www.ep-ad.org

European Prevention of Alzheimer's Dementia Consortium

Grant Agreement nº115736

D4.1 Report on standardisation and harmonisation of EPAD Trial Delivery Centres

WP4 – EPAD Cohort and EPAD Trials

V2.0

Final

Lead beneficiary: UEDIN
Date: 21/10/2015
Nature: Report
Dissemination level: Public (PU)

TABLE OF CONTENTS

DOCUMENT INFORMATION

Grant Agreement Number	115736	**Acronym**	EPAD
Full title	Prevention of Alzheimer's Dementia Consortium		
Project URL	www.ep-ad.org		
IMI Project officer	Elisabetta Vaudano (elisabetta.vaudano@imi.europa.eu)		

Deliverable	D4.1	**Title**	Report on standardisation and harmonisation of EPAD Trial Delivery Centres
Work package	WP4	**Title**	EPAD Cohort and EPAD Trials

Delivery date	**Contractual**	Month 9	**Actual**	21/10/2015	
Status	Current version / V2.0		Draft ☐ Final ✓		
Nature	Report ✓ Prototype ☐ Other ☐				
Dissemination Level	Public ✓ Confidential ☐ Other ☐				

Authors (Partner)	UEDIN, Janssen, KI, BI + WP4 contributors			
Responsible Author	Craig Ritchie		**Email**	Craig.ritchie@ed.ac.uk
	Partner	UEDIN	**Phone**	+44 131 537 6264

Description of the deliverable	This deliverable will report on the activities undertaken to select and harmonise EPAD TDCs in preparation for the Cohort and Trial
Key words	TDCs, Certification, LCS, PoC

DOCUMENT HISTORY

NAME	DATE	VERSION	DESCRIPTION
Craig Ritchie, Judith Syson	07.08.2015	1.0	First draft
Craig Ritchie, Judith Syson	28.08.2015	1.2	Internal review completed
Judith Syson, WG4.1	14.09.2015	1.3	Additional changes post WG1 meeting
Sean Knox, David Ruvolo, Shirlene Badger	12.10.2015	1.4	Incorporated reviewers comments
Judith Syson	21.10.2015	2.0	Final version

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.** Barcelona Beta 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.** 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)
- **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.

GLOSSARY

- **ACCORD –** Academic & Clinical Central Office for Research & Development
- **CSMO –** Chief Sponsor Medical Officer
- **LCS –** Longitudinal Cohort Study
- **PI –** Principal Investigator
- **SPOC –** Single Point of Contact
- **TDC –** Trial Delivery Centre

EXECUTIVE SUMMARY

The University of Edinburgh will lead the Trial Delivery Centre (TDC) Certification process. The standards required will be based on accepted Clinical Trial standards and applicable regulations based on Good Clinical Practice. In addition the technical certification of staff qualification and equipment will be assessed based on the requirements of the EPAD protocols. Finally, the TDC and the EPAD representatives will ensure that the TDC Certification process is a key element of building the community of professionals contributing to EPAD as a cohesive and productive "family".

1. INTRODUCTION

This document presents the EPAD Trial Delivery Centre (TDC) Certification process. The aim of TDC Certification is to ensure delivery, quality and fidelity to the aims of EPAD. In addition the process will ensure compliance with applicable regulations and standards including but not limited to Good Clinical Practice.

The development of this process focused on TDCs satisfying specific criteria in 4 domains:

[1] Access and proximity to research participants from parent cohorts,

[2] Availability of physical and human infrastructure,

[3] Track record of success in Alzheimer's disease trials and

[4] Acceptance of the EPAD TDC Contract, which includes the EPAD Cohort Replenishment Policy.

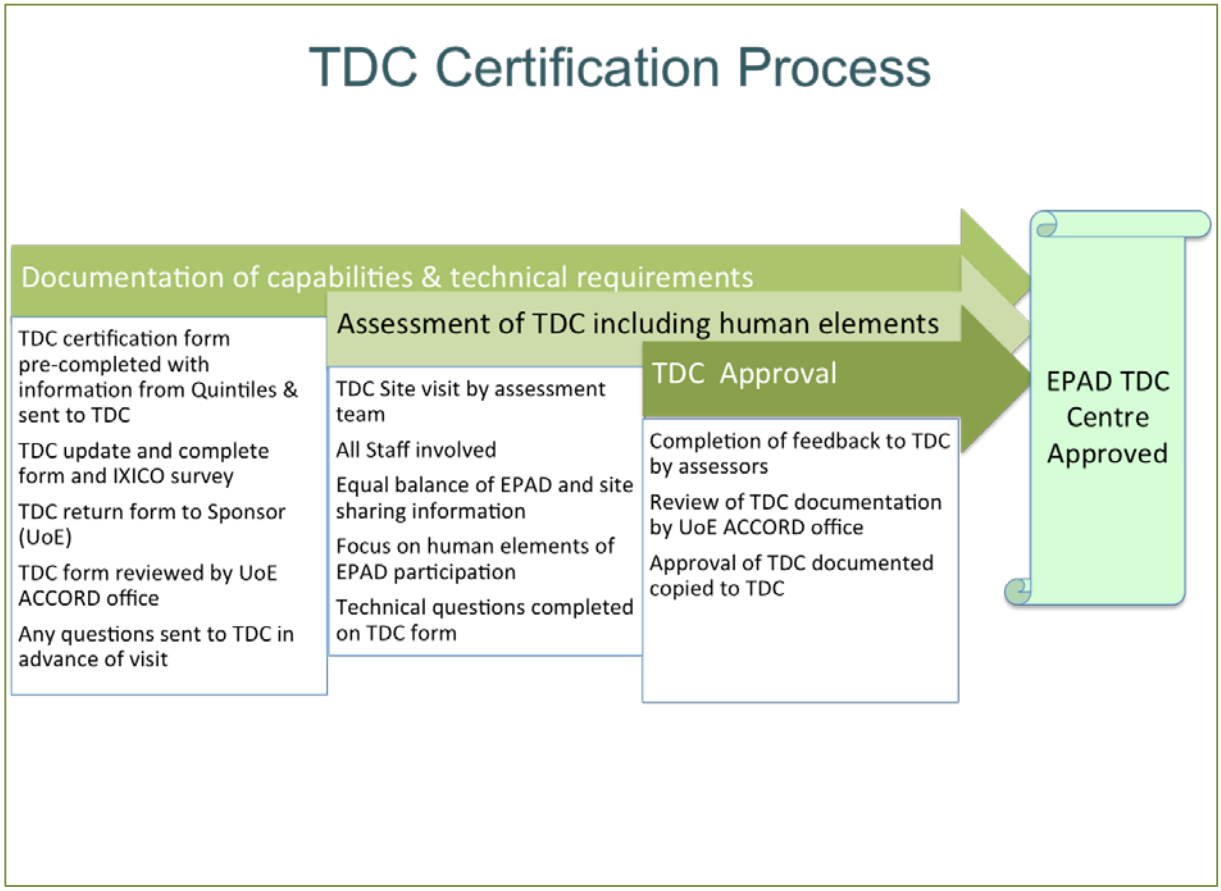
A 5th domain of the "human" engagement was added to ensure that the ethos of the EPAD family was clearly represented in the TDC certification process.

This document will detail the process and the documentation to record the TDC certification and approval to participate in EPAD.

2. TDC Certification Process

2.1. Three steps to TDC Certification

The pathway is summarised by the diagram shown below:



2.1.1. Pre-visit processes (6 weeks prior to the TDC certification visit)

These tasks will be undertaken during the 6-8 weeks prior to the TDC visit.

The TDC will be contacted and a link established between the EPAD Administrator (or delegate) and the nominated TDC Single Point of Contact (SPOC) supporting the Certification process. The TDC Certification team will include a representative of the Chief Sponsor Medical Officer (CSMO), the WP4 Leadership Team and can include representatives from the lead EFPIA Company (Janssen), the CRO Partner (Quintiles) and where appropriate the National Leader for the region. A mutually convenient date for the TDC Certification Visit (the Visit) will be arranged by the EPAD Administrator and confirmed by email/meeting invitation.

The EPAD Administrator will liaise with the designated Quintiles representative to facilitate the pre-completion of the TDC Certification Form from information held on the Quintiles site database. The TDC Certification Form is attached in Annex 1.

The EPAD Administrator will send the pre-completed form to the TDC SPOC, at least 4 weeks prior to the Visit.

In parallel, the EPAD Administrator will provide IXICO with the contact details of the TDC SPOC and the relevant TDC Imaging Team. IXICO will send the TDC imaging team the IXICO Imaging Survey. IXICO will work directly with the TDC Imaging Team to complete the Survey. The urvey will be returned to IXICO who will review the detail and resolve any issues with the TDC. Once IXICO can confirm that the TDC meets the imaging requirements the completed form will be sent to the EPAD Administrator to be included in the TDC Certification Documents.

The IXICO Imaging Survey documentation is attached in Annex 1.

The TDC SPOC will work with the Principal Investigator and other relevant staff to ensure the TDC form is completed. The completed TDC form will be returned to the EPAD Administrator who will circulate to the Sponsor representatives from The University of Edinburgh & NHS Lothian; The Academic & Clinical Central Office for Research & Development (ACCORD) and Chief Sponsor Medical Officer (CSMO); at least 2 weeks prior to the Visit.

The Sponsor representatives will review the information provided and list any questions and/or comments for resolution/discussion at the TDC Certification Visit. A copy of any questions/comments will be send to the TDC SPOC at least 1 week prior to the Visit.

The TDC representative will ensure that all relevant staff members, including researchers where available from Parent Cohorts, are prepared for the Visit.

2.1.2. Assessment of TDC & Human Elements

There are two main objectives for the TDC visit:

- Sponsor certification of the TDC according to EPAD requirements and applicable standards and regulations,
- To engage all participants at the TDC in the EPAD family and foster long term working relationships in the ethos of the EPAD project.

The TDC assessment will be led by the CSMO – with support from the leadership of EPAD WP4. The CSMO may appoint a delegate from WP4 to lead the TDC certification visit and report back to the CSMO. Other members of the TDC certification team can include representatives from the lead EFPIA Company (Janssen), the CRO Partner (Quintiles) and the National Leader for the region.

The TDC Principal Investigator (PI) will ensure that all relevant site staff members are appropriately engaged in the Visit.

The agenda will be the responsibility by the TDC PI and TDC SPOC who will arrange the agenda to suit the site and travel arrangements of the visitors. The template agenda is attached in Appendix 2.

The agenda should reflect an equal balance of time for EPAD and TDC sharing information so that all those involved come to a common understanding of the requirements of EPAD and how the TDC meets these requirements. Time will be allowed for informal interactions to facilitate the human elements of engagement in the EPAD family.

The TDC PI and the CSMO (or delegate) will ensure that the technical elements of the TDC certification requirements and any outstanding questions from the visit preparation are completed during the Visit.

2.1.3. TDC approval & follow-up activities

The TDC visit will be completed with feedback to the TDC PI from the EPAD CSMO to summarise the assessment. The WP4 representative will complete a report of the visit recording the assessment of the Visit.

The TDC certification documents; the TDC Certification Form, the completed IXICO Survey and the TDC Visit report; will be collated by the EPAD Administrator. The CSMO and the ACCORD office will review the certification documents.

The CSMO and the TDC PI will resolve any questions.

ACCORD will certify that the TDC has met the required elements as an EPAD TDC. The TDC PI will be informed. The EPAD Administrator will file the original signed copies of the certification documents in the Trial Master File and send a copy to the TDC.

2.2. Management of changes at TDCs

Changes that materially impact of the conduct of the EPAD trials at the TDC will be notified to the CSMO by the TDC PI, e.g. key staff changes, new imaging facilities, significant changes in study conduct facilities. Any additional changes identified by the CRO Partner during monitoring visits will be highlighted to the PI for review and communication as appropriate. The CSMO will review these changes with the ACCORD office and if require a further TDC certification visit will be undertaken to ensure EPAD standards are maintained.

2.3. Documentation of TDC Certification

2.3.1. TDC Form – to be attached in Annex 1

2.3.2. Approved signatories

EPAD CSMO

ACCORD

2.3.3. Document management

The completed TDC form and IXICO imaging assessment forms will be file in the Trial Master file by the EPAD Administrator

2.3.4. Documentation of changes at TDC

Any material changes will be documented by a Note to File in the Trial Master File or a TDC certification visit form if required.

ANNEXES

Annex I. TDC Certification Documents

These forms will be updated and maintained to reflect the details of the EPAD Longitudinal Cohort Study and the EPAD Proof of Concept Study.

Trial Delivery Centre (TDC) Assessment Form

1. Study Staff Qualifications & Experience

1.1 Staff suitability

Title	**Forename:** Click here to enter text.	**Surname**: Click here to enter text.
Institute and Department Name: Click here to enter text.		
Address (Line 1): Click here to enter text.		
Address (Line 2): Click here to enter text.		
Town/City: Click here to enter text.	**County/Region:** Click here to enter text.	
Country: Click here to enter text.	**Postcode:** Click here to enter text.	
Phone: Click here to enter text.	**Mobile:** Click here to enter text.	**Fax:** Click here to enter text.
Email: Click here to enter text.		
Setting		
Medical Speciality of the Principal Investigator at your site: ☐ Psychiatry ☐ Neurology ☐ Geriatric Medicine ☐ Other (Specify): Click here to enter text.		

Role	Name	Phone	Email	Number of other relevant studies in which this person is involved	% Time dedicated to EPAD
Study Coordinator					
Study Coordinator					
Sub-Investigator					
Sub-Investigator					
Lead Neuropsychologist					
Clinical Trial Pharmacist					
Medical Physicist					
MRI Center Primary Contact					
PET Center Primary Contact					
Other (please specify) Click here to enter text.					
Other (please specify) Click here to enter text.					

Cognitive Rater Name		Phone	Email	How long working as a Cognitive Rater?	
				Total	At site
1.					
2.					
3.					
4.					

What clinical trial experience relevant to EPAD do you (Principal Investigator) have? Please comment on whether these were registration trials for submission to health authorities and whether they were single-centre or multi-centre trials.	
Phase II	Click here to enter text.
Phase III	Click here to enter text.
What experience do you have of observational studies in this subject population?	
Click here to enter text.	

1.2 GCP Knowledge and Certification

	Yes	**No**
Has your institution/practice ever been inspected by a local Regulatory Agency or FDA?	☐	☐
If you have been inspected, have all findings been resolved?	☐	☐
Are the investigator & research staff GCP certified within the last 2 years?	☐	☐
Please give a description of GCP training and how certification is maintained. Click here to enter text.		

2. Facilities, Equipment and Processes

2.1 Clinical and Rating Scale Assessment

Who at your TDC (Investigator; Clinical Rater/Psychometrician/Neuropsychologist) has experience of administering and scoring the following instruments/scales?

Scales	Experience		Any current certification? By whom?	Proposed rater name
	Yes	No		
Eriksen Flanker Task (NIH EXAMINER/Toolbox)	☐	☐		
Coding Test (RBANS)	☐	☐		
List Learning (RBANS)	☐	☐		

Story Memory (RBANS)	☐	☐		
Figure Copy task (RBANS)	☐	☐		
Line Orientation task (RBANS)	☐	☐		
Picture Naming task (RBANS)	☐	☐		
Semantic Fluency task (RBANS)	☐	☐		
Digit Span test (RBANS)	☐	☐		
Dot Counting task (NIH Examiner)	☐	☐		
Four Mountains Task (Cambridge Cognitive Neurosciences)	☐	☐		
Face Name Associative Memory task (UCSF)	☐	☐		
Virtual Reality Supermarket Trolley (University College London)	☐	☐		
Clinical Dementia Rating Scale (CDR)	☐	☐		
Mini-Mental Status Exam (MMSE)	☐	☐		
Geriatric Depression Scale (GDS)	☐	☐		

	Yes	**No**
Does your site have a minimum of 2 raters that can be blinded for this study?	☐	☐
Could your site ensure at a minimum the CDR rater remained blinded to other assessments?	☐	☐
Does your site have a dedicated area available suitable for conducting rating scales?	☐	☐
Would your site be willing to conduct neurocognitive assessments on an electronic device?	☐	☐

Describe your source document filing and storage of paper and electronic records
Click here to enter text.

Describe how your electronic medical records comply with regulatory requirements

Click here to enter text.

Describe your biological sample collection & processing:

Click here to enter text.

Do you have access to:	**Yes**	**No**
Freezer that stores at -20ºC	☐	☐
Freezer that stores at -70ºC	☐	☐
Dry ice	☐	☐
Centrifuge	☐	☐
Refrigerated Centrifuge	☐	☐
A refrigerator (2ºC - 8ºC or 36ºF - 46ºF) in a secure area with an alarm and limited access that can be locked to be used to store the investigational product?	☐	☐

Equipment required for biological sample processing and storage (short and long term)

Equipment	**Monitoring**	**Back-up**

Note: Requirements to be defined by the LCS and PoC Study laboratory manuals.

Incidental findings

Describe how incidental findings are managed in your TDC

Click here to enter text.

2.2 Lumbar Puncture and CSF samples

Is LP part of routine diagnostic procedures in your department / clinic?	☐ Yes	☐ No
Who would perform LPs at your site?	Select Click here to enter text.	
In the past 5 years, how many studies involving collection of CSF have you undertaken?		
For the CSF studies, was LP (CSF collection) an optional sub-study component or mandatory study procedure?	☐ OPTIONAL ☐ MANDATORY	
If optional, how many patients were you able to consent for the LP/CSF substudy?	Click here to enter text.	
What techniques so you use to help subjects understand the CSF collection process?		
Click here to enter text.		
What is the maximum CSF volume per LP that you would collect / are comfortable or allowed to collect per institutional policy?	☐ 5mL ☐ 10mL ☐ 15mL ☐ 20mL ☐ Other: Click here to enter text.	
What percentage of patients who are approached about this study do you feel would be willing to have a lumbar puncture as part of study procedure?	☐ <25% ☐ 26-50% ☐ 51-75% ☐ 76-100%	

2.3 Imaging (*this topic is covered by the IXICO survey)*

IXICO Survey		
Survey completed	☐ Yes	☐ No
When Survey is completed the TDC certification form notes will be completed with confirmation that the TDC has appropriate experience and facilities for the Imaging requirements		

2.4 ECG

Describe the ECG technique and equipment at your TDC		
Click here to enter text.		
Do you have access to 12 lead ECG?	Yes ☐	No ☐

	List Role
ECG Technician	
ECG Review	

2.5 IT Infrastructure

Do you have access to:	**Yes**	**No**
Fax Machine in clinic area (with ISD – International Standard Dialling)	☐	☐
Telephone in clinic area (with ISD – International Standard Dialling)	☐	☐
Internet access	☐	☐
Do you have a computer at your site that you could use for completing CRF's, and study-related documents online?	☐	☐
Comments: Click here to enter text.		
Would there be any issues connecting the neurocognitive assessment electronic capture device to the internet at your site?	Yes ☐	No ☐
If yes, please explain what support might be needed: Click here to enter text.		

2.6 Pharmacy

	Yes	No
Does your site have a resource that would allow for a blinded pharmacist to prepare study medication?	☐	☐
How many days/week is there a pharmacist available?		
How many hours/day is there a pharmacist available?		
Please describe your experience with the medications used in adaptive design trials and with IVRS systems		
Click here to enter text.		
Describe your pharmacy record keeping and study documentation		
Click here to enter text.		
Pharmacy IMP and storage facilities		
Click here to enter text.		
Pharmacy facilities for sterile IMP preparation		
Click here to enter text.		

2.7 Archiving

Describe your protected and secure archiving facilities
Click here to enter text.

2.8 Standard Operating Procedures

List the SOPs at your TDC relevant to EPAD participation
Click here to enter text.

Describe your SOP maintenance and training procedures
Click here to enter text.

2.9 Clinical Research Quality Management

Describe your audit and inspection experience and outcomes
Click here to enter text.
Describe the management of source documents, data entry and query management, use of IWRS/IVRS at your TDC
Click here to enter text.
What is the availability of staff for quality control activities at your TDC?
Click here to enter text.
What is the Availability of staff for audit and inspection activities at your TDC?
Click here to enter text.

3. Parent Cohort Links and EPAD

What Parent Cohorts will you be linked to?

Name of Cohort	Name of PI	Description of Cohort

4. Developing and Maintain the EPAD participant engagement

Please describe the plans in your TDC for developing and maintaining individual and group engagement of EPAD participants and their study partners in EPAD activities
Click here to enter text.

5. Research Environment

Insurance: Are there any site-specific indemnification requirements?	Yes ☐	No ☐
If **Yes** please specify: Click here to enter text.		
What language translations would your site require for this study?		
Click here to enter text.		

Ethics Committee

Describe the Ethics Committee processes and timelines at your TDC
Click here to enter text.
What patient group/lay person membership does your EC have?
Click here to enter text.
What experience does you TDC have of observational protocols?
Click here to enter text.
What experience does your TDC have of master and appendix protocols?
Click here to enter text.

5.2 Other authorities required to give approval for TDC participation

Are there any other processes and timelines required for TDC participation?	Yes ☐	No ☐
If **Yes** please specify: Click here to enter text.		

5.3 Institution research environment

What are the funding sources for staff in your TDC?
Click here to enter text.
How do your approach recruitment and retention for replacement staff?
Click here to enter text.

6. Contractual Environment

Research/Institution Engagement

Describe the parties involved, roles and responsibilities in R&D approval at your TDC?
Click here to enter text.

Describe the engagement and maintenance of agreements with:
Imaging: Click here to enter text.
Pharmacy: Click here to enter text.
Biological sample handling: Click here to enter text.
Specialists for lumbar puncture: Click here to enter text.
Emergency unit: Click here to enter text.
Other facility/equipment providers: Click here to enter text.

Describe the process and timelines for negotiation of agreements
Click here to enter text.

Explain the management of funds between parties
Click here to enter text.

Name & email of person completing this form (contact for questions):	
Name: Click here to enter text.	**Email**: Click here to enter text.
Date: Click here to enter a date.	

EPAD MRI Site Survey

IXICO has been contracted to conduct the imaging setup and data analyses on the **EPAD project for the longitudinal cohort**. This project aims to develop an infrastructure that efficiently enables the undertaking of adaptive, multi-arm Proof of Concept studies for early and accurate decisions on the ongoing development of drug candidates or drug combinations in Alzheimer's disease. This includes evaluating patients' reactions to a drug early in a clinical trial and modifying the trial according to these reactions.

The purpose of this document is to assess your site's ability to meet the MRI imaging needs of this project and to allow IXICO to tailor the training and ongoing support appropriately.

The project is estimated to run for **5 years** (from 2016 - 2021).

According to the clinical protocol version ******, subjects consented for participation will be imaged under:

- Volumetric MRI (vMRI)
- Resting State functional MRI (rs-fMRI) (subset of subjects)
- Diffusion Tensor Imaging (DTI) (subset of subjects)
- Arterial Spin Labelling (ASL)

Our minimum requirement is a **3T MRI scanner** able to run the above sequences.

Does your site have the appropriate hardware, software and expertise to contribute to this study?

☐ Yes ☐ No

If No, please comment in the space provided below and send this page back to IXICO:

If Yes, please help us by completing this form with as much detail as possible and send it back to IXICO as soon as possible. We will then review your answers and be in touch shortly.

For your information, we will be looking to perform the following steps to **qualify** your imaging centre prior to the first subject visit.

- Typically one scanner will be qualified per site and the same scanner should be used to scan all subjects across all time-points at your site.
- IXICO will provide the scan parameters tailored to your scanner to enable the scanner set-up.
- IXICO will provide an imaging manual to cover study overview including imaging expectations (e.g. scanning protocol, data transfer, query management).
- Phantom scanning(s) with the approved imaging protocol, to ensure the protocol has been set up correctly and no image quality issues exist.
- IXICO will conduct a remote Webex training session. We request the MRI technologist/radiographer, physicist and study co-ordinator to be available for this meeting, as a minimum.

NOTE: Please enter N/A if a section is Not Applicable. Provide additional information, where appropriate. Please select all options that apply, in case of multiple possible answers.

Please complete this form with as much detail as possible and please scan/fax the signed form back to ***********@ixico.com/+44 ***************

Thank you for your help and cooperation!

1. Basic Information

Please input the contact information for all relevant personnel at the site. If anyone serves more than one role, or if multiple people are accessible at the same address, the address information does not need to be repeated.

1.1 Site Details

Site Name:	
Address :	
City:	
State/Province:	
Zip/Postal Code:	
Country:	

1.2 Principal Investigator contact details

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.3 Study Coordinator contact details

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.4 MRI personnel contact details

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.5 MRI Pysicist contact details

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.6 IT/System Administration contact details

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.7 Who will serve as the primary contact for this study for technical questions?

☐ Study Coordinator ☐ Physicist ☐ MR Department ☐ Radiologist

☐ Other, please provide their contact details and role at your imaging site:

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.8 Who will serve as the primary contact for this study for administrative questions?

☐ Study Coordinator ☐ Physicist ☐ MR Department ☐ Radiologist

☐ IT/System Administration ☐ Other, please provide their contact details and role at your site:

Name:	
Role:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

2. Experience Levels

2.1 Does your site have previous experience with clinical trials involving patients with Alzheimer's Disease, specifically projects involving MRI?

☐ Yes ☐ No

2.2 Confirm your site's previous experience in:

☐ Volumetric MRI (vMRI) ☐ Resting State Functional MRI (rs-fMRI) ☐ Diffusion Tensor Imaging (DTI)

☐ Arterial Spin Labelling (ASL)

If you checked any of the above please provide details:

2.3 Details of MRI technologists that will be involved in the study:

How many MRI technologists will be involved in this study?			
Details	**Tech 1**	**Tech 2**	**Tech 3**
Name			
Email			
Phone number			
Lead? (Yes/No)			
Back-up? (Yes/No)			
Years of experience scanning for clinical trials			
Board certification? If no, please detail experience with operating MR scanners			

3. MRI Scanner Information

3.1 MRI Scanner details

This study requires the use of a 3.0 Tesla MRI Scanner with the necessary associated equipment and software packages for performing vMRI, rs-fMRI, DTI and ASL. Please confirm you are able to provide access to such an MRI Scanner.

Key Information	Specifics
Access to the same 3T MRI Scanner throughout study duration:	☐ Yes ☐ No If No, provide details under 3.3, as applicable
MRI scanner Manufacturer:	☐ Philips ☐ Siemens ☐ GE
MRI Scanner Model Name (e.g. Achieva, Signa, Symphony):	
Software Version:	
Head coil type:	
Number of channels (if you have multiple headcoils available, please list them all):	
Age of scanner, years	

Additional Information	Specifics	
Diffusion Tensor Imaging		
How many diffusion directions do you normally apply?		
Is there a limit to the number of directions that can be applied?		
Is is possible to apply 41 directions?	☐ Yes	☐ No
Is is possible to apply 64 directions?	☐ Yes	☐ No
Do you have a research agreement or science key already in place with the scanner manufacturer/ vendor?	☐ Yes Details:	☐ No

3.2 Location of the MRI Scanner (i.e. room/department/building within hospital, or distance from the hospital if off-site separate location)

3.3 Please indicate if any of the following events are planned or anticipated for this MRI scanner for the timescale of this study:

☐ Software Upgrade ☐ Hardware Upgrade (e.g. head coils, gradients) ☐ Relocation of MRI Scanner

☐ MRI scanner going offline (permanently or temporary)

If you checked any of the above please provide details:

3.4 If you have more than one suitable 3T scanner, please describe.

3.5 How much lead time is required to schedule study scans (including phantom scans)?

3.6 Do you have/can you get the ASL software installed?

If yes, is this ASL acquisition software approved for use on patients, or is it a "work in progress" or R&D sequence?

4. Data Management information

4.1 Please provide a brief description of the long term MRI image archiving procedure

(PACS, proprietary media, long term tape archive, etc.). Please include the length of time that images are stored in the archive for Clinical Trials.

4.2 Data de-identification and export from MRI Scanner

Please provide a brief description of your standard procedure for data de-identification, exporting DICOM data from the MRI Scanner (e.g. burn CD, send directly to PACS etc.) and coordination of patient data with clinical sites.

4.3 Are you able to transfer data from your site electronically?

☐Yes ☐No

(IXICO's preferred method of data transfer is through an online **Site Interface** to Trial*Tracker*™, a web-based JAVA run platform. Other option for data transfer is SFTP. CD contingeny may be explored if either of the above are not feasible)

If No, Please specify the reason you do not use electronic transfer:

☐ Firewall issues

☐ Hospital Regulations

☐ Previous issues with electronic transfer

☐ Other, Please specify ……

If you answered Yes to 4.3,

Do you have regular access to a computer with internet access which you are able to use for electronic data transfer?

☐Yes ☐No

Do you have Java version, 6.0 or above, installed on the computer that you intend using for data transfer?

☐Yes ☐No

5. Phantom Information and Sequence Testing, including QA processes

5.1 Do you have a local Manufacturer's phantom available?

☐ Yes ☐ No

Please list all the other MRI imaging phantoms available for MRI scanning.

Provide details of phantoms you use for testing structural MRI sequences and if you use any phantoms (including in-house built) for testing vMRI, rs-fMRI, DTI & ASL.

5.2 Please state how often the following QA procedures are performed and what phantom is used to perform them.

QA Procedure	Frequency	Method (phantom)	QA Specification (manufacturer or local spec.)
SNR measurements on head, neck and/ or spine coil			
MRI scanning geometry phantom			
Gradient calibration (linear)			
Gradient calibration (non-linear)			
B0 uniformity			
Centre frequency drift			
EPI ghosting level			
EPI Stability			
Diffusion data quality			
fMRI data quality			
ASL data quality			

If you answered 'Local Specification' to any of the QA procedures in the table above, please specify the details of your local specification below.

5.3 If you have other QA Procedures not listed in the table above, please provide details below.

5.4 What action is taken in the event of a QA breach?

e.g. contacting system engineer

6. Questionnaire follow-up contact details

Who has been the person primarily responsible for completing this form?

Name:	
Signature:	
Date:	

If not already entered in the previous sections:

Name:	
Job Title:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

Please fax back to IXICO at ************* or email to *******@ixico.com.**

If you have any questions please feel free to contact IXICO either by telephone at +44 20 3763 7495, fax or e-mail as shown above.

Thank you for completing this survey. We will be in contact with you concerning further information and instructions related to this study.

EPAD PET Site Survey

IXICO has been contracted to conduct the imaging setup and data analyses on the **EPAD project for the longitudinal cohort.** This project aims to develop an infrastructure that efficiently enables the undertaking of adaptive, multi-arm Proof of Concept studies for early and accurate decisions on the ongoing development of drug candidates or drug combinations in Alzheimer's disease. This includes evaluating patients' reactions to a drug early in a clinical trial and modifying the trial according to these reactions.

The purpose of this document is to assess your site's ability to meet the PET imaging needs of this project and to allow IXICO to tailor the training and ongoing support appropriately.

According to the clinical protocol version ******, subjects consented for participation will be imaged under:

- Amyloid PET
- Dynamic early frame amyloid PET (subset of subjects)

For your information, we will be looking to perform the following steps to **qualify** your imaging centre prior to the first subject visit.

- Typically one scanner will be qualified per site and the same scanner should be used to scan all subjects across all time-points at your site.
- IXICO will provide the scan parameters tailored to your scanner to enable the scanner set-up.
- IXICO will provide an imaging manual to cover study overview including imaging expectations (e.g. scanning protocol, data transfer, query management).
- Phantom scanning(s) with the approved imaging protocol, to ensure the protocol has been set up correctly and no image quality issues exist.
- IXICO will conduct a remote Webex training session. We request the study coordinator, PET technologist, PET physicist and Nuclear Medicine Physician to be available for this meeting, as a minimum.

NOTE: Please enter N/A if a section is Not Applicable and provide additional information, where appropriate. Please select all options that apply, in case of multiple possible answers.

Please complete this survey with as much detail as possible and please scan/fax the completed form back to **********@ixico.com/+44 **********.

Thank you for your help and cooperation!

1. Basic Information

Please input the contact information for all relevant personnel at the site. If anyone serves more than one role, or if multiple people are accessible at the same address, the address information does not need to be repeated.

1.1 Site Details (please refer to MRI survey section 1.1)

Site Name:	
Address :	
City:	
State/Province:	
Zip/Postal Code:	
Country:	

1.2 Principal Investigator Details (please refer to MRI survey section 1.2)

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.3 Study Coordinator Details (please refer to MRI survey section 1.3)

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.4 Lead PET Technologist Details

Name:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.5 PET Physicist Details

Name:	
Job Title:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different from above):	
Experience performing PET imaging	..... Years
Experience with clinical research studies	☐ Yes ☐ No ..... Years
License/Certification?	☐ Yes ☐ No Please provide details:

1.6 Nuclear Medicine Physician Department Details

Name:	
Job Title:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different from above):	
Experience performing PET imaging	..... Years
Experience with clinical research studies	☐ Yes ☐ No ..... Years
License/Certification?	☐ Yes ☐ No Please provide details:

1.7 Primary contact for Image Acquisition and Image Quality

If 'Other' is selected, then this person should also attend the training session

☐ PET Technologist ☐ PET Physicist ☐ Nuclear Medicine Physician

☐ Other, please provide their contact details and role at your site:

Name:	
Role:	
E-mail:	
Phone Number:	

Fax Number:	
Address (if different than above):	

1.8 Primary contact for technical questions (i.e. data transfer/IT)

If 'Other' is selected, then this person should also attend the training session

☐ PET Technologist ☐ PET Physicist ☐ Nuclear Medicine Physician

☐ Other, please provide their contact details and role at your site:

Name:	
Role:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

1.9 Primary contact for administrative questions

If 'Other' is selected, then this person should also attend the training session

☐ PET Technologist ☐ PET Physicist ☐ Nuclear Medicine Physician

☐ Other, please provide their contact details and role at your site:

Name:	
Role:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

2. Experience Levels

2.1 Does your site have previous experience with clinical trials involving patients with Alzheimer's Disease, specifically projects involving PET?

☐ Yes ☐ No

2.2 Confirm your site's previous experience in:

☐ Amyloid PET ☐ Dynamic early frame amyloid PET

If you checked any of the above please provide details:

2.3 Details of PET technologists that will be involved in the study

How many PET technologists will be involved in this study?			
Details	**Tech 1**	**Tech 2**	**Tech 3**
Name			
Email			
Phone number			
Lead? (Yes/No)			
Back-up? (Yes/No)			
Years of experience peforming PET imaging			
Years experience with clinical research studies			
License/Certification? If no, please detail experience with operating PET scanners			

3. PET Scanner Information

3.1 Please list any site accreditations you have for PET (e.g. ACR, EARL)

3.2 PET Scanner details

Note: Please only provide details of the scanner proposed for use in the study.

Type of scanner	☐ PET	☐ PET-CT	
PET Scanner Make	☐ Philips	☐ Siemens	☐ GE
Model of the scanner and year of installation			
Scanner Software Version			
Date of last upgrade			
Please briefly describe what was upgraded			
Capability of list-mode	☐ Yes	☐ No	
Capability of dynamic scanning	☐ Yes	☐ No	
Capability for 3D data acquisition	☐ Yes	☐ No	

3.3 Please indicate if any of the following events are planned or anticipated for this PET Scanner for the timescale of this study:

☐ Software Upgrade ☐ Firmware Upgrade ☐ Hardware Upgrade ☐ PET Scanner going offline
☐ Other, please specify .....

If you checked any of the above please provide details:

3.4 How much lead time is required to schedule study scans?

4. Phantom Information and Sequence Testing

4.1 Please check which of these phantoms you have available for scanning

☐ NEMA ☐ Hoffman 3-D Brain

4.2 Please list all other phantoms that you use for routine scanner quality control

4.3 Please outline what QA processes for PET and CT are performed on a regular basis and how you document the results

PET	CT
Daily	
Weekly	
Montly	
Quaterly	
Yearly	
Other (please specify)	

If you have other QA Procedures not listed in the table above, please provide details below.

4.4 What action is taken in the event of a QA breach?

e.g. contacting system engineer

5. Data Management information

5.1 Please provide a brief description of the long term PET image archiving procedure

(PACS, proprietary media, long term tape archive, etc.). Please include the length of time that images are stored in the archive for Clinical Trials and whether there is the ability to archive raw data.

5.2 Data de-identification and export from PET Scanner

Please provide a brief description of your standard procedure for data de-identification, exporting DICOM data from the PET Scanner (e.g. burn CD, send directly to PACS etc.), and coordination of patient data with clinical sites.

5.3 Are you able to transfer data from your site electronically?

(IXICO's preferred method of data transfer is via Trial*Tracker*™, a web-based JAVA run platform)

☐Yes ☐No

If No, Please specify the reason you do not use electronic transfer:

☐ Firewall issues
☐ Hospital Regulations
☐ Previous issues with electronic transfer
☐ Other, Please specify ……

5.4 If you answered yes to 5.3, do you have regular access to a computer with internet access which you are able to use for electronic data transfer?

☐Yes ☐No

6. Preparation Procedures, Radiopharmaceutical Administration and Radioisotope Production

6.1 Briefly describe your preparation procedures for a radiopharmaceutical tracer

6.2 Briefly describe your procedures for quality control of dosing equipment

6.3 Briefly describe how you record time between the injection of a radiopharmaceutical and the beginning of emission scan

Please also confirm if you calibrate clocks between injection and scanner room or use a stop watch

6.4 Briefly describe how you assay the dosage of a radiopharmaceutical before and after injection

Please also confirm if re-assaying the dose after injection is done as standard procedure at your site

6.5 Indicate the source of radiopharmaceutical that you routinely use

☐ Produced on site ☐ Provided by a commercial supplier (Name and addres of commercial supplier): ……

7. Questionnaire follow-up contact details

Who has been the person primarily responsible for completing this form?

Name:	
Signature:	
Date:	

If not already entered in the previous sections:

Name:	
Job Title:	
E-mail:	
Phone Number:	
Fax Number:	
Address (if different than above):	

Please fax back to IXICO at ******** or email to *******@ixico.com.**

If you have any questions please feel free to contact IXICO either by telephone at +44 20 3763 7495, fax or e-mail as shown above.

Thank you for completing this survey. We will be in contact with you concerning further information and instructions related to this study.

Annex II. TDC site visit agenda – sample

EPAD Trial Delivery Centre Certification Meetings - Planning

Agenda

Dates	**TBA Sep/Oct/Nov 2015**
Time	**Day 1: 13:00-17:00** **Day 2: 8:30-13:00**
Attendees	**PI & TDC Centre Staff** **Miia Kivipelto or Craig Ritchie** **Judi Syson or Stefan Borg** **Mila Etropolski or Isabelle Coste** **Lynne Hughes or Andrea Morton-Moyes or local CRA**
Location	

Day 1		
Time	**Topic**	**Discussion lead**
13:00	**Welcome and Introduction**	
13:15	**Meeting with PIs**	**PI** **Miia Kivipelto or Craig Ritchie**
15:00	**Coffee break**	
15:15	**Facilities:** • **Clinics & Rating/EDC** • **Scanning (Brain Imaging)** • **Labs (Bloods & CSF & ECG recording)** • **Pharmacy**	
17:30	**Dinner with Key staff**	

Day 2		
Time	**Topic**	**Discussion lead**
8:30	**Intro to R and D organisation (Hospital/University administration)**	
10:00	**Coffee break**	
10:15	**Staff:** • **Raters/Cognitive testing** • **Physicians**	
11:30	**Discussion:** • **TDC Certification Requirements** • **EPAD Funding Engagement**	
13:00	**End of Meeting**	