSBase does not come with funding, sites wishing to participate will need to implement local

processes to provide translated documentation and interpreters etc.

A33-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to participants in Wales?

While MSBase is a global registry the UK document set has been specifically designed to align with UK governance requirements and there are not any plans to provide translated versions.

As site participation in MSBase does not come with funding, sites wishing to participate will need to implement local processes to provide translated documentation and interpreters etc.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? Tick one option only.

- ☐ The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.
- ☒ The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.
- ☐ The participant would continue to be included in the study.
- ☐ Not applicable – informed consent will not be sought from any participants in this research.
- ☐ Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

If you plan to retain and make further use of identifiable data/tissue following loss of capacity, you should inform participants about this when seeking their consent initially.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)? (Tick as appropriate)

- ☒ Access to medical records by those outside the direct healthcare team
- ☐ Access to social care records by those outside the direct social care team
- ☒ Electronic transfer by magnetic or optical media, email or computer networks
- ☒ Sharing of personal data with other organisations
- ☒ Export of personal data outside the EEA
- ☒ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☐ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☐ Use of audio/visual recording devices
- ☒ Storage of personal data on any of the following:
- ☒ Manual files (includes paper or film)
- ☒ NHS computers

- ☐ Social Care Service computers
- ☐ Home or other personal computers
- ☐ University computers
- ☒ Private company computers
- ☒ Laptop computers

Further details:

Access outside of direct healthcare team will only be undertaken with consent.

Electronic data transferred will be codified and encrypted.

Only anonymous data will be shared with other organisations.

Only anonymous data will be shared outside of EEA and with consent.

Sensitive data including address will only be held locally and not transferred.

Paper records such as ICFs will be appropriately stored in line with local data protection requirements.

Data stored on NHS computers will be subject to appropriate controls and systems protections.

Anonymous data stored within MSBase is subject to appropriate controls access and password protection and release and access is subject to the Foundation steering Committee.

A37. Please describe the physical security arrangements for storage of personal data during the study?

MSBase is an ongoing, longitudinal, strictly observational registry that tracks outcomes of routine clinical practice for patients with MS. Routine clinical data will be maintained in line with each site/Organisations records management policy and procedure.

Personal identifiable data held to maintain a record those patients participating in the MSBase Registry e.g. site file copy of ICF, enrollment logs will be maintained in a locked cabinet within a locked office and will be access controlled to only those members of the MSBase team at site.

A38. How will you ensure the confidentiality of personal data? *Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

Participant data is entered into data-collection software- either a system called the "MSBase Data Entry Software", or "MSBase iMed data collection software and visualisation tool" – both of which have been designed specifically for MS and other NIDs care. Some sites may use these systems routinely without linkage to MSBase registry. The systems are fully password protected.

When a patient agrees to participate in MSBase, information from either of these systems can then be sent electronically to the MSBase central registry secure storage location (hosted by Microsoft Azure Servers in Australia). The data transferred is pseudonymised by the system with the link held only at the participating site.

The information accessible to The MSBase Registry Operations team is non-identifiable and includes:

- Month and Year of birth,
- Medical history,
- Results of any tests and investigations like MRI scans, spinal fluid tests or blood tests,
- Results of neurological tests and examinations such as the Expanded Disability Status Scale (EDSS),
- Information about any family history of neuroimmunological diseases like MS,
- Concomitant medications

Codified data collected on the registry can be sent securely to approved MSBase members for research projects. MSBase members must submit a data request to access data. Data requests are reviewed by the MSBase Scientific Leadership Group. The requester must sign a data use agreement including assurances about how data will be used and protected. Participants will not be able to be identified from this data.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

Only the direct care team and the MSBase team locally at site will have access to participants personal identifiable data. Personal data as part of the registry will not be able to be linked to an individual by either the MSBase Registry Operations team in Australia or by any researchers who, by application to MSBase, have been provided access to the registry data.

Access to identifiable and personal data is covered within the PIS and each participant will sign an ICF to this effect.

Storage and use of data after the end of the study

A41. Where will the data generated by the study be analysed and by whom?

There are three types of data analysed:

1. Investigator - initiated analysis

Centres, through its PIs, and the SLG, can request to receive MSBase Registry patient data and perform analyses on the entire Registry dataset or Registry data subsets. The procedures for proposing and conducting scientific analyses are outlined in detail in the MSBase Participation Agreement. If approved by the SLG, the anonymised data required for a particular study is forwarded to the requesting PI to perform the analysis. Any PI can request statistical support from MSBase. If approved, the MSBase Statistician would also gain access to the anonymised data.

2. Investigator-initiated sub-studies

Investigator-initiated prospective sub-studies can be created and managed on the Registry website. Sub-studies capture specific sub-cohort information (e.g. national, regional, thematic). Centres exclusively decide if they wish to participate and share their Centre data, in any proposed sub-studies. Governance and data use frameworks of sub-studies are defined by the sub-study lead PI, and are described in the MSBase Registry Participation Agreement. We request permission for involvement in any sub-study that uses observational data only. A sub-study involving any other type of data or intervention, would require a separate, individual ethics opinion. The MSBase web platform will enrol patients according to the inclusion criteria specified by the Principal Investigators of a sub-study, and will provide accumulated data to the study leader in a format suitable for statistical analysis.

3. Global analysis by MSBase operational team.

The MSBase registry SLG may perform global analyses on the entire dataset. The global analyses work on an "opt out" system whereby a two stage process of permission will be sought from centre PIs. Analyses occur for research publication and for contract reports requested by Pharmaceutical companies. The MSBase operational team would receive anonymised data for this analysis. Analyses for contract reports are conducted by the MSBase Foundation team and only the reports are released to the company, with a copy to the PI.

The MSBase Scientific Leadership Group (SLG) acts as the Scientific Advisory Board to the MSBase Foundation Ltd. The SLG has been delegated the role of custodian of the composite data, while individual datasets at all times remain the property of the participating centre, under management of the Principal Investigator (PI). The MSBase SLG will ensure data integrity and monitor all MSBase activities including core study designs, promotion and implementation, and perform composite data analyses.

A42. Who will have control of and act as the custodian for the data generated by the study?

	Title	Forename/Initials	Surname
	Professor	Helmut	Butzkueven
Post	Managing Director MSBase Foundation Ltd		
Qualifications			
Work Address	Lvl 6 / 99 Commercial Road		
	Melbourne		
	Australia		
Post Code	VIC 3004		
Work Email	info@msbase.org		
Work Telephone			
Fax			

A43. How long will personal data be stored or accessed after the study has ended?

- ☐ Less than 3 months
- ☐ 3 – 6 months

- ☐ 6 – 12 months
☐ 12 months – 3 years
☒ Over 3 years

If longer than 12 months, please justify:

The study is a research registry.

Data will be retained for as long as the registry exists/has funding to continue.

A44. For how long will you store research data generated by the study?

Years: 100

Months:

A45. Please give details of the long term arrangements for storage of research data after the study has ended. Say where data will be stored, who will have access and the arrangements to ensure security.

The study is a research registry and data will be retained for as long as the registry exists/has funding to continue.
Data collected is part of the routine clinical record.

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

☐ Yes ☒ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

☐ Yes ☒ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

☐ Yes ☒ No

NOTIFICATION OF OTHER PROFESSIONALS

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

☐ Yes ☒ No

Please give details, or justify if not registering the research.

MSBase is a research registry. Individual research projects run from the registry may be publicly registered.

Registration of research studies is encouraged wherever possible.

You may be able to register your study through your NHS organisation or a register run by a medical research charity,

or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? Tick as appropriate:

- ☒ Peer reviewed scientific journals
- ☒ Internal report
- ☒ Conference presentation
- ☒ Publication on website
- ☒ Other publication
- ☒ Submission to regulatory authorities
- ☒ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☐ Other (please specify)

A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when publishing the results?

Identifiable data will not be published.
Participants will not be able to be identified from within published data.

A53. Will you inform participants of the results?

☒ Yes ☐ No

Please give details of how you will inform participants or justify if not doing so.
Results are available on the MSBase website.
A patient area of the MSBase website is currently under construction.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? Tick as appropriate:

- ☐ Independent external review
- ☐ Review within a company
- ☒ Review within a multi-centre research group
- ☐ Review within the Chief Investigator's institution or host organisation
- ☐ Review within the research team
- ☐ Review by educational supervisor
- ☒ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:

The MSBase Scientific Leadership Group (SLG) acts as the Scientific Advisory Board to the MSBase Foundation Ltd. The SLG has been delegated the role of custodian of the composite data, while individual datasets at all times remain the property of the participating centre, under management of the Principal Investigator (PI). The MSBase SLG will ensure data integrity and monitor all MSBase activities including core study designs, promotion and implementation, and perform composite data analyses

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports,

together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

- ☒ Review by independent statistician commissioned by funder or sponsor
- ☐ Other review by independent statistician
- ☐ Review by company statistician
- ☐ Review by a statistician within the Chief Investigator's institution
- ☒ Review by a statistician within the research team or multi-centre group
- ☐ Review by educational supervisor
- ☐ Other review by individual with relevant statistical expertise
- ☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title Forename/Initials Surname
	Dr Tim Spelman
Department	
Institution	MSBase Foundation
Work Address	Level 6
	99 Commercial Road
	Melbourne, Australia
Post Code	VIC 3004
Telephone	
Fax	
Mobile	
E-mail	

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

MSBase is an ongoing, longitudinal, strictly observational registry that tracks outcomes of routine clinical practice for patients with MS. No experimental intervention is involved.

The MSBase observational registry aims to:

- collect clinical information from a large number of patients with diagnosed neuroimmunological diseases and people who have had symptoms that are suggestive of MS,
- enable researchers to observe the effects and safety of current and future treatments,
- enable researchers to document disease outcomes in different parts of the world.

A58. What are the secondary outcome measures? *(if any)*

N/A

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size:

Total international sample size (including UK):

Total in European Economic Area:

Further details:

N/A Registry.

The prevalence of MS varies significantly within the UK. It is estimated that there are approx. 130,000 cases in total in the UK, 105,000 in England (prevalence 190/100,000), 5,500 in Wales (prevalence 179/100,000), 5,500 in Northern Ireland (prevalence 258/100,000) and 15,000 in Scotland (prevalence 295/100,000).

Due to the broadness of the eligibility criteria it is anticipated that most patients will be able to be approached by the direct care team at participating sites for involvement in MSBase

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

N/A Registry

A61. Will participants be allocated to groups at random?

☐ Yes ☒ No

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

The statistical methods used will be dependant on the specific research question for any individual analysis, as determined by the statistician involved. For example, in studies comparing the effectiveness of different Disease Modifying Treatments in MS. Propensity Score analysis is used as the statistical method.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co-applicants, protocol co-authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

Title Forename/Initials Surname

Post

Qualifications

Employer

Work Address

Post Code

Telephone

Fax

Mobile

Work Email

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead SponsorStatus: ☐ NHS or HSC care organisation☐ Academic☐ Pharmaceutical industry☐ Medical device industry☐ Local Authority☐ Other social care provider (including voluntary sector or private organisation)☒ Other

Commercial status: Non-Commercial

If Other, please specify: Non-UK Foundation/Charity**Contact person**

Name of organisation MSBase Foundation Ltd

Given name Helmut

Family name Butzkueven

Address Lvl 6 / 99 Commercial Road

Town/city Melbourne

Post code VIC 3004

Country Australia

Telephone 000

Fax 000

E-mail info@msbase.org

A65. Has external funding for the research been secured?*Please tick at least one check box.*☐ Funding secured from one or more funders☐ External funding application to one or more funders in progress☒ No application for external funding will be made

What type of research project is this?

☐ Standalone project☐ Project that is part of a programme grant☐ Project that is part of a Centre grant☐ Project that is part of a fellowship/ personal award/ research training award☒ Other

Other – please state:

Registry funded by The MSBase Foundation Ltd (a not-for-profit charitable organisation incorporated as a company in Australia)

A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? Please give details of subcontractors if applicable.

☐ Yes ☒ No

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

☐ Yes ☒ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

	Title Forename/Initials Surname Research Manager
Organisation	South Eastern Health and Social Care Trust
Address	Home 3 Ulster Hospital
Post Code	BT161RH
Work Email	research.development@setrust.hscni.net
Telephone	02890553101
Fax	
Mobile	02890553101

Details can be obtained from the NHS R&D Forum website: <http://www.rdforum.nhs.uk>

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/01/2021

Planned end date: 31/12/2050

Total duration:

Years: 29 Months: 11 Days: 31

A71-1. Is this study?

☐ Single centre
☒ Multicentre

A71-2. Where will the research take place? (Tick as appropriate)

- ☒ England
- ☒ Scotland
- ☒ Wales
- ☒ Northern Ireland
- ☒ Other countries in European Economic Area

Total UK sites in study Unknown

Number of sites anticipated in the Community N/A

Does this trial involve countries outside the EU?

☒ Yes ☐ No

☒ USA

☒ Other international (please specify)

Global study

A72. Which organisations in the UK will host the research? *Please indicate the type of organisation by ticking the box and give approximate numbers if known:*

☒ NHS organisations in England

☒ NHS organisations in Wales

☒ NHS organisations in Scotland

☒ HSC organisations in Northern Ireland

☐ GP practices in England

☐ GP practices in Wales

☐ GP practices in Scotland

☐ GP practices in Northern Ireland

☐ Joint health and social care agencies (eg community mental health teams)

☐ Local authorities

☐ Phase 1 trial units

☐ Prison establishments

☐ Probation areas

☐ Independent (private or voluntary sector) organisations

☐ Educational establishments

☐ Independent research units

☐ Other (give details)

Total UK sites in study:

0

A73-1. Will potential participants be identified through any organisations other than the research sites listed above?

☐ Yes ☒ No

A74. What arrangements are in place for monitoring and auditing the conduct of the research?

The SLG will closely monitor all MSBase Registry activities and supervise the general conduct of the Registry.

Since this is a non-interventional study, there will be no regular on-site monitoring and no source data verification, unless a for-cause clinical audit is requested by the SLG. However, the physician agrees to cooperate fully with all reasonable requests for information or training related to this Registry from the SLG. Written or telephone requests for information, training or meetings shall be answered in a timely manner. The SLG has the right to request an

independent, clinical audit to verify patient files or source documents.

A76. Insurance/ indemnity to meet potential legal liabilities

***Note:** in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland*

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? Please tick box(es) as applicable.

***Note:** Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.*

- ☐ NHS indemnity scheme will apply (NHS sponsors only)
- ☒ Other insurance or indemnity arrangements will apply (give details below)

Msbase Foundation Limited

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? Please tick box(es) as applicable.

***Note:** Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.*

- ☐ NHS indemnity scheme will apply (protocol authors with NHS contracts only)
- ☒ Other insurance or indemnity arrangements will apply (give details below)

Msbase Foundation Limited

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

***Note:** Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.*

- ☒ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)
- ☐ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

A78. Could the research lead to the development of a new product/process or the generation of intellectual property?

☐ Yes ☒ No ☐ Not sure

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For further information please refer to guidance.*

Investigator identifier	Research site	Investigator Name
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PART D: Declarations**D1. Declaration by Chief Investigator**

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. I undertake to fulfil the responsibilities of the chief investigator for this study as set out in the UK Policy Framework for Health and Social Care Research.
3. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.
4. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.
5. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.
6. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.
7. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.
8. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.
9. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 2018.
10. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:
 - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
 - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
 - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
 - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
 - May be sent by email to REC members.
11. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 2018.
12. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the Health Research Authority (HRA) together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after the issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

HRA would like to include a contact point with the published summary of the study for those wishing to seek further

information. We would be grateful if you would indicate one of the contact points below.

- ☒ Chief Investigator
☐ Sponsor
☐ Study co-ordinator
☐ Student
☐ Other – please give details
☐ None

Access to application for training purposes (Not applicable for R&D Forms)

Optional – please tick as appropriate:

☒ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Dr Orla Gray on 20/11/2020 15:32.

Job Title/Post: Consultant Neurologist
Organisation: South Eastern Trust
Email: orla.gray@setrust.hscni.net

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co-sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.
3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
6. The responsibilities of sponsors set out in the UK Policy Framework for Health and Social Care Research will be fulfilled in relation to this research.

Please note: The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.
8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by Professor Helmut Butzkueven on 23/11/2020 12:24.

Job Title/Post: Managing Director
Organisation: MSBase Foundation
Email: helmut.bu