Publishable Summary of the Part I: Prognostic Natural History Study (PNHS)

The AMYPAD project raises a number of important ethical issues, some of which are novel. This first part of this guidance document covers questions related to the AMYPAD Prognostic Natural History Study (PNHS) and its relation to the EPAD Longitudinal Cohort Study (LCS) and Proof of Concept trial (PoC). As a sub-study of EPAD, the AMYPAD-PNHS raises ethical issues that overlap to a great extent with the ethical issues that are raised in the EPAD-LCS. Recommendations stated here explicitly address specific ethical guidance on questions that relate to the AMYPAD-PNHS and not to the EPAD project as a whole. Background information on the ethical recommendations for the PNHS stated can be found in the EPAD guidance document (D8.1 'Initial ethics policy review and information governance framework', EPAD Grant Agreement number: 115736). **This document is meant *for guidance* and to support the development of study governance, protocols and ethics review submissions. It does not replace the need for ethical review procedures.**

This document identifies issues and sets out recommendations for the AMYPAD project in the following areas:

- The integration of informed consent for AMYPAD-PNHS into the EPAD project
- Return of results and disclosure of Alzheimer's disease risk
- The management of incidental findings
- The experience of participation in the AMYPAD-PNHS
- Data sharing and governance
- Continuity between the EPAD-LCS and the AMYPAD-PNHS.

Publishable Summary of the Part II: Diagnostic value of amyloid PET imaging in patients with cognitive decline where AD is a differential diagnosis

The second part of this document offers ethics policy and guidance for the diagnostic study of AMYPAD. Ethics guidance for the diagnostic study is presented separately from ethics guidance for the PNHS of AMYPAD (part I of this document), because the two studies raise different ethical issues. Unlike the PNHS, the diagnostic study of AMYPAD is embedded in the clinical setting of a memory clinic. Participants have sought medical counsel for their memory complaints, resulting in a syndromic 'diagnosis' of either SCD PLUS, MCI or dementia. Therefore, they may wish to learn about their biomarker status and, in some cases, will have a limited capacity to consent. Additional precautions apply to these participants since they are more vulnerable and may have limited decision-making capacities. The need to adopt special cautions in research involving individuals with compromised

capacity, particularly in non-therapeutic research, has been highlighted by most declarations and laws on research ethics. Legal requirements will differ in all countries involved in AMYPAD, starting with different local requirements for the consent procedure. Meeting these requirements is the responsibility of national leads and PIs of the TDC. **This document is meant *for guidance* and to support the development of study governance, protocols and ethics review submissions. It does not replace the need for ethical review procedures.**

This document identifies issues and sets out recommendations for the project in the following areas:

- Social value of the research objectives
- Risks and burdens of participation
- Informed consent
- Return of results
- The management of incidental findings
- The experience of participation
- Data sharing and governance.

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