2D BioPAD

Supple Graphene Bio-Platform for point-of-care early detection and monitoring of Alzheimer's Disease

Ethical Consideration Roadmap Self-Assessment

WP2 T2.4

Funded by the European Union

Purpose

The present Self-Assessment for the 2D-BioPAD offers a framework for Consortium partners to review the ethics of the project activities throughout the research cycle. The Self-Assessment must to cover all identified possible ethics issues identified for the 2D-BioPAD project's design, development/experimentation, and deployment phases. The Self-Assessment provides a timely means to identify ethical issues for the research conducted. The method does not resolve the ethical issues, however, strives to identify ethical risks and shape future discussions that enable prevention of ethical harms and improvement of ethics in project activities.

Responsibility

- The Self-Assessment is not intended to be performed by consortium members alone, but be performed as a group, discussed, and documented by each WP task leader representing different partners in the Consortium.
- WP/Task leaders are responsible to complete, and archive completed Self-Assessment form in the folder 2D-BioPAD SharePoint Site Ethical Deliverables.

Procedure

The Self-Assessment shall be read through and then completed with information regarding the name of the Organization, Country, WP task leader name, Work Package and Task numbers.

- Notes for the WP task leader:
    - All passages/text in italics and highlighted in grey are intended to support the WP Task leader during Self-Assessment preparation. These passages shall be deleted prior to delivery of the document so the Self-Assessment only comprises results of the Self-Assessment.
    - Where the answer is YES or NO, please tick NO if NOT APPLICABLE.
    - Where a specific document is requested to be kept on file and provided on request, please tick "Document available" check box if available.

Disclaimer

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1.1 Respondent of Self-Assessment

Organization	Country	WP/Task Leader		WP/Task	Date	Signature
				WP1 Needs, Requirements & System Architecture Co-Design		
			☐	**T1.3**:System Architecture co-design		
				WP2: Biomarkers binding and quantitative analysis		
			☐	**T2.1**: Identification, synthesis, and evaluation of aptamers for AD protein hallmarks		
			☐	**T2.2**: Optimization and functionalisation of aptamers		
			☐	**T2.3**: Synthesis and characterisation of magnetic nanoparticles as carriers and enablers		
			☒	**T2.4**: Functionalization of Conjugated MNPs/Aptamers/Biomarkers	1/4/2025	M. Angelakeris
				WP3: Graphene-based platform design and implementation		
			☐	**T3.1:** Functionalized graphene synthesis and ssDNA conjugation		
			☐	**T3.2:** Functionalized Janus Fluorographene synthesis and ssDNA conjugation		
			☐	**T3.3**: Fabrication and Testing of the Graphene-based Electrochemical biosensor		
			☐	**T3.4:** Fabrication and Testing of the Graphene-based FET biosensor		
			☐	**T3.5:** AI-based optimisation graphene/ssDNA – MNPs/Aptamer/Biomarker optimisation		
				WP4: 2D-BioPAD Device Development and System Integration		
			☐	**T4.1:** Advanced Microfluidics for Identifying Multiple Biomarkers		
			☐	**T4.2:** Intelligent decision support module & User Interfaces		

Organization	Country	WP/Task Leader		WP/Task	Date	Signature
			☐	**T4.3**: Casing prototyping and assembly of the 2D-BioPAD system		
			☐	**T4.4**: Integration, lab testing, and fine-tuning		
				WP5: Clinical Pilot Studies Design, Deployment, Evaluation & Validation		
			☐	**T5.1:** Pilot Studies' Deployment & Evaluation Design		
			☐	**T5.2:** Retrospective pilot study deployment and technical validation		
			☐	**T5.3:** Prospective pilot study deployment and clinical validation		
			☐	**T5.4:** Cross-regional pilot studies evaluation and validation		
				WP6: Dissemination, Communication & Exploitation		
			☐	**T6.1:** Dissemination and communication strategy, plan, and activities		
			☐	**T6.2**: Innovation management, exploitation, and sustainability		
			☐	**T6.5:** Networking & joint activities with relevant initiatives		

1.2 Public Good

Public Good: evaluation of potential Risks and Benefits of the project		YES	NO	Description
Is there potential for your work to be used to make decisions about individuals (e.g., as may be the case with predictive modelling projects) or to identify individuals?		☐	☒	
If **YES**	What ramifications may this have for these individuals?			
Is there potential for your work to be used to make decisions about, or to identify, particular groups or communities within society?		☐	☒	
If **YES**	What ramifications may this have for them?			
Are there any potential data gaps in your work that could lead to harm, stigmatisation or distress for individuals or groups who are under-represented in your analysis (i.e., those who may be missing from your data)?		☐	☒	
If **YES**	How could this be mitigated?			
Is there potential for harm, stigmatisation or distress for individuals or groups who are (a) included as data subjects in your project or (b) may be impacted as a result of the findings of the research (including		☐	☒	

Public Good: evaluation of potential Risks and Benefits of the project		YES	NO	Description
social, environmental, economic, physical or mental health impacts)?				
If **YES**	How can these risks be minimised?			
Is there potential for negative impacts for organisations who are (a) included as data subjects in your project or (b) may be impacted as a result of the findings of the research (including reputational impacts)?		☐	☒	
If **YES**	How can these risks be minimised?			
Is there potential for harm or distress to members of the research team, research facilitators, or other individuals involved in activities related to conducting the project?		☐	☒	
If **YES**	How can these risks be minimised?			
Are there specific envisaged public benefits of your work?		☒	☐	*Yes, conjugation of magnetic nanoparticles with aptamers and Alzheimer biomarkers hold significant promise in biomedical research and have the potential to offer several public benefit for Alzheimer's disease diagnosis may assist in early biomarker detection, Point-of-Care Testing (2D-BioPAD Objective & Deliverable) and personalized medicine approaches. By tailoring diagnostic tests to individual patients, clinicians can better assess disease progression, monitor treatment response, and optimize therapeutic strategies.*
If **YES**	How will you achieve these benefits?	*By evaluating protocols and sequences on different biomarkers to provide validation*		
Is there any evidence-base behind your justification of potential benefits?		☐	☒	*Please specify. See Pharmaceutics 2023, 15, 2316. https://doi.org/10.3390/pharmaceutics15092316*
If **YES**	Is it peer-reviewed?	*Yes*		
	How confident are you that these benefits will be realised?	*Quite confident since it is an emerging field attracting important scientific interest. In* www.scopus.com *"magnetic nanoparticles and Alzheimer" appear more in more than 700 publications with the score of more than 70/year for the last five years.*		
Are there any limitations in your project approach that may limit the impact of potential benefits?		☒	☐	Despite the beneficial role of MNPs in biomedical applications there are certain limitations in the use of magnetic nanoparticles (MNPs) for Alzheimer's disease (AD) that can affect the

Public Good: evaluation of potential Risks and Benefits of the project		YES	NO	Description
				impact and translation of their potential benefits. The proposed framework and methodology consider among others : 1. Blood–Brain Barrier (BBB) Penetration: Efficient and targeted delivery of magnetic nanoparticles across the BBB remains difficult. The BBB restricts most therapeutic agents and nanoparticles from reaching brain tissue, limiting their efficacy. Workarounds being explored: Surface modifications (e.g., PEGylation, antibody-functionalization) or using external magnetic fields to guide MNPs. 2. Toxicity and Biocompatibility: Long-term safety of MNPs in the brain is not fully understood. Accumulation in organs (liver, spleen), Oxidative stress or inflammation in neural tissue, Iron metabolism disruption. We are exploring comprehensive in vivo toxicity and clearance assessments. 3. Standardization and Reproducibility: Variability in synthesis methods leads to inconsistencies in particle size, shape, surface charge, and coating. These properties influence distribution, targeting ability, and toxicity. We proposed Development of standardized, scalable manufacturing protocols.
If **YES**	What are these and how have they been minimised?	*Please specify.*		
Is the work focused on enhancing trust in statistics or statistics producers (e.g., challenging or validating official statistics)?		☒	☐	Our proiect clearly explains methodology and data sources, since sources of data (e.g., experimental results, simulations) are clearly described and proposed methodologies are reproducible. Our project applies proper statistical techniques rigorously (Quality), with respect to data integrity and sample size & cross-validation.
If **YES**	By what means will it do this?	*Please specify.*		

Public Good: evaluation of potential Risks and Benefits of the project		YES	NO	Description
Is the work addressing a topic that requires urgent or timely data to aid decision-making?		☐	☒	*Please specify.*
If **YES**	What is the rationale for this?	*Please specify.*		
Is the work addressing data gaps in statistics?		☐	☒	*Please specify.*
If **YES**	Which ones?	*Please specify.*		
Will your work effectively communicate findings so that public benefit can be maximised across different audiences who may engage with your project results?		☒	☐	*Publications in International peer-review journals* *Oral & Poster presentations in International Conferences* *Public presentations to media and TV to inform general audience*
If **YES**	What communication methods and channels will you use to ensure this?	*2D BioPAD social media, TV, Radio Channels, Open Science Days in Academic Institutions*		
Does your project approach uphold the principles of trustworthiness, quality and value in statistics?		☒	☐	The focus of the work is not on enhancing trust in traditional statistical systems or producers, but rather on biosensing using aptamer-functionalized MNPs for detecting biomarkers like amyloid beta. Validating specificity/sensitivity claims, analyzing methodological robustness, and comparing performance against officially accepted diagnostic thresholds for amyloid beta detection can enhance trust in biosensor-generated statistics and contribute to data robustness and model trustworthiness within the scientific domain Overall, this project offers insights or applications beneficial to Alzheimer's research or treatment, by contributing meaningful insight or tools for detection, diagnosis, or treatment of AD. Magnetic nanoparticles could be translated into clinical applications while stakeholder engagement (needs of clinicians, patients, or researchers) dictates how we design and interpret our study.
If **YES**	In what way?	*Please specify.*		

1.3 Data security and confidentiality

Data security and confidentiality	YES	NO	Description	Document available	Document available (tick if yes)
Does your activity involve processing of personal data?	☐	☒		1) Informed consent forms and information Sheets (if relevant).	☐
				2) Data management plan (if relevant).	☐

Data security and confidentiality		YES	NO	Description	Document available	Document available (tick if yes)
					3) Data protection impact assessment (if relevant).	☐
If **YES**	Does it involve the processing of special categories of personal data (e.g. sexual lifestyle, ethnicity, genetic, biometric and health data, political opinion, religious or philosophical beliefs)?	☐	☒			

Data security and confidentiality			YES	NO	Description	Document available	Document available (tick if yes)
	If **YES**	Does it involve process-ing of genetic, bio-metric or health data?	☐	☒		1) Declaration confirming compliance with the laws of the country where the data were collected.	☐
	Does it involve profiling, systematic monitoring of individuals, or processing of large scale of special categories of data or intrusive methods of data processing (such as, surveillance, geolocation tracking etc.)?		☐	☒		1) Opinion of the data controller on the need for conducting data protection impact assessment under art 35 GDPR. (if relevant).	☐

Data security and confidentiality	YES	NO	Description	Document available	Document available (tick if yes)
Does your activity involve further processing of previously collected personal data (including use of pre-existing data sets or sources, merging existing data sets)?	☐	☒		1) Confirmation that the data controller has a lawful basis for the data processing and that the appropriate technical and organisational measures are in place to safeguard the rights of the data subjects.	☐
				2) Permission by the owner/manager of the data sets (e.g. social media databases) (if applicable).	☐
				3) Informed Consent Forms + Information Sheets + other consent documents (if applicable).	☐
Is it planned to export personal data (data transfer) from the EU to non-EU countries?	☐	☒		1) Confirmation that data transfers will be made in accordance with Chapter V of the General Data Protection Regulation 2016/679.	☐

Data security and confidentiality	YES	NO	Description	Document available	Document available (tick if yes)
Is it planned to import personal data (data transfer) from non-EU countries into the EU or from a non-EU country to another non-EU country?	☐	☒		1) Confirmation of compliance with the laws of the country in which the data was collected.	☐
Is it planned to use Artificial Intelligence in your project/activity?	☒	☐	1) *Akey aspect of this project is to find the "best combination" of aptamers to be conjugated with MNPs and provide early stage detection of AD.* This exploration process is incrementally guided as the selected aptamers by deep learning models capable of predicting structures of high affinity, easing the process after each iteration. The evolution of the pools is monitored by NGS sequencing, and the sequence analyses which use a proprietary algorithm. Candidates chosen based on the bioinformatics analysis will be chemically synthesized and their binding to proteins will be characterized by SPR or BLI. *2)*	1) Bashir, A. et al., Machine learning guided aptamer refinement and discovery *Nat Commun* 12, 2366 (2021). 2) Shin, I. et al., AptaTrans: a deep neural network for predicting aptamer-protein interaction using pretrained encoders *BMC Bioinformatics* 24, 447 (2023). 3)	☐

Data security and confidentiality		YES	NO	Description	Document available	Document available (tick if yes)
If **YES**	Are you going to inform participants about the use of AI?	☐	☒		1) Informed Consent Forms + Information Sheets + other consent documents (if applicable).	☐
	Is there any measure taken to avoid bias in input data and algorithm design?	☐	☒			☐
	Will the AI model contain data and parameters sensitive to people's personal and professional life?	☐	☒		1) Study protocol and DMP.	☐
	Have you assessed the main ethical risks for the use of AI technology?	☐	☒		1) Risk Management documents, Study protocol and DMP.	☐

1.4 Methodological Quality

Methodological Quality	YES	NO	Description	Documents to be kept on file and provided on request	Document available (tick if yes)
Is the activity conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).	☐	☒	1) *While this task does not involve direct interactions with participants, the overall project framework ensures that any future activities involving human data will strictly adhere to these principles. Ethical reviews and approvals will be sought for all research involving human.* 2) *Electrochemical biosensors will be used in clinical studies that will be conducted in accordance with GCP principles, including obtaining informed consent, ensuring data integrity, and maintaining participant confidentiality."*		
Is the activity supported by non-clinical and clinical information available as state of the art and acquired during the first steps of the project?	☐	☒	1) *The activity is supported by both state-of-the-art non-clinical and clinical information. The selection of aptamers and target biomarkers (such as amyloid beta) is grounded in well-established scientific literature and diagnostic benchmarks. Early steps of the project focus on reviewing and integrating existing kinetic models,*		

Methodological Quality	YES	NO	Description	Documents to be kept on file and provided on request	Document available (tick if yes)
			aptamer binding characteristics, and biomarker concentration ranges in biological fluids		
Is the activity conducted with products manufactured, handled and stored in accordance with applicable Good Manufacturing Practice (GMP) and used in accordance with the approved protocol.	☒	☐	1) *Conjugation Protocol of different AD. All products used in the activity are, or will be, manufactured, handled, and stored in compliance with applicable GMP standards. Their use is aligned with the approved study protocol (see document details in next columns) to ensure adherence to regulatory and quality requirements.*	1) A Material Safety Data Sheet (MSDS), Certificate of Analysis (COA), 2) Handling protocol for handling Aβ-40, Aβ--42 3) MNPs conjugation protocol with aptamers 4) Both protocols appear as appedixes in D2.3 (01/04/2025)	☒
Is the activity conducted in compliance with recognised standards of data integrity and quality.	☒	☐	*1) This activity follows recognized laboratory and regulatory standards (GLP, FDA, ISO), rigorous statistical methods with transparent reporting, proper nanoparticle, aptamer characterization and toxicity assessment*		
Is the activity conducted by researchers skilled in the chosen methodology.	☒	☐	*1) Dr. A. Makridis* *2) Dr. G, Katsipis* *3) Dr. E. Tzekaki* *4) PhD student K. Kazeli*	1) Team members Curricula Vitae.	☒
Does your activity involve interventions (physical also including imaging technology, behavioural treatments, tracking and tracing, etc.) on the study participants?	☐	☒			
Does your activity involve the use of human cells or tissues?	☐	☒			

Methodological Quality		YES	NO	Description	Documents to be kept on file and provided on request	Document available (tick if yes)
If **YES**	Are they available commercially?	☐	☐		1) Copies of import licences (if relevant).	☐
	Are they obtained within this project?	☐	☐		1) Copies of ethics approvals.	☐
					2) Informed consent forms and information sheets.	☐
	Are they obtained from another project, laboratory or institution?	☐	☐		1) Authorisation by primary owner of cells/tissues (including references to ethics approvals).	☐
					2) Copies of import licences (if relevant).	☐
					3) Statement from the primary laboratory/institution that informed consent has been obtained.	☐

1.5 Legal/regulatory compliance

Legal/regulatory compliance	YES	NO	Description
Are the activity and methods employed consistent with Global legal requirements set up in ECR?	☒	☐	*Although this project activity T2.4 and phase of the project focuses on preclinical development, ethical considerations for future human testing are integrated from the outset, ensuring alignment with the Declaration of Helsinki and compliance with regulatory frameworks such as IVDR and GCP. Ethical foresight for human testing: Even though early development does not involve human participants, future clinical performance studies will, and ethical considerations are integrated . Transparency in data sharing: The T2.4 project activity commits to transparency in research dissemination, ensuring that results—whether positive or negative—are published in accordance with ethical reporting standards*
Are the activity and methods employed consistent with European legal requirements set up in ECR?	☒	☐	*T 2.4 activity complies with the principles of:* *Reliability in ensuring the quality of research, reflected in the design, methodology, analysis, and use of resources.* *Honesty in developing, undertaking, reviewing, reporting, and communicating research in a transparent, fair, full, and unbiased way.* *Respect for colleagues, research participants, research subjects, society, ecosystems, cultural heritage, and the environment.* *Accountability for the research from idea to publication, for its management and organization, for training, supervision, and mentoring, and for its wider societal impacts.*
Are the activity and methods employed consistent with National legal requirements set up in ECR?	☐	☒	*1) Specify which are the National requirements applicable to the activity. If not applicable put N/A*

1.6 Public Views and Engagement

Public Views and Engagement		YES	NO	Description
Is the public widely supportive of the project aim and method?		☐	☒	
If **YES**	Does the research involve regular engagement with the public and/or stakeholders?	☐	☒	
	Do activities' findings reflect the experiences and opinions of the participant group?	☐	☒	

1.7 Transparency

Transparency		YES	NO	Description of the required characteristic	Documents to be kept on file and provided on request	Document available (tick if yes)
Does your activity involve human participants?		☐	☒			
If **YES**	Are they volunteers?	☐	☐		1) Copies of ethics approvals (if required by law or practice).	☐
					2) Informed consent forms and information sheets.	☐
	Are they healthy volunteers for medical studies?	☐	☐		1) Copies of ethics approvals (if required by law or practice).	☐
					2) Informed consent forms and information sheets.	☐
	Are they patients for medical study?	☐	☐		1) Copies of ethics approvals (if required by law or practice).	☐
					2) Informed consent forms and information sheets.	☐
	Are they potentially vulnerable individuals or groups?	☐	☐		1) Copies of ethics approvals.	☐

Transparency		YES	NO	Description of the required characteristic	Documents to be kept on file and provided on request	Document available (tick if yes)
					2) Informed consent forms and information sheets.	☐
Are informed consent form and information sheet required for your activity?		☐	☒			
If **YES**	Are they written in a language and in terms involved persons can fully understand?	☐	☐			
	Do they describe the aims, methods and implications of the project activity, the nature of the participation and any benefits, risks or discomfort that might ensue?	☐	☐			
	Do they explicitly state that participation is voluntary and that anyone has the right to refuse to participate and to withdraw their participation, samples or data at any time — without any consequences?	☐	☐			
	Do they state how biological samples and data will be collected, protected during the	☐	☐			

Transparency		YES	NO	Description of the required characteristic	Documents to be kept on file and provided on request	Document available (tick if yes)
	project and whether they will be destroyed or reused afterwards?					
	Do they state what procedures will be implemented in the event of unexpected or incidental findings?	☐	☐			
	Are there other persons unable to give informed consent?	☐	☐			
Will research outcomes be openly available to the public?		☐	☒			
If **YES**	How will research outcomes be disseminated?			*1)D As stated in the D6.1 Dissemination and Communication Plan and Activities, Version 1. submitted on 31/12/2023 the framework and guidelines for the successful implementation of dissemination and communication activities throughout the lifespan of the project and beyond has been set. This document also provides the monitoring mechanism of the dissemination activities, which is based on targeted KPIs. By communicating the project's tangible and intangible assets through the most effective channels and tools to timely reach the targeted groups, As the project evolves, the DCP will be updated, results will be presented and progress against targets will be measured in version 2 and version 3 (M24 and M48 respectively).*		

1.8 Need for self-assessment revision/addition

Need for self-assessment revision/addition	YES	NO	Reason for self-assessment revision/addition	Expected timepoint
Do you expect to make an ethics self-assessment again at a later stage in the project i.e., revision/addition to the ECR.?	☐	☒		

2D BioPAD

Supple Graphene Bio-Platform for point-of-care early detection and monitoring of Alzheimer's Disease

GA 101120706

Partners

CATRIN Czech Advanced Technology and Research Institute

Q-PLAN INTERNATIONAL

ICN2 Institut Català de Nanociència i Nanotecnologia

Grapheal

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