MSBase Registry Participation Agreement

for Centres from the United Kingdom
participating in the
MSBase Registry Observational Study

Formerly a part of the "MSBase Observational Plan"

United Kingdom Version 3.0 dated: 21 December 2020

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CONTENTS

VERSION CONTROL

Version	Date	Author	Summary of changes
1.0	12/08/2019	MSBase Operations	1. The MSBase Participation Agreement supersedes the 9th edition of the MSBase Observational Plan dated 11 February 2015.
2.0	09/06/2020	MSBase Operations *	1. The Foundation owns and operates the iMed software (Clause 2, Subclause 2.3 and 'Background' heading in Schedule 2 (MSBase Observational Study Protocol)). 2. GDPR-compliant data transfer from iMed to MSBase Registry (Subclause 8.5 and throughout the Schedules to this Agreement). 3. Icometrix and ProSynergie Sàrl added to Appendix 1B - 'Approved Sub-Processors' in Schedule 1 (Data Processing Agreement).
2.1	2/09/2020	MSBase Operations	United Kingdom-specific updates 1. Changes to Clause 4.1 to indicate requirement for use of Patient Information Sheet (PIS) and Informed Consent Form (ICF) in the United Kingdom. 2. Changes to Clause 9.0 to reflect that under GDPR the lawful basis for processing data in the U.K. is "legitimate interests". Under "legitimate interests" the ability for a data subject to remove or transfer existing information is limited.
3.0	16/12/2020	MSBase Operations *	1. Changes in relation to MSBase role as joint Data Controller for certain data processing activities. 2. Removal of signature pages from the Data Processing Agreement and addition of text confirming tripartite execution of Participation Agreement encompasses execution of all Schedules.

* This Participation Agreement has been independently reviewed by a registered legal firm in Stockholm, Sweden, with relevant expertise in GDPR.

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
PIS	Participant Information Sheet
ICF	Informed Consent Form
GDPR	General Data Protection Regulation
IRB	Institutional Review Board
EC	Ethics Committee

DEFINITIONS

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

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

"Investigator" or "I" means a person working for an MSBase 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 Registry and perform tasks as delegated by the Centre or its PI.

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

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

"Participation Agreement" means the MSBase Registry Participation Agreement, to which this MSBase Registry Observational Study Protocol is a Schedule.

"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.

"Pseudonymised" means the act of "pseudonymisation" as defined in the GDPR.

"Processor", "Controller" and "Joint Controller" means a "processor", "controller" and "joint controller" as defined in the GDPR.

1. BACKGROUND AND RATIONALE

Neuro-immunological 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 suitable 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 REGISTRY AND THE MSBASE REGISTRY OBSERVATIONAL STUDY

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

MSBase runs the MSBase 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, 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 (Data Controllers) are responsible for the management of their patients according to the laws of their jurisdiction and their Centre's Governing Policies and Procedures. MSBase's expectations regarding patient consent are described in Clause 5.1.

This Participation Agreement includes the following schedules:

- Schedule 1 – Data Processing Agreement (with sub-schedules)
- Schedule 2 – MSBase Registry Observational Study Protocol
- Schedule 3 – Roles and Responsibilities of the MSBase Principal Investigator

The Data Processing Agreement (Schedule 1) pertains to the certain processing activities that MSBase must perform to facilitate the Study, such as hosting the pseudonymised personal data transferred to the Registry.

For analyses and sub-studies that require MSBase to perform processing activities that involve additional sharing of the hosted pseudonymised personal data to third parties, MSBase has the role of joint controller together with the involved parties. For these special analyses and studies, eligible Centres shall be informed about the analysis or study and must enter into additional Data Sharing Agreement(s) should they wish to participate.

2.1 THE MSBASE FOUNDATION LTD

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 REGISTRY

The Registry (www.msbase.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.

2.3 THE MSBASE DATA ENTRY SYSTEMS (MDS AND IMED)

The Registry can receive pseudonymised data from locally installed, compatible data entry systems, including the MSBase Data-entry Software (MDS) and the iMed software, both of which are owned and operated by the MSBase Foundation. Online data entry directly into the MSBase 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 REGISTRY OBSERVATIONAL STUDY

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

The Study is governed by the MSBase Registry Observational Study Protocol, attached in Schedule 2. Clause 5 of this Agreement discusses the MSBase 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 must also sign to acknowledge the terms and conditions of this Agreement.

Neurologists and their healthcare teams can participate in the MSBase Registry Observational Study by becoming members of the MSBase 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 Investigators (MSBase 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 DATA PROCESSING AGREEMENT

The MSBase Data Processing Agreement sets forth the Centre's rights and obligations as a Data Controller and MSBase Foundation's rights and obligations as a Data Processor. MSBase 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 REGISTRY OBSERVATIONAL STUDY PROTOCOL

The MSBase 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 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 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 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 SLG members are listed on the MSBase Website, www.msbase.org.

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 Scientific Leadership Group (SLG).

4.2 THE MSBASE SCIENTIFIC LEADERSHIP GROUP (SLG)

The MSBase Foundation has appointed a Scientific Leadership Group (SLG) to, *inter alia*, supervise the general conduct of the data contained in the Registry and to monitor all Registry activities. Members of the SLG meet up to 6 times a year and form sub-committees to oversee scientific projects. The SLG sets the governance framework to ensure the integrity of the Registry database and act as the data custodians for the MSBase Foundation and participating MSBase Centres.

4.3 THE MSBASE OPERATIONS TEAM

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

4.4 MSBASE REGISTRY CENTRES

The Centre delegates to the Principal Investigator (PI) all appropriate authority to transfer pseudonymised patient data to the Registry. 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 REGISTRY PRINCIPAL INVESTIGATORS

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. 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 MSBase and nominate a new PI in accordance with section 10.3 - 'Replacement of a Principal Investigator'.

4.6 MSBASE 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 Registry Healthcare Team, which is managed through their Centre Profile within the Registry.

5. MSBase Registry Observational Study

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

5.1 Participant Information Sheet (PIS) and Informed Consent Form (ICF)

The Centre PI, or an authorised Centre Investigator, must provide all potential participants with a Participant Information Sheet (PIS), explain the MSBase Registry Observational Study and provide the opportunity for questions to be asked.

All patients who agree to participate shall be required to sign an Informed Consent Form (ICF) that will authorise the release of their highly pseudonymised (coded) 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.

The Centre, through its PI, must always inform the participant following the requirements in their jurisdiction and obtain a signed PIS and ICF.

The UK PIS and ICF (in English) is available on the MSBase Registry Website Documents and Resources page.

5.2 Protocols for analysis of composite data

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

Data Request Forms define the aim of the request, 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 MSBase Operations Team to assess feasibility. If feasible, they are submitted to the 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, through its PI, may opt out of any data request. Peer-review and comment is encouraged.

The MSBase 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

MSBase 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 SLG and are performed by MSBase-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 Registry Website provides 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 PI's 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 PI's 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 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 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 patients 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 PI's 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 (the MSBase MDS Data Dictionary documents a comprehensive list of these fields) as outlined in the MSBase 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 PI's must ensure that they fulfil any additional regulatory, legal requirements. For example, obtainment of additional ethical approvals and/or updates to the 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 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 the Registry, as stated in the MSBase Data Use Agreement. A copy of any submitted or accepted publications using Registry-derived datasets must be submitted to the Operations Team.

The MSBase Authorship Policy is mandated and determined by the SLG.

8. DATA PROTECTION

Both MSBase and all Centres must adhere to their respective data protection roles, as defined in the Data Processing Agreement (Schedule 1), and where a joint Data Controllership role exists, as agreed between the relevant parties in the relevant Data Sharing Agreement.

For the purposes of each Centre's applicable local legislation relating to personal data and the General Data Protection Regulation ("GDPR"), every Centre must act independently as the Data 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 MSBase, as a Data Processor, on behalf of each Centre is governed by the Data Processing Agreement in Schedule 1.

As regards the processing of personal data in commercial analyses, as well as special sub-studies where personal data is transferred to third parties, MSBase has the role of joint controller, and has a shared controllership with the involved parties. Consequently, agreeable parties must execute an additional Data Sharing Agreement, determining their respective responsibilities and roles for compliance with the data privacy obligations in a transparent matter.

NOTE: The Data Processing Agreement (Schedule 1) pertains to data processing activities that are necessary for MSBase to the run the Registry and must always remain in place. Data Sharing Agreement(s) shall document the additional data processing activities, roles and responsibilities of MSBase in the role of joint Data Controller for commercial analyses and sub-studies sharing data to third parties.

The Centres, their lead PI's and approved healthcare teams must hold all appropriate authority and approvals to transfer pseudonymised patient data to the Registry. 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 the Agreement and all laws, rules and directives applicable in their jurisdiction and practice setting.

8.1 PATIENT CONFIDENTIALITY

The MSBase 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 gender are shared to the Registry 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 MSBase. 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 DATA CONTROLLER

Each participating Centre (led by their PI) is a Data Controller. The Data Controller must adhere to the obligations provided in the General Data Protection Regulation (GDPR), which, *inter alia*, include 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
- Give a copy of his/her personal data to the individual, on request

8.3 MSBASE OBLIGATIONS AS DATA PROCESSOR

- MSBase, as a Data Processor, must process personal data on the instructions of the Data Controller, as provided in the Data Processing Agreement.
- MSBase must maintain the data secure from unauthorised access, disclosure, destruction or accidental loss.

8.4 MSBASE OBLIGATIONS AS JOINT DATA CONTROLLER

- MSBase, as a joint Data Controller, must enter into a Data Sharing Agreement with the involved parties, determining their respective responsibilities and roles for compliance with the data privacy obligations in a transparent matter.

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 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 to the Health Information Trust Alliance Common Security Framework (https://www.microsoft.com/en-us/trustcenter/Compliance/NHS).

MSBase's 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 highly pseudonymised Registry data is stored and backed up in the Australian Microsoft Azure servers (Azure cloud).

9. Data ownership

The primary data is always 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 SLG has been delegated the role to supervise the general conduct of the data contained in the Registry and to monitor all Registry activities. The SLG 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 MSBASE 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 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. 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.

10.3 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 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.

10.4 ORPHAN DATA

If a replacement PI is not nominated, the MSBase Operations Team will contact the Centre over a period of 12 months to attempt to re-establish a Centre PI. If no PI can be nominated over this time, or if the Centre is closed, the pseudonymised Centre data will remain in the MSBase Registry global data pool.

11. FUNDING AND REIMBURSEMENTS

MSBase may receive funding from external sources to conduct contract analyses or sponsored sub-studies. MSBase 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 Registry Observational Study, including all ethics/waivers/consents and all required reporting of Serious Adverse Events.

13. AGREEMENT SIGNATURE

This Agreement has been executed and takes effect on the date of last signature written below. It has been drawn up in two (2) identical copies of which the parties have received one each.

Name of centre (e.g. hospital or clinic): Click or tap here to enter text.

Authorised centre representative:

_____ _____
Signature Date

_____
Name written in full

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

_____ _____
Signature Date

Click or tap here to enter text.

Name written in full

The MSBase Foundation Ltd

MSBase Foundation Director: Helmut Butzkueven

_____ _____
Signature Date