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European Prevention of Alzheimer's Dementia Consortium

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D1.8 Establishment of the EPAD LCS Research Access Committees

WP1 – Scientific Expertise

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TABLE OF CONTENTS

DOCUMENT INFORMATION 3
DOCUMENT HISTORY 4
DEFINITIONS 5
EXECUTIVE SUMMARY 7
1. INTRODUCTION 8
2. OVERVIEW OF PLANNED RAC PROCESS & STRUCTURE: 8
3. EPAD LCS DATA ACCESS 9
4. MRI DATA 10
5. REPORTING 10
6. EPAD LCS SAMPLE ACCESS COMMITTEE 10
7. SECRETARIAT 12

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DEFINITIONS

- Partners of the EPAD Consortium are referred to herein according to the following codes:
  - **Janssen**. Janssen Pharmaceutica NV (Belgium)
  - **UEDIN**. The University of Edinburgh (United Kingdom)
  - **UOXF.** Masters and Scholars of the University of Oxford (United Kingdom)
  - **BBRC.** BarcelonaBeta Brain Research Center (Spain)
  - **SYNAPSE.** Synapse Research Management Partners S.L (Spain)
  - **KI.** Karolinska Institutet (Sweden)
  - **VUMC.** Stichting VUmc (Netherlands)
  - **UCAM.** Masters and Scholars of the University of Cambridge (United Kingdom)
  - **MRC.** Medical Research Council (United Kingdom)
  - **BERRY.** Berry Consultants LLP (United Kingdom)
  - **UNIGE.** Université de Genève (Switzerland)
  - **RUMC.** Stichting Katholieke Universiteit (Netherlands)
  - **CU.** Cardiff University (United Kingdom)
  - **CHUT.** Centre Hospitalier Universitaire de Toulouse (France)
  - **IQVIA.** IQVIA, Ltd (United Kingdom)
  - **AE.** Alzheimer Europe (Luxemburg)
  - **EMC.** Erasmus Universitair Medisch Centrum Rotterdam (Netherlands)
  - **APHP.** Hôpital de la Salpêtrière (France)
  - **INSERM.** Institut National de la Santé et de la Recherche Médicale (France)
  - **ULEIC.** University of Leicester (United Kingdom)
  - **IXICO.** IXICO Technologies Ltd (United Kingdom)
  - **ARACLON.** Araclon Biotech S.L (Spain)
  - **FRAUNHOFER.** Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V. (Germany)
  - **Eisai.** Eisai Inc (United States)
  - **SARD.** Sanofi-Aventis Recherche & Développement (France)
  - **NOV.** Novartis Pharma AG (Switzerland)
  - **BI.** Boehringer Ingelheim International GmbH (Germany)
  - **Eli Lilly.** Eli Lilly and Company Ltd (United Kingdom)
  - **HLU.** H. Lundbeck A/S (Denmark)
  - **Takeda EU.** Takeda Development Centre Europe Ltd (United Kingdom)
  - **AC Immune.** AC Immune SA (Switzerland)
  - **Biogen**. Biogen Idec Limited (United Kingdom)
  - **Amgen.** Amgen NV (Belgium)
  - **Pfizer.** Pfizer Limited (United Kingdom)
  - **UCB.** UCB Biopharma SPRL (Belgium)
  - **ARIDHIA**. Aridhia Informatics Ltd (United Kingdom)
  - **ROCHE**. F. Hoffmann - La Roche (Switzerland)
  - **UKK**. University Hospital of Cologne (Germany)
  - **MSD**. Merck Sharp & Dohme (United States)

- **Grant Agreement.** The agreement signed between the beneficiaries and the IMI JU for the undertaking of the EPAD project (115736).
- **Project.** The sum of all activities carried out in the framework of the Grant Agreement.
- **Work plan.** Schedule of tasks, deliverables, efforts, dates and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.
- **Consortium.** The EPAD Consortium, comprising the above-mentioned legal entities.
- **Project Agreement.** Agreement concluded amongst EPAD participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.
- **EPAD LCS.** The EPAD Longitudinal Cohort Study.
- **AD.** Alzheimer's Dementia.
- **MRI.** Magnetic Resonance Imaging
- **DICOM.** Digital Imaging and Communications in Medicine is a standard for handling, storing, printing, and transmitting information in medical imaging.
- **Samples –** biological samples and products such as cells and DNA derived from biological samples
- **DICOM Data & Images –** the MRI DICOM Data collected at TDCs, standardised by IXICO to derive the Images used (also included in this definition) for the EPAD LCS MRI Active Core sequence data.
- **CSF -** Cerebrospinal fluid.

EXECUTIVE SUMMARY

The EPAD Longitudinal Cohort Study represents a valuable resource to the scientific community for the study of risk factors for Alzheimer's Dementia. Data, biological samples and MRI data are collected and stored as described in D4.13. This includes clinical data, human biological samples and MRI data (raw DICOM data and derived images). EPAD LCS Data will be available to EPAD Partners according to the terms of the EPAD Project agreement. In order to facilitate research collaboration within EPAD and to support external researchers, data set releases will be defined and made available via collaborative workspaces. These data set releases will only include data which has been cleaned and released via a quality control process, with EPAD partners also having access to the underlying raw data as well as the possibility to transfer such data to their own databases. While the data released can be made available on an open access basis, the collection of biological samples represents a finite resource and therefore access to these samples must be controlled to maximise the scientific value of the resource – this resource will be referred to as Samples in this process. The EPAD project has set up an appropriate governance structure, called the EPAD LCS Sample Access Committee, that will oversee access the EPAD LCS Samples. The original data from MRI scans represents a high-volume data resource and use of this data and the derived images requires specialist knowledge and skills. In accordance with the EPAD Project Agreement Partners may access the raw image data on request. To facilitate imaging research the Active Core scan will be made available and access will be provided via an XNAT currently hosted at VUmc (with EPAD partners also having the possibility to transfer such data to their own databases).

1. INTRODUCTION

The EPAD Longitudinal Cohort Study (LCS) represents a valuable resource to the scientific community for the study of risk factors for Alzheimer's Dementia (AD). Data, biological samples and MRI data are collected and stored as described in D4.13. While the clinical data collected and derived can be made available on an open access basis, the collection of biological samples represents a finite resource and therefore access to these samples in the EPAD Bioresource must be controlled to maximise the scientific value of the resource. The EPAD project has set up an appropriate governance structure called the EPAD LCS Sample Access Committee for access to Samples. The original data from MRI scans and derived images represents a high-volume data resource and use of this data requires specialist knowledge and skills. In accordance with the EPAD Project Agreement Partners may access the raw image data on request. To facilitate imaging research the Active Core scan will be available and access will be provided via an XNAT currently hosted at VUmc (with EPAD partners also having the possibility to transfer such data to their own databases). Maintenance of the LCS data access provisions for EPAD partners and third parties (including but not limited to associated Trial Delivery Centres and Parent Cohort (PC) Principal Investigators (PIs)) as described in the EPAD project agreement will be managed by UEDIN.

In addition, it is best practice to expect that as part of the Research Access Process researchers that work with EPAD LCS Samples or MRI data to comply with expected quality standards, e.g. Good Clinical Laboratory Practice for the processing of Samples and GDPR standards for working with MRI Image Data.

Several aspects provided for in this Deliverable are still in the process of being implemented in the Project Agreement. Their implementation is therefore the subject of agreement by all EPAD partners on corresponding amendments to the Project Agreement.

2. Overview of planned RAC process & structure:

The EPAD LCS Chief Investigator (CI) will oversee the administration of the EPAD LCS Research Access Processes and the associated Committee.

An on-line tool will be accessed via the EPAD website (www.ep-adp.org/erap) and will be Administered by UEDIN. This tool will utilise Zengine, an on-line platform provided by Wizehive configured to EPAD LCS specifications. The Wizehive tool will collect information about the researchers and (subject to exceptions when it concerns LCS data access by EPAD partners) the research that is planned to streamline request management, facilitate committee review and deliver downstream information processing as follows:

1. For Data Access – Aridhia (EPAD Partner) will provide workspaces in the Aridhia workspace platform with the data set requested to the specified researchers. EPAD partners can also

request access to the raw data set (as made available to the Balancing Committee), also delivered via the workspace platform, and have the possibility to transfer the raw data from the platform to their own databases.

2. The Sample Access Committee will make access decisions for Samples in accordance with the EPAD Project Agreement, and the CI will confirm these decisions on behalf of the Sponsor.
3. For Samples Access – EPAD Bioresource (UEDIN EPAD Partner) will retrieve from Bioresource storage, package and transport approved Sample requests to the specifications requested and Aridhia will provide the associated Data as described in point 1
4. For MRI Image Access – VUMC (EPAD Partner) will provide access to an XNAT for the retrieval and processing of the Active Scan Core sequences and MRI image data. Aridhia will provide the associated Data as described in point 1. EPAD partners will have the possibility to transfer the MRI data and images from XNAT to their own databases and receive access to the raw MRI data. Other arrangements for the Advance Active Scans are being fully explored and developed to ensure full compliance with the project agreement.

An important principle that will be maintained is that access to all EPAD LCS data will be provided to EPAD Partners according to the terms of the EPAD Project Agreement. Research proposals will be focused on specific EPAD data sets described in D4.13.

3. EPAD LCS Data Access

Data Access requests will be coordinated by UEDIN. The basic role of UEDIN will be research oversight rather than approval as open data access will be provided for EPAD partners following each LCS data release and for external non-EPAD partners following an embargo period of 6 months following each LCS data release.

Access will in principle only be provided to quality-controlled data sets. However, EPAD Partners can also request, via the Wizehive system, a data transfer of any such quality controlled LCS data and also of raw LCS data (as made available to the Balancing Committee) to allow them to perform their research use outside of any EPAD controlled platform. This access will be provided via the Aridhia platform and the Partner will have administrator access to download such data without any approvals.

All requests for access to LCS data need to be made through the Wizehive system (to the extent operational). EPAD partners are not obliged to disclose their research question and will also not be subject to mandatory publication rules of their research results, be required to grant back a license on their research results or demonstrate that they are self-funding. EPAD partners requesting access to LCS data will therefore not be required to provide any information about research plans. EPAD partners requesting access to data sets will have the option to provide information about research plans to facilitate collaboration and publication coordination.

All data access requests (including the provision of clinical data to support Samples or MRI Image research) will be provisioned by the Aridhia workspace platform. The researchers will be provided with access to their requested Data Set, via a semi-automated process which transfers the request and required researcher email and contact information direct to Aridhia from the Wizehive system. There is no approval step in this process to provide data access. If requested, an EPAD partner can transfer the data out of the workspace. Alternatively, the researcher can collaborate, invite other researchers and utilise the tools & applications available in the Aridhia workspace to facilitate research.

4. MRI data

In principle all data access requests will be supported by UEDIN. Except for EPAD partners who decide not to identify a research question, the research questions will be made available via the ERAP webpage, and collaborations formed where research proposals intersect.

All requests for EPAD LCS MRI data from EPAD partners will be recorded by the Wizehive system with automatic approval in accordance with the EPAD Project agreement. EPAD partners and external researchers will have the possibility to transfer data for the Active Scans from an XNAT, currently managed at VUMC, to their own databases. Other arrangements for the Advance Active Scans are being fully explored and developed to ensure full compliance with the project agreement. EPAD partners will have the possibility to receive access to the raw MRI data.

5. Reporting

A bi-annual report of all research access requests and the progress of those requests from concept to delivery of publication will be collated from the Wizehive system by the Secretariat. UEDIN will review the progress of research with the EPAD LCS data. In addition, UEDIN will be responsible for deciding on the future releases of EPAD LCS Data Sets.

For the avoidance of doubt, EPAD partners do not have to identify a research question, share any results of their research with any committee established hereunder or any other EPAD partner, publish the results of their research, or demonstrate that they are self-funding.

6. EPAD LCS Sample Access Committee

Membership for the Sample Access Committee (SAC)

Jean Manson (chair)

Judi Syson (Secretariat)

Membership will be a mix of eight industry and academic EPAD representatives and will also include external experts. The committee may also draw on specific expertise for advice when required.

Description of the EPAD LCS Bioresource

The EPAD LCS Bioresource is a collection of samples generated from the EPAD Longitudinal Cohort Study (LCS) of participants who have no or limited signs of Dementia. The resource has trials level rigor (Good Clinical Laboratory Practice) with associated measures of Alzheimer's Dementia pathology using both CSF and MRI. The participants undergo follow-up and sample collection over several years. The EPAD Bioresource consists of blood, urine and saliva collected annually from each participant and a sample of cerebral spinal fluid collected at baseline visit. The resource is currently collected from 28 approved Trial Delivery Centres across Europe with an expectation that this will increase during 2019/20 resulting in up to 40 sites. The resource incorporates a database and information management system which provides traceability and sample validation at every stage along the sample pathway, from collection through processing to storage. The resource aims to facilitate research to generate data for risk factor assessment, support for proof of concept and other trials in AD. The EPAD LCS Bioresource thus consists of a unique set of samples for the study of early brain changes leading to AD and is designed to increase the likelihood of successful development of new treatments for the secondary prevention of Dementia. Jean Manson is the PI for the EPAD LCS Bioresource and chair of the EPAD LCS Sample Access committee.

Terms of reference for EPAD LCS Sample Access Committee

1. The SAC will review and prioritise all requests for the use of samples from the EPAD LCS Bioresource.
2. The SAC will utilise an on-line tool (Wizehive Zengine) to review and manage requests from end to end.
3. The SAC will hold meetings bi-annually in person or by tele/video conference to prioritise and finalise recommendations. (This bi-annual review has been chosen because of the finite nature of the Bioresource and the need to consider requests in batches to facilitate prioritisation between requests and avoid depleting the Bioresource based on a "first come first served" basis.)
4. Requests will be available to the SAC via the on-line tool, review time will be available 6 weeks ahead of a meeting, completed reviews will be required 2 weeks ahead of a meeting.
5. Six members of the committee (out of eight) including the chair or delegate will be required to be present for the meeting to be quorate.
6. Decisions on requests will be made by consensus following a standardised review process. The chair will have the casting vote.
7. The SAC will recommend release of samples for appropriate studies to the Chief Investigator.

8. The minutes of the SAC meetings will be made available to SAC members and the EPAD Executive Committee (ExCom) via TeamWork.
9. The SAC will report directly to WP1 bi-annually following the review meetings.
10. SAC will use criteria, principles and guidelines through which requests will be assessed, which will be available on the EPAD website.
11. The SAC and its membership will be reviewed annually by WP1 and EPAD Executive Committee.

There is an expectation that results of the research will to be shared back with EPAD partners for research use where appropriate.

7. Secretariat

The Samples Access Committee will be supported by the Chief Investigator and resources from within their office. This resource will provide secretariat services to the Chairperson and members of the committee to ensure the smooth running of the committee.

EPAD has commissioned the implementation of a Wizehive system adapted from grant management systems to support the user and committee member interface with the research access process. The cloud-based service allows applicants to inform EPAD of their research plans and request access to make an application. Opportunities for potential collaborations will be identified at this early stage so that researchers complete novel applications that are of interest to EPAD. Applicants will be able to provide details of the researchers involved, research plans, scientific and statistical justifications and details of data management and publication plans. Applicants will be required to be self-funding for Sample access request costs. For the avoidance of doubt, in the case of LCS data access, EPAD partners do not have to identify a research question, share any results of their research with any committee established hereunder or any other EPAD partner, publish the results of their research, or demonstrate that they are self-funding.

There are costs at the EPAD LCS Bioresource associated with preparing batches of Samples to fulfil approved Samples requests, e.g. the biological sample handling, management and shipping, the cost of these services will be made visible (on the EPAD website) calculated based on access to Sample sets that match the data set releases. The researcher will be required to provide compensation/payment for these costs to UEDIN. The Secretariat will provide support if bespoke costings are required for a potential researcher to make a funding application prior to completing a full application to EPAD for samples.

Once an application has been received it will be routed by the Wizehive system to the committee as agreed by the Terms of Reference of the committee. The Wizehive system will include an on-line review tool for committee members to assess each application. The Committee have developed

criteria for assessment of applications, which are aligned with this Deliverable and the Project Agreement. The Secretariat will coordinate the distribution and collation of the committee assessments as required by the committee. On-line collaboration or meetings can be arranged to come to a consensus decision on each application. This will be routed by the Secretariat to the CI for confirmation of the decision by the CI and on behalf of the EPAD LCS Sponsor (UEDIN)

The Secretariat will provide supporting materials for applicants via the EPAD website including the EPAD LCS Data Set Library, Information for Applicants, EPAD Publication guidance etc.