MSBase and MGBase Registry Participation Agreement

for Centres participating in the

MSBase/MGBase Registry Observational Study

Version 6.1: 7 April 2023

Contact details:

MSBase Foundation Ltd

Managing Director: Professor Helmut Butzkueven

Central Clinical School, Level 6, The Alfred Centre
99 Commercial Rd, Victoria 3004, Australia

Phone: +61 3 9903 8264
Email: info@msbase.org

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ABBREVIATIONS

MS	Multiple Sclerosis
NIDs	Neuro-immunological Diseases
NMO	Neuromyelitis Optica
MG	Myasthenia Gravis
PI/Centre PI	Principal Investigator/Centre Principal Investigator
I	Investigator
SLG	Scientific Leadership Group
SAE	Serious Adverse Event
IT	Information Technology
MDS	MSBase Data-entry Software
MDS SLA	MDS Software License Agreement
iMed	MSBase iMed Data-entry Software
iMed SLA	iMed Software Licence Agreement
PICF	Patient Information and Informed Consent Form
GDPR	General Data Protection Regulation
IRB	Institutional Review Board
EC	Ethics Committee

DEFINITIONS

"Applicable Data Protection Legislation" means all privacy and personal data legislation applicable to the personal data processing that is carried out under this Participation Agreement, which may include regulations and decisions of competent authorities applying the GDPR Laws.

"Centre" means a medical institution, such as a hospital, university or private clinic that has joined the MSBase or MGBase Registry and holds a unique MSBase and/or MGBase Centre Identification Code.

"Centre Authority" means a person or persons who a Centre has officially delegated the authority to execute agreements on behalf of the Centre.

"Controller" means a party acting as a data controller under Applicable Data Protection Legislation.

"GDPR" means the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons regarding the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC.

"GDPR Laws" means the GDPR and/or the UK General Data Protection Regulation (the "UK GDPR") and any EU Member State and/or UK laws made under or pursuant to the GDPR and/or UK GDPR.

"Principal Investigator" or "PI" means a legally qualified, practicing neurologist at a MS or neuro-immunological disease ("NIDs") Centre, who has been given authority from the Centre to transfer pseudonymised data and collaborate in the MSBase/MGBase Registry Observational Study.

"Investigator" or "I" means a person working for an MSBase/MGBase Centre as part of a healthcare team (e.g. nurses, training doctors, administrative staff, data scientists, research assistants) who has been authorised by the Centre or its PI to join the MSBase/MGBase Registry and perform tasks as delegated by the Centre or its PI.

"MSBase Members" means any approved member of the MSBase/MGBase Registry, as authorised by MSBase and the Centre at which they work on the MSBase/MGBase Registry Observational Study.

"MSBase Foundation" means the not-for-profit charitable organisation incorporated as a company in Australia, which provides and administers the web-based MSBase/MGBase Registry and runs the MSBase/MGBase Observational Study.

"The MSBase Registry" (www.msbase.org) is the database and MSBase Website that hosts all pseudonymised patient data and functions used for sharing, tracking and evaluating outcomes of MS and other NIDs (NMO etc).

"The MGBase Registry" (www.mgbase.org) is the database and MGBase Website that hosts all pseudonymised patient data and functions used for sharing, tracking and evaluating outcomes of MG.

"MSBase Website" means the MSBase Registry Website at www.msbase.org

"MGBase Website" means the MGBase Registry Website at www.mgbase.org

"Participation Agreement" means this MSBase and MGBase Registry Participation Agreement.

"Pseudonymised" means the act of "pseudonymisation" as defined in or interpreted under the Applicable Data Protection Legislation.

"Processor" means a party acting as a data processor under Applicable Data Protection Legislation.

1. BACKGROUND AND RATIONALE

Neuroimmunological diseases ("NIDs") including multiple sclerosis ("MS"), neuromyelitis optica ("NMO") and myasthenia gravis ("MG") are chronic inflammatory diseases of the nervous system and are common causes of neurological disability in adults. The effects of NIDs are characterised by attacks of neurological symptoms and signs with variable recovery. MS patients can additionally develop a progressive clinical course. The clinical course of NIDs is highly variable. People with NIDs often receive immunosuppressive or immunomodulatory treatments, sequentially or in combination.

There is a global requirement for patients, doctors, regulators and the pharmaceutical industry to understand the risk factors, course and outcomes of these diseases including:

- Short and long-term outcomes of NIDs as assessed by standard clinical rating scales and outcome measures
- Clinical and paraclinical outcome predictors including imaging results, blood tests and self-monitoring devices and applications
- Medication exposure patterns and their short and long-term efficacy
- Individualised prediction of treatment response
- Safety of medications in the real-world setting, in particular long-term safety
- Pregnancy and infant risks and outcomes in women exposed to medications during conception, in pregnancy and during breastfeeding

The challenges for multi-centre investigator-initiated clinical research of this nature include harmonisation of protocols and minimum datasets, a suitably flexible data collection platform, retention of data ownership, the identification of collaborators, ongoing communication between study sites, data quality assurance, legal data storage, data management platforms and study governance.

The MSBase Foundation provides Investigators with the best possible logistic solutions to meet these challenges at no cost.

2. SCOPE OF THE MSBASE/MGBASE REGISTRY AND THE MSBASE/MGBASE REGISTRY OBSERVATIONAL STUDY

The MSBase/MGBase Registry ("Registry") is a collaborative study management platform designed and run by neurologists, for neurologists. The MSBase Foundation provides and administers the web-based Registry located at www.msbase.org and www.mgbase.org and the locally installed compatible data-entry software tools – the MSBase Data-Entry and Visualisation Software Tool ("MDS") and the iMed Data-Entry and Visualisation Software Tool ("iMed").

The MSBase Foundation runs the MSBase/MGBase Observational Study ("Study") and aims to provide operational and administrative support to enable Investigators to conduct research analyses and studies by using the Registry and its compatible data-entry systems.

This Participation Agreement is targeted at Centres and their healthcare teams who treat patients with MS and other NIDs (MG, NMO etc), and who wish to participate in the Study.

The participation of Centres joining the Registry should not be confused with the participation of patients. Participating Centres (Controllers) are responsible for the management of their patients according to the laws of their jurisdiction and their Centre's Governing Policies and Procedures. The MSBase Foundation's requirements regarding patient consent are described in Clause 5.1.

This Participation Agreement includes the following schedules:

1. Schedule 1 – Data Processing Agreement
2. Schedule 2 – MSBase/MGBase Registry Observational Study Protocol
3. Schedule 3 – Roles and Responsibilities of the MSBase/MGBase Principal Investigator

2.1 The MSBase Foundation Limited

The MSBase Foundation is a Not-For-Profit Company incorporated in Victoria, Australia. It is registered with the Australian Charities and Not-for-profits Commission (ACNC) and holds deductible gift recipient (DGR) status.

2.2 The MSBase/MGBase Registry

The Registry (www.msbase.org/www.mgbase.org) is the database and Website that hosts all pseudonymised patient data and functions used for sharing, tracking and evaluating outcomes of MS,and other NIDs (MG, NMO etc).

2.3 The MSBase Data-Entry Systems (MDS and iMed)

The MSBase/MGBase Registry can receive pseudonymised data from locally installed, compatible data-entry systems, including MDS and iMed, both of which are owned and operated by the MSBase Foundation. Online data-entry directly into the MSBase/MGBase Registry is not currently possible.

Should a Centre wish to use MDS, the MDS Software License Agreement ("MDS SLA"), will apply. Should a Centre wish to use iMed, the iMed Software License Agreement ("iMed SLA") will apply. A Software License Agreement must be entered into by the Centre prior to installing either of these Software Tools.

2.4 The MSBase/MGBase Registry Observational Study

The MSBase Foundation runs and administers the MSBase and MGBase Registry Observational Study. The MSBase/MGBase Registry Observational Study is an international study open to all neurologists practicing in the field of multiple sclerosis and other supported neuroimmunological diseases, worldwide.

The Study is governed by the MSBase/MGBase Registry Observational Study Protocol set out at Schedule 2 of this Agreement. Clause 5 of this Agreement discusses the MSBase/MGBase Registry Observational Study in further detail.

A Centre Authority must review and agree to the terms and conditions of the Participation Agreement as the head signatory. Execution of the Participation Agreement encompasses agreement and sign-off on the schedules contained in this Participation Agreement. The Principal Investigator(s) must also sign to acknowledge the terms and conditions of this Agreement. The Participation Agreement and the schedules may be signed in counterparts.

Neurologists and their healthcare teams can participate in the MSBase/MGBase Registry Observational Study by becoming members of the MSBase Registry and/or the MGBase Registry. Investigators are invited to join and are led by their Centre PI. The Centre PI agrees to follow the 'Roles and Responsibilities of the Centre Principal Investigator' (Schedule 3) and to inform the Centre's MSBase/MGBase Investigators (MSBase or MGBase Healthcare Team) of the rules and responsibilities associated with their Investigator role.

3. INTRODUCTION TO THE SCHEDULES OF THIS PARTICIPATION AGREEMENT

3.1 SCHEDULE 1 – MSBASE/MGBASE DATA PROCESSING AGREEMENT

The MSBase/MGBase Data Processing Agreement sets forth the Centre's rights and obligations as a Controller and the MSBase Foundation's rights and obligations as a Processor. The MSBase Foundation will only process the pseudonymised personal data of patients participating in the Study, on behalf of the Centre, and in accordance with the instructions documented in the Data Processing Agreement.

3.2 SCHEDULE 2 – MSBASE/MGBASE REGISTRY OBSERVATIONAL STUDY PROTOCOL

The MSBase/MGBase Registry Observational Study is a longitudinal, real-world study of MS and other NIDs, which invites participation from practicing neurologists and their teams, worldwide. It is jointly owned by all MSBase/MGBase Registry Observational Study Investigators.

The Study aims to advance Investigator-initiated, collaborative epidemiological and outcomes research by utilising a uniform minimum dataset to systematically collect and analyse pseudonymised data from consented patients with MS and other NIDs. Detailed information on the Study can be found in Schedule 2 of this Agreement and in Clause 5.

3.3 SCHEDULE 3 – ROLES AND RESPONSIBILITIES OF THE MSBASE/MGBASE PRINCIPAL INVESTIGATOR

The roles and responsibilities of Principal Investigators participating in the Study are explicitly set out in Schedule 3. It should be referred to by Principal Investigators and Investigators on a regular basis to ensure that all MSBase/MGBase Members participating in the Study understand their role and

responsibilities and participate according to the terms and conditions set out in this Agreement.

4. ROLES AND RESPONSIBILITIES OF THE MSBASE FOUNDATION

All current staff, contractors, board members and Scientific Leadership Group ("SLG") members are listed on the MSBase Website, www.msbase.org. The MGBase Website lists the members of the MGBase SLG.

4.1 THE MSBASE FOUNDATION BOARD OF DIRECTORS

The MSBase Foundation is governed by a Board of Directors who have all powers and duties of direction and management of the Foundation. The Board integrates and prioritises the scientific initiatives as determined by the strategic plan, formulated by the SLGs.

4.2 THE MSBASE AND MGBASE SCIENTIFIC LEADERSHIP GROUPS (SLGS)

The MSBase Foundation has appointed Scientific Leadership Groups to, *inter alia*, supervise the general conduct of the data contained in the MSBase and MGBase Registries and to monitor all Registry activities. The SLGs set the governance framework to ensure the integrity of the Registry databases and act as the data custodians for the MSBase Foundation and participating MSBase/MGBase Centres.

4.3 THE MSBASE FOUNDATION OPERATIONS TEAM

The MSBase Foundation Operations team manages and administers the MSBase and MGBase Registries under the direction of the MSBase Foundation Board of Directors. The Operations Team provide various forms of support to MSBase/MGBase Centres and their teams participating in the Study. These functions include general administrative and operational support, IT support, and statistical support (the latter subject to SLG approval), to enable and facilitate Investigator-initiated research. Statistical and IT support may also be provided through contractors who have agreements in place with the MSBase Foundation.

4.4 MSBASE/MGBASE REGISTRY CENTRES

The Centre delegates to the Principal Investigators (PIs) all appropriate authority to transfer pseudonymised patient data to the Registries. Each Centre governs the data that the PI is authorised to share with the Registry and each Centre is legally responsible for ensuring that the Registry is used in accordance with this Agreement and all laws, rules and directives applicable in their jurisdiction and practice setting.

4.5 MSBASE/MGBASE REGISTRY PRINCIPAL INVESTIGATORS (PIS)

PIs are authorised by their Centre to perform the roles and responsibilities listed in Schedule 3 and throughout this Agreement.

Each Centre shall nominate a PI for MS (NMO, MOG etc) and/or a PI for MG. Alternatively, a PI may approach their Centre to discuss the participation of their

Centre under the lead of the PI according to the roles and responsibilities of this Participation Agreement. Should the nominated PI resign, leave or be replaced, the Centre shall notify the MSBase Foundation and nominate a new PI in accordance with section 10.4 - 'Replacement of a Principal Investigator'.

4.6 MSBase/MGBase Registry Investigators and Healthcare Teams

Investigator roles are permitted and managed by the Centre PI and typically include the healthcare professionals, administrators, data managers and scientists working with the PI as a member of their neurology healthcare team. The PI can assign certain roles and responsibilities to each Investigator member of their MSBase/MGBase Registry Healthcare Team, which is managed through their Centre Profile within the Registry websites.

5. MSBase/MGBase Registry Observational Study

The MSBase Foundation runs and administers the longitudinal, real-world MSBase and MGBase Registry Observational Study. The Registry enables the longitudinal, real-world MSBase/MGBase Registry Observational Study, open to all practicing neurologists and their healthcare teams, worldwide. It is governed by the MSBase/MGBase Registry Observational Study Protocol, attached as Schedule 2.

5.1 Patient Informed Consent Form (PICF)

People with MS ("PwMS") or other NIDs must receive a sufficient level of detail to learn about the Study and enable them to make a well-informed decision prior to participating. They should be given the opportunity to ask questions prior to providing their consent to participate.

All patients who agree to participate are required to read and sign a Patient Information and Informed Consent Form ("PICF") that will authorise the release of their pseudonymised demographic and medical information to the Registry. The consent form must be signed in the patient's treating hospital or clinic, in a language fully understood by the patient. A copy must be provided to the patient.

An Institutional Review Board ("IRB") or the responsible Ethics Committee ("EC") must approve the Study unless it is exempt from approval in the applicable jurisdiction. If no responsible EC, IRB, or equivalent legal entity exists, the Centre, through its PI, shall still inform the participant following the requirements in their jurisdiction and obtain a signed PICF.

A template English PICF is available on the MSBase and MGBase Registry Website Documents and Resources page as a point of reference, however each Centre is responsible for ensuring that it collects informed patient consent in a manner that meets the requirements of the Centre's jurisdiction and provides for use of the patient data in the manner described in this Participation Agreement.

5.2 Protocols for Analysis of Composite Data

Centre PIs, and the SLGs, can submit data requests to obtain pseudonymised data to conduct observational research. A Data Request Form is also available on the MSBase and MGBase Registry Website Documents and Resources page.

Data Request Forms define the aim of the research, provide an analysis plan, list the identity of the data handlers, the data variables required and the Co-authorship Policy. All approved data requests include a guarantee from the Centre that shared data will be destroyed after an appropriate period.

Data Request Forms are first submitted to the Operations Team to assess feasibility. If feasible, they are submitted to either the MSBase or MGBase SLG for review and approval. Following SLG approval, a permission request is sent with the data request and project proposal to all Centre PIs. Each Centre, though its PI, may opt out of any data request. Peer-review and comment is encouraged.

The MSBase Foundation Statistician works with the pseudonymised data to collect the required variables, and 'cleans' the dataset before sending it in encrypted format to the requesting Centre PI. Research is performed by the researching party, i.e. the requesting Centre, in the interest of all involved Centres.

5.3 COMMERCIAL ANALYSES

The MSBase Foundation obtains funding from commercial entities to provide summary results in reports derived from analyses of the global dataset or subsets thereof. All commercial analyses are commissioned by the SLGs and are performed by MSBase Foundation-contracted statisticians. Pseudonymised patient level data are not shared with commercial entities unless previously agreed in a Data Sharing Agreement with each participating Centre.

Commercial scientific analyses also require a Data Request Form to be completed which follows the same internal process as described above in Clause 5.2. Centre PIs will always be informed and given the option to either participate or opt-out of each and any data request on behalf of their Centre.

Reports are shared with all Centres whose data was used for the analysis.

6. SUB-STUDY FUNCTIONALITY

The MSBase and MGBase Registry Websites provide a free logistic support tool for Investigator-initiated prospective 'sub-studies'. Sub-studies typically contain a subset of the pseudonymised data pool pertaining to a particular research topic. Sub-studies currently active within the Registry include topics such as pregnancy and NIDs, demographics and NIDs, familial NIDs and drug safety/drug efficacy studies. These sub-studies may be national or international collaborations between member investigators with similar research interests. The sub-study module also enables the set-up and management of national, supranational, and regional registries.

Centre PIs who initiate a sub-study on behalf of the Centre, become the leader of the sub-study. Once established, the sub-study can be joined by other Centres. The sub-studies leading PI can download encrypted datasets of the pseudonymised patient data records available within the sub-study.

Note: by clicking 'JOIN' on a sub-study, each collaborating PI gives the leading PI permission to download, manage and use the shared subset of pseudonymised patient data for research. Collaborating PIs should read the study criteria carefully prior to joining any sub-study to ensure that they agree with the leading PI's terms and conditions and ensure that their Centre Authority is agreeable with their Centre's participation (as part of the PI delegated responsibilities).

6.1 SUB-STUDY INCLUSION CRITERIA AND FLEXIFIELDS

Filters are available within the sub-study module to allow leading sub-study PIs to customise their Centre's sub-study when they set it up. This enables the filtering of a defined sub-set of patient records containing specific patient profile and/or disease attributes. The filters can be used to restrict enrolment based on location to allow demographics studies and the creation of national, supranational and regional registries.

When creating a sub-study, the lead PI begins by defining the sub-study inclusion criteria in the Registry, which can be customised in three 'dimensions', as follows:

6.1.1 CENTRE SELECTION

A sub-study may be open to:

- All MSBase/MGBase Centres, or
- Centres from a specific country or countries
    - Only PIs from the selected country/countries/region may join the sub-study which allows for the creation of regional, national, or supranational registries and other demographics studies, or
- Specific selected Centre(s)
    - Only PIs from selected Centres may join the sub-study which enables Centre-Centre sub-study collaborations.

6.1.2 PATIENT PROFILE AND DISEASE ATTRIBUTES SELECTION

A sub-study may be set-up to select:

- All patient records, enabling all patients to be enrolled in the sub-study, or
- A sub-set of patient records, according to defined inclusion criteria. This enables filtering of the sub-study analytical population according to the defined specific attributes/inclusion criteria and entered as field values at the time of the sub-studies set-up.

6.1.3 METHOD OF PATIENT ENROLMENT

A sub-study can be set-up to allow either automatic or manual enrolment of eligible patient records, as follows:

- If set to automatic enrolment, all eligible patient records will be enrolled.
- If set to manual enrolment, each PI collaborating in the sub-study must first review their eligible patient records prior to manually clicking 'ENROL'.

6.1.4 FLEXIFIELDS

The leading PI can add unique data-fields, termed flexifields. Each flexifield created for a sub-study relates only to the sub-study that it was created in and are only visible to the PIs collaborating in that sub-study. Flexifields automatically appear in the supported data-entry software tool (MDS or iMed) when a patient has been enrolled in the sub-study.

6.2 SPONSORED SUB-STUDIES

Sponsored sub-studies attract grants from funders or grantees such as government agencies, independent funders or the pharmaceutical industry. The MSBase Foundation may provide grants to Centres to support data collection and onsite study governance for specific projects. In these cases, funding will only be provided to official institutional bank accounts of participating Centres and will be subject to tripartite Grant Agreements executed between the MSBase Foundation, the PI and the Centre through its Centre Authority.

6.3 GOVERNANCE OF SUB-STUDIES

All collaboration in sub-studies is voluntary and joining a sub-study implies a mutual agreement between the Sub-Study Leader and each other participating Centre to share data for the purpose of the sub-studies aim(s) and objective(s).

Many sub-studies can be conducted using the dataset available in the Registry as outlined in the MSBase/MGBase Registry Observational Study Protocol. Some sub-studies also require the collection of additional data fields or require interventions that are not covered by the Study Protocol. For these collaborative sub-studies, Centres and their authorised PIs must ensure that they fulfil any additional regulatory and legal requirements, including, for example, obtainment of additional ethical approvals and/or updates to the Patient Informed Consent Form.

7. PUBLICATIONS AND AUTHORSHIP

All data requests explicitly state authorship criteria. Investigators need to comply with authorship identification guidelines of The International Committee of Medical Journal Editors (ICMJE). A confidential draft manuscript will be forwarded to each contributing Centre PI for comment, discussion and approval prior to manuscript submission. If the PI does not wish to be a named co-author on the paper after the analyses has been performed, they will be acknowledged as an "MSBase/MGBase Investigator" for contributing their data to the analysis (unless removal from acknowledgements is also requested).

All publications using Registry-derived datasets must acknowledge the broader collaborative effort of either Registry, as stated in the MSBase/MGBase Data Use Agreement. A copy of any submitted or accepted publications using Registry-derived datasets must be submitted to the Operations Team.

The MSBase/MGBase Authorship Policy is mandated and determined by the SLGs.

8. DATA PROTECTION

Both the MSBase Foundation and all Centres must adhere to their respective data protection roles, as defined in Schedule 1 - Data Processing Agreement ("DPA"), where the MSBase Foundation is a Processor of the Centres.

For the purposes of each Centre's Applicable Data Protection Legislation, every Centre must act independently as the Controller for the personal data they upload to the Registry. It is the responsibility of each Centre to process the personal data lawfully and in accordance with the applicable legislation in its jurisdiction.

Processing of pseudonymised personal data performed by the MSBase Foundation, as a Processor, on behalf of each Centre is governed by the Data Processing Agreement in Schedule 1.

Centres may be invited to join special sub-studies where personal data is transferred to external third parties. In this scenario, the MSBase Foundation and the Centre share the role of joint controller and jointly determine the purpose and means of processing. A separate Joint Controller Agreement between the MSBase Foundation and the Centre will be required, and a draft agreement would be provided to the Centre by the MSBase Foundation. The centre will be under no obligation to enter into such an agreement.

The Centres, their lead PIs and approved healthcare teams must hold all appropriate authority and approvals to transfer pseudonymised patient data to the Registries. Each Centre governs the data that they have uploaded to the Registry and each Centre is legally responsible for ensuring that the use of the Registry is conducted in accordance with this Participation Agreement and all laws, rules and directives applicable in their jurisdiction and practice setting.

8.1 PATIENT CONFIDENTIALITY

The MSBase/MGBase Registry does not collect the following identifying information: patient name, address, phone number, day of birth, and most other identifying personal information. This is done to preserve patient confidentiality.

Only month and year of birth and sex are shared to the Registries due to the importance of these data fields in the effective disease management for PwMS and other NIDs and to scientific investigations into MS and other NIDs.

Data stored in the Registry servers are highly pseudonymised. This means that patients sharing data to the Registry through their Centre cannot be easily

identified without the use of additional information that is not collected by the MSBase Foundation. As part of the pseudonymisation process, each patient record shared to the Registry is assigned a code number called a "Globally Unique Identification Number" (GUID). This hexadecimal GUID also incorporates encoded site and country identity. Association of identifying information and the patient record's GUID is only possible at the patient's treating Centre through their local database.

8.2 CENTRE OBLIGATIONS AS CONTROLLER

Each participating Centre (led by their PI) is acting as a Controller when providing data to the MSBase Foundation under this Participation Agreement. The Controller must adhere to the obligations provided in the Applicable Data Protection Legislation, (including the GDPR, when applicable), which, *inter alia*, may be expected to include obligations to:

- Obtain and process personal data lawfully
- Keep personal data only for one or more specified, explicit and lawful purposes
- Use and disclose personal data only in ways compatible with these purposes
- Keep personal data safe and secure
- Keep personal data accurate, complete and up to date
- Ensure that personal data is adequate, relevant and not excessive
- Retain personal data for no longer than is necessary for the purpose or purposes
- Provide a copy of his/her personal data to the individual, on request

8.3 THE MSBASE FOUNDATION OBLIGATIONS AS PROCESSOR

- The MSBase Foundation is acting as a Processor when receiving data from Centres under this Participation Agreement.
- The MSBase Foundation, as a Processor, must process personal data on the instructions of the Controller, as provided in the Data Processing Agreement.
- The MSBase Foundation must maintain the data secure from unauthorised access, disclosure, destruction or accidental loss.

8.5 SECURITY OF THE REGISTRY DATA

Highly pseudonymised data is transferred from MDS, iMed or other data sources to the Registry. Communications between MDS or iMed and the Registry use end-to-end encryption. Each Centre is responsible for ensuring adequate security measures are in place to secure their confidential patient data. To be compliant with Applicable Data Protection Legislation (including, where relevant, the GDPR), appropriate technical and organisational measures should be put in place, such as

encryption, to ensure a level of security appropriate to the risk associated with the transfer of data.

The Registry database is an encrypted SQL Database using Windows Azure's Real Time SQL Transparent Data Encryption (TDE). TDE encrypts the entire database with the 256-bit AES algorithm and uses a symmetric key called the database encryption key. A built-in server certificate protects the encryption key. Each server certificate is unique for each SQL Database server. Microsoft automatically rotates these certificates at least every 90 days.

The Azure SQL Database meets regulatory compliances such as ISO/IEC 27001 & FedRAMP/FISMA, SOC and PCI DSS. In addition to this, Azure is certified to HITRUST, the Health Information Trust Alliance Common Security Framework (https://www.microsoft.com/en-us/trustcenter/Compliance/HITRUST) and also complies with standards for the UK NHS regulations (Regulatory Compliance details for UK OFFICIAL and UK NHS - Azure Policy | Microsoft Learn)

The MSBase Foundation security measures in relation to the processing of personal data as a Data Processor is set out the in a sub-schedule to the Data Processing Agreement in Schedule 1.

8.6 Location of the Registry data

The pseudonymised Registry data is stored and backed up in the Australian Microsoft Azure servers (Azure cloud).

9. Data ownership

For Centres using MDS and iMed, the primary data is stored locally in each Centre's Data-entry Software's database, potentially on the local hospital network, and within each Centre's jurisdiction.

Patient datasets from a Centre will remain under the control of that Centre and its PI. Depending on local regulations, the Centre, the PI and/or the patient may own the patient data associated with each Centre, however, patient data will always be governed by the Centre according to the rules and regulations of the Centre's jurisdiction.

The MSBase Foundation does not own any of the data contained in the Registry. Patients (through their PI), Centres and their PIs, can request to withdraw data from the Registry at any time.

All research outputs will remain the joint property of the participating Centres, as applicable, always. The SLGs have been delegated the role to supervise the general conduct of the data contained in the Registry and to monitor all Registry activities. The SLGs will ensure data integrity and govern data access rules. The MSBase Foundation owns the infrastructure of the patient database and the digital envelope in which the data extract is contained, but never the data itself.

10. DATA REMOVAL

10.1 PATIENT REQUEST FOR WITHDRAWAL FROM THE MSBASE/MGBASE OBSERVATIONAL STUDY

If a patient chooses to withdraw from the Study, they must notify the PI or the Centre Authority at the Centre where they were consented. The PI must then unenroll the patient record within their local data-entry software, which will stop prospective data collection. Previously uploaded data in relation to the patient will remain in the database.

10.2 PATIENT REQUEST FOR COMPLETE REMOVAL OF DATA FROM THE MSBASE/MGBASE REGISTRY

If a patient wishes to completely remove their data from either Registry, they must notify the Centre PI at the Centre where they were consented. The PI must inform the MSBase Operations Team in writing (including the patient's MSBase ID) to info@msbase.org. The MSBase Operations Team will action the removal of the patient's entire record, including all data relating to the patient, within 60 days and will notify the Centre PI when the action has been completed.

10.3 CENTRE REQUEST FOR COMPLETE REMOVAL OF CENTRE DATA

A Centre PI, or the Centre Authority, can request deletion of their entire dataset by submitting a written request to the MSBase Operations Team at info@msbase.org. The Centre data will be completely removed within 60 days and MSBase Operations will confirm when this action has been completed by email to the PI or Centre Authority.

10.4 REPLACEMENT OF A PRINCIPAL INVESTIGATOR

The PI or the Centre Authority must notify the MSBase Operations Team if they can no longer act in their role as PI. The PI should notify the MSBase Operations Team at info@msbase.org at their earliest convenience and up to 90 days after finishing. The Centre Authority or PI can nominate a replacement PI for approval by the MSBase Operations Team.

10.5 ORPHAN DATA

If a replacement PI is not nominated, or where the existing PI or Centre Authority does not respond to communications from the MSBase Operations Team, the Operations Team will continue to contact the Centre over a period of 12 months to attempt to re-establish a Centre PI.

If no PI can be nominated over the course of this time, the MSBase Operations Team will ask the Centre Authority how they wish to proceed with respect to retaining the pseudonymised orphan data that are still useful and necessary in relation to the Observational Study research purposes, for which they were collected.

If the Centre Authority cannot be contacted over the course of this time, or if the Centre is closed, the MSBase Operations Team will remove the orphan data from the Registry.

11. FUNDING AND REIMBURSEMENTS

The MSBase Foundation may receive funding from external sources to conduct contract analyses or sponsored sub-studies. The MSBase Foundation may then be able to provide participating Centres with grants to help reimburse administrative costs incurred during the period of participation. Administrative costs can include additional time or personnel required for data entry, costs incurred for ethics approval and other associated costs that are necessary for the Centre's participation in the sponsored sub-study. Reimbursements are subject to execution of a financial Grant Agreement between the Centre, the PI and the MSBase Foundation and must be paid to an Institutional Bank Account of the Centre.

12. RESEARCH INTEGRITY

The Centre guarantees and warrants that it will follow all applicable rules and regulations for participating in the MSBase/MGBase Registry Observational Study, including all ethics/waivers/consents and all required reporting of serious adverse events.

13. AGREEMENT SIGNATURE

This Agreement, including its applicable schedules, has been executed and takes effect on the date of last signature written below.

Name of MSBase/MGBase centre (e.g. hospital or clinic):

Centre Authority *(Head of Department, or similar)*

_____ _____

Signature Date

_____ _____

Name written in full Position

MSBase Principal Investigator *(Signs to acknowledge the Agreement):*

_____ _____

Signature Date

_____

Name written in full

OR

MGBase Principal Investigator *(Signs to acknowledge the Agreement):*

_____ _____

Signature Date

_____

Name written in full

The MSBase Foundation Ltd

MSBase Foundation Director: Helmut Butzkueven

_____ _____

Signature Date