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European Prevention of Alzheimer's Dementia Consortium

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D8.2 Guidance on recruitment into EPAD LCS from Parent cohort studies

WP8 – Ethical, Legal and Social Implications

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[1] If "Other" type of dissemination level, please inform the PMO team (mgt@ep-ad.org) accordingly.

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DEFINITIONS[2]

- 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)
  - **VU-VUMC.** Stichting VU-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)
  - **QUINTILES.** Quintiles, 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.** Boehriger 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, Inc (United States)
  - **Amgen.** Amgen NV (Belgium)
  - **Pfizer.** Pfizer Limited (United Kingdom)

[2] To be completed with terms and abbreviations related to the actual content of the document

- **UCB.** UCB Biopharma SPRL (Belgium)

- **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.

EXECUTIVE SUMMARY[3]

This deliverable summarises the ethical issues associated with the development of the EPAD virtual register and data discovery tool. It focuses on the relationship between parent cohorts ("**PCs**") and the EPAD project, particularly related to (i) the transfer and/or access of PC data by the EPAD project, (ii) contacting and enrolling participants from whom data has been included in the PC; and (iii) the transfer and/or access of certain EPAD data by the PCs. The deliverable complements D8.1, which focusses on ethical issues arising within the EPAD project itself, as well as D3.3 related to the fingerprinting of parent cohorts, and EPAD legal documents including the Parent Cohort Engagement and Associated Scientific Collaborator Agreement.

[3] Maximum 2,000 characters (including spaces).

1. INTRODUCTION

The EPAD project draws on the accumulated data of existing studies to develop a platform for the identification of potential participants. This represents a novel approach to recruitment, and the relationship between EPAD and these parent cohorts (PCs) warrants close attention. This is provided in this deliverable.

The background to the document is provided by national and international frameworks for the conduct of ethical research in biomedical science[1,2] and interpretations of these[3,4], in dementia research[5,6] and in the development of platforms for data sharing[1,2,7–11]. However, it is important to note that the EPAD project will operate across regulatory jurisdictions within Europe. As such, study and trial arrangements must conform to national and international ethical regulations[4], including those related to recruitment, informed consent and data governance. This may need to be reflected in local changes to the study protocol, recruitment, consent and disclosure procedures. Responsibility for ensuring that EPAD adheres to local regulatory frameworks will ultimately lie with national leads and EPAD TDCs

2. BACKGROUND

In the following sections we consider specific issues related to EPAD's interaction with parent cohorts. In particular, we cover issues associated with the movement transfer and/or access of PC data by the EPAD project and contacting and enrolling participants whose data is included in the PC between PCs and EPAD**,** specifically although not exclusively related to consent and data access. The document sits alongside, and provides the ethical justification related to, legal agreements between EPAD and Parent Cohorts (PCs), specifically the Parent Cohort Engagement document and the Associated Scientific Collaborator Agreement. It also parallels D3.3. It complements D8.1, which covers ethical issues raised within the EPAD longitudinal cohort and proof of concept studies.

The engagement with parent cohorts will involve a series of steps:

1. The identification of relevant parent cohorts

[4]See the International Compilation of Human Research Standards http://www.hhs.gov/ohrp/international/

2. The establishment of relationships with the PIs of potential PCs
3. The fingerprinting of parent cohort data
4. Data discovery to enable the identification of sets of potential EPAD participants
5. The recontacting of PC participants by the PC PI to investigate their willingness to participate in EPAD
6. The return of data from the EPAD LCS to parent cohorts

Steps subsequent to the contacting of participants form part of the EPAD LCS recruitment and consent process, and are discussed in more detail in D8.1.

3. ETHICAL REQUIREMENTS FOR THE INCLUSION OF PARENT COHORTS

3.1. Access to PC data within the EPAD register for data discovery

The EPAD Register is a virtual resource that enables subject characteristics across all participating PCs to be explored remotely, without actual display of individual subject data. **Therefore, no informed consent from the individual subjects from the PCs is necessary for data inclusion for data discovery. This exemption from consent is acceptable when all of the conditions below are met.**

However, if in the future, EPAD feels it necessary to request data from parent cohorts, such as legacy imaging data, **consent should be in place for this data to be shared**.

1) For data discovery in the EPAD Register, subject-level (coded, indirectly identifiable) data are not visible to EPAD researchers or researchers from other PCs. IDs employed should not be coded and directly/easily related to PC participant, but instead employ one-way irreversible encryption of original participant IDs such that only the PC can ever interpret these derivative IDs (DerIDs) The ‘open access’ option within the PREPAD tool will not be used. No data are or can be made accessible to anyone other than those who own the data (PI of PC). Should other software be applied in the future, the same limitations apply.
2) The EPAD Register is built in a ‘one-node’ way: **EPAD researchers should only view summary counts**. PIs of PCs will not have access to each other’s data. Only the PI of a PC will have access to the individual data of his PC.

3) Confidentiality is further imposed by a minimum count of 3 subjects that may be reported following a discovery query. This should be ensured by the developers of the PREPAD tool.
4) Although the EPAD Register builds on the work done in EMIF-AD, the governance, rules and regulations of EPAD, not EMIF-AD, will apply to all EPAD activities.

The conditions for the incorporation of PC data into the virtual register are set out in the legal agreements between EPAD and the PC PI, namely the Parent Cohort Engagement (PCE) document, the Associated Scientific Collaborator Agreement (ASCA). The PCE provides for the profiling of the cohort by EPAD to determine the general content and characteristics of the Parent Cohort. The ASCA provides the basis for 'participant access' by EPAD, including fully anonymized responses to searches, but **excluding the ability to control, process or access personal data or raw participant level data** included in the PC. It provides the basis for EPAD to request PC PIs to contact participants in their research in order to introduce EPAD research. If PCs are controlled by EPAD partners, a simplified version of the ASCA will be used.

Initial first contact with participants from PCs who are potentially eligible for EPAD LCS will be established by PC teams, designated by the PIs of the respective PCs. EPAD will not approach eligible research participants from PCs directly (see D8.1 section 5)

3.2. Re-contacting eligible participants from PCs in the EPAD register

EPAD has a moral responsibility to ensure that eligible research participants are appropriately approached and that data are appropriately gathered. It is essential that the modes of action for consent for re-contact in the PC are transparent to EPAD. PIs of PCs are required to explain their modes of action regarding the re-contacting of their eligible research participants during the EPAD Register stage.

1) **In some PCs, arrangements have already been made for the re-contacting of participants.** Some PCs have asked participants and documented, as part of the PC informed consent, whether they agree to being re-contacted in the future for other research projects (with other purposes). If consent to being re-contacted for future research with another purpose (which would cover EPAD) is already included in the informed consent document of the PC, the following modes of action are recommended:
    - Eligible participants who have provided consent are approached by the PI of the PC with information materials about EPAD in general and asked to participate in the EPAD LCS. Where EPAD TDC PI and PC PI are the same individual, it is important that it is clear to (potential) participants that EPAD is a different study

from the one they are already participating in. Participants will then 'opt in' and contact an EPAD TDC.

- Eligible participants who have dissented to re-contacting will not be approached by the PI of the PC.

2) If consent to being re-contacted for future research with another purpose is not included in the informed consent document of the PC, local (national) legislation will determine whether or not participants can be approached.

a) In some jurisdictions (e.g. in the UK), **PIs should have consent for re-contact in place** before they may approach research participants in the PC for other research for other purposes. In those jurisdictions, the following modes of action are recommended:

- It is the responsibility of the PI of the PC to obtain ethical approval from a local ethics committee to approach research participants for consent to being re-contacted for future research for other purposes (by amendment of protocol).
- If ethical approval from the ethics board is in place, the PI of the PC can approach eligible participants to ask consent to be re-contacted for future research for other purposes.
- Subsequently, the PI of the PC approaches eligible participants who have consented to being re-contacted with information materials about EPAD in general and asks to participate in the EPAD LCS. Participants will 'opt in' and actively contact an EPAD TDC.

b) In other jurisdictions (e.g. the Netherlands), **PIs can re-contact their own participants** about other research projects when no arrangements for re-contact have been made in the informed consent of the PC. It is the responsibility of the EPAD National Lead to determine whether national legislation allows for the re-contacting of participants for participation in EPAD in the absence of prior consent for re-contact arrangements in the informed consent document of the PC. Mode of action recommended:

- Eligible participants are approached by the PI of the PC with information materials about EPAD in general and are asked to participate in the EPAD LCS. Participants will 'opt in' and actively contact an EPAD TDC.

4. PARENT COHORT ACCESS TO EPAD DATA

The EPAD project will draw on the prior effort of researchers and participants in parent cohorts. However, it also intends to provide parent cohorts with data on these participants collected through the EPAD project, in accordance with the Project Agreement and the ASCA. The sharing of data between EPAD and the parent cohort requires some conditions to be in place. Most importantly, for data sharing to occur, participants must have been informed about it during the EPAD LCS consent process and given informed consent. However, as it is not an exclusion criteria for the LCS, it is included in the 'optional' consents.

This has potential advantages for both parent cohorts and participants. Firstly, it provides augmented data to cohorts. The more cohort participants take part in the EPAD LCS, the more additional data will be available to the parent cohort and the greater its value. However, conversely, having EPAD data on few participants may be of limited appeal.

For participants, the sharing of data between EPAD and the PC may make it possible to limit the number of investigations they take part in. Researchers should make efforts to minimise the burden on participants, particularly where the same researchers are involved in both EPAD and the PC. If certain data are collected in the context of either EPAD or the PC, and a test has been conducted within EPAD within the timeframe expected for the PC, reasonable efforts should be made to avoid the unnecessary duplication of testing. This will require data to be made available to PCs during the EPAD project, rather than solely at its conclusion.

There are potential implications related to disclosure if EPAD provides information to parent cohorts that relates to Alzheimer's disease risk or dementia status or incidental findings. EPAD's approach to disclosure is discussed in more detail in D8.1. However, it should be clear to the parent cohort what, if anything, has been communicated to the participant within EPAD. Responsibility for decisions related to the subsequent disclosure or non-disclosure of these results by PC PIs rests with the parent cohort. However, EPAD should provide its policy on the return of results and incidental findings to facilitate consistency.