Funded by
the European Union

ADDIT-CE

Alzheimer's Disease Diagnostics Innovation and Translation to Clinical Practice in Central Europe

HORIZON-WIDERA-2022-ACCESS-04

D7.2 Quality Plan, Ethics Requirements and Project Visual Identity, Website and Social Media

Work Package:	WP7
Task:	T7.2, T7.3, T7.5
Deliverable due date:	28/02/2023
Responsible partner:	MU
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Deliverable number:	D7.2 (D23)
Deliverable type:	Report
Dissemination level:	PU
First Created:	26/01/2023
Last Updated:	19/04/2023
Version:	1.0

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Executive summary

Deliverable 7.2 provides a summary of set-up related to T7.2 Quality and Risk Management, T7.3 Management of project communication tools and channels, and last but not least ethics approvals from participating institutions and templates of informed consent. The report is structured into three chapters; T7.2, T7.3, and Ethics requirements.

The first chapter describes the organizational structure of the project consortium as it was set in order to secure proper and timely project implementation meeting all objectives with maintaining a desired level of excellence. Furthermore, it includes a description of risk management, including risk identification, description, evaluation, and suggestions for mitigating measures and control mechanisms.

The second chapter is dedicated to the preparation and maintenance of communication tools according to the CDE Plan as well as the project's visual identity, project communication tools and channels, and its management.

The last chapter includes the approvals of ethics committees and templates of informed consent from all relevant partner institutions.

1 T7.2 Quality and Risk Management

The organizational structure of the consortium quality and risk management is the following; Vertically, the Project Coordinator (PC) oversees the project management and interfaces with the European Commission (EC). The PC supervises project actions and coordinates the decision-making process. A dedicated Project Manager (PM) along with WP leaders ensures proper day-to-day implementation of the project and communicates with Grant administration Offices or Project Management Offices at partner institutions to handle formal matters. The PM ensures continuous quality management and is responsible for the continuous assessment and earliest possible identification of any risks. The PC (or the Steering Committee, if appropriate) will determine the corresponding action, and the WP leaders are responsible to implement such actions and recommendations.

During the Kick-off meeting in M1 each WP, Task, Deliverable, and each Milestone was assigned to a specific responsible person. WP Leaders are responsible for the coordination of actions within their WP and are organizing working meetings either via teleconference or in person as necessary. PM is overseeing the schedule and deadlines and is regularly informed about the progress on WPs by WP Leaders.

Project meetings will take place every six months (May and November) and their organization will be joined with AD workshops (day 1 project meeting, day 2 workshop) as many members of the consortium will attend the AD workshop. A Steering Committee will be held yearly in November within the November project meeting. In M36, the SC meeting will convene with the External Advisory Board (EAB) meeting (WP3) to assist in the

evaluation of the Joint Strategy. The SC and the EAB will continue beyond the project implementation and guide the scientific projects toward the application and development of new interaction topics in the joint ecosystem between the Brno and Bratislava regions.

Any other meetings will happen via teleconference or in person based on the actual need and upon request of any member of the consortium.

The Risk assessment will be conducted continuously during the whole project duration to ensure that the Consortium will meet the project objectives on time and on budget, under the supervision of the PM. The risk management process consists of the following steps: (1) Risk identification and characterization, (2) Risk evaluation (qualitative and quantitative), (3) Risk prioritization, (4) Risk response (mitigation strategies and contingency planning), and (5) Risk control, monitoring and reporting. The outcomes of the Risk management will be included in the Periodic Reports. The PM is also responsible for the creation of internal communication tools and the maintenance of internal communication flow to share project-related documents and keep all participants updated. The PM also coordinates the interim and final technical and financial reports required by the HE program rules.

Table 1: Critical risks & risk management strategy

Description	WP	Impact	Likelihood	Mitigation Measures	Control
Project activities and deliverables will not be delivered on time	WP1, WP2, WP3, WP4, WP5, WP6, WP7	Medium	Medium	Each task and each deliverable were assigned to a specific responsible person who will be accountable for timely implementation. Each WP was assigned to a responsible person coordinating the actions within the WP via organizing WP-related working group meetings (online and in person). Deadlines were clearly set with PM overseeing the schedule.	Regular project meetings of all partners, feedback, and regular communication with the coordinator (PM)
Internal rules and processes of the partnered institutions can be incompatible, making the implementation (i.e. job shadowing, hands-on internships etc.) inefficient.	WP3, WP4, WP6, WP7,	Medium	Low	(i) Possible incompatibilities were presumed and resolved within the Consortium Agreement (ii) PM will be monitoring possible conflicts that might occur during the implementation of the project and will ensure their timely handling.	Regular project meetings of all partners, feedback, and regular communication with the coordinator (PM)
Key research staff from an academic institution will leave during the project, causing discontinuity of research, training, and strategy development.	WP1, WP2, WP6, WP4	High	Medium	All researchers are highly motivated to participate in the project. In case of inevitable personal reasons to leave, there is enough professional capacity within the research teams for a substitute.	Regular communication between the PM, HR department, and PI

A business partner will leave the project by external forces (i.e. economic decline).	WP1, WP2, WP3, WP6, WP4	High	Low	Due to the war in Ukraine, the economy of Central Europe can become more vulnerable in this decade. Therefore, all companies will focus either on the enlargement of their product portfolio or on more intensive collaboration with pharma partners to mitigate the risk of economic decline.	Regular project meetings of all partners, feedback, and regular communication with the coordinator (PM)
Rise of new epidemics resulting in state-wide lockdowns and border closures, blocking dissemination and training vectors.	WP6, WP5	Low	Low	All partners already have vast experience with online spaces for networking and dissemination. If the need arises, we are able to convert workshops, lectures, discussions etc. into an online format. The epidemic situation in the Czech and Slovak Republic will be monitored.	Regular monitoring of an epidemiologic situation worldwide.
Low interest of civil society in the project, resulting in an inefficient communication campaign.	WP5	High	Low	Partners involved in communication with society are excellent disseminators with established outreach. The WP5 leader will continuously evaluate the efficiency of the campaign and adjust according to needs.	Regular project meetings of all partners, WP working meetings
Deterioration of the economy (spiraling inflation) raising the cost of services and materials above planned budget.	WP7, WP6, WP4	Medium	Medium	The planned expenditures have been carefully budgeted. The PM will regularly monitor the spending of the budget and the SC will make decisions on budget shifts if necessary.	Expenditures control and regular monitoring by each partner, regular project meetings with all partners
New epidemics preventing patients from participation intervention studies	WP5	High	Low	Cannot be influenced nor mitigated	Regular monitoring of epidemiologic situation
One of the biggest risks in joint project preparation is a lack of alignment between project partners. This can include differences in objectives, work plans, and timelines, which can make it difficult to coordinate activities and deliverables – in our case submission of 4 joint research projects, 10 above threshold	WP2	Low	Low	• Detailed work plan • Regular communication and clear communication channels to ensure that all partners are aware of project updates and any potential issues. • Regular monitoring of potential funding opportunities and informing members of consortia about them	Highly motivated consortium is committed to fully implement the project and to build Hub of Excellence. Regular project meetings and status updates may help identify a potential lack of alignment.

proposals.					
Risk of technological obsolescence - New technology concurrently developed by groups other than consortium members can render approaches outlined in the project obsolete. Risks can be further amplified by slow progress of TRL advancement by consortium members.	WP2	Medium	Medium	• Engage external experts: The project consortium may need to engage with external experts to provide technical expertise, legal advice, or other support. • Monitoring of scientific literature, WIPO database, and diagnostics solutions introduced to the market. • Adjusting R&I development and resource deployment to reflect cutting-edge technological developments.	Regular monitoring and screening of potentially competitive technologies supplanted by regular scientific meetings of consortium members.
Patent restrictions - The results of patent searches will prove that commercial use of the outputs is not possible.	WP3	Medium	Medium	Conducting a patent search before planning outputs	Regular project meetings of all partners, feedback, and regular communication with the coordinator (PM)
Lack of suitable outputs with commercial potential.	WP3	High	Low	Continuous monitoring of results and evaluation of their commercial potential	Regular project meetings of all partners
Risk arising from demanding regulatory requirements for new diagnostic devices (IVDR).	WP3	Medium	High	Increasing knowledge of new IVD regulations and requirements, experience with other products	Regular project meetings of all partners
Risk arising from the complexity of the processes in determining IP and transfer conditions.	WP3	Low	Low	Ongoing communication with the involved Technology Transfer Centers	Regular project meetings of all partners
A dramatic change in the political leadership in CZ or SK significantly changing the long-term plans toward proactive knowledge-based economy activities	WP1	High	Low	Ongoing communication with the representatives of involved institutions and the Ministry of Education of CR and SK	Monitoring of the political situation in CZ and SK
Phosphorylation of Tau protein variants at particular sites may be very difficult by the particular kinases. In such cases we plan to insert phospho-serines (pSer) at particular sites by the extended genetic code technology. However, it is currently applicable only for pSer on a small number of sites.	WP4	High	Medium	In case when a version of Tau phosphorylated in a larger number of sites needs to be prepared or if also phopho-threonines should be incorporated, we will try to prepare them in mammalian expression cell lines. A universal back-up plan is to insert phosphomimicking mutations (GLU, ASP) at the given positions. This is a straightforward approach (heavily used in the	The incorporation of the particular phosphorylated residues at the specific sites will be validated by mass-spectrometry. In the case of the insertion of phosphomimicking mutations – the behavior of such Tau variants will be compared with their phosphorylated

				community), although in multiple cases, it is not a fully realistic approximation.	counterparts by solution NMR spectroscopy to analyze their possible differences.
Biomolecular solution NMR spectroscopy requires a high concentration of soluble molecules of Tau protein variants. We have already optimized the yield of the expression of Tau proteins, but we cannot prevent the possibility that some variants will be aggregating during the concentrating of the samples or during the NMR measurement.	WP4	Medium	Medium	In such cases, we will try to optimize the buffer conditions in order to increase the protein solubility. If it is still insufficient, we may try at their ends to incorporate the solubilization tags. However, we are aware that the presence of a solubilization tag on the N- or C-terminus may affect the overall behavior of Tau variants. Therefore some of those Tau variants we will analyze, mostly in their fibril form and in the monomeric form, will be rather used biophysical interaction methods.	The behavior of Tau fragment in the optimized buffer conditions or the variants with the solubilization tags will be checked by solution NMR spectroscopy. In the low solubility cases, they will be analyzed by SAXS measurements requiring much lower protein concentrations.
In addition to the characterization of Tau fibrils from different origins, we will search for the in-vitro conditions inducing similar morphology of the Tau fibrils similar as observed in AD disease	WP4	Medium	Medium	We are prepared to apply large-scale screening of conditions for the Tau fibrils formation in combination with fast AFM and negative staining EM. Even when no exact match of morphologies is found – the most similar cases will have a high value for future analysis. In parallel, we will analyze the in-vivo Tau fibrils samples from AD patients.	The pre-selected Tau fibrils based on AFM analysis will finally be checked and validated by cryoEM analysis using a helical reconstruction procedure.
Inadequate analytical parameters of the developed kit - The developed kit will not meet the required analytical criteria	WP4	High	Low	The experience of the development team, the design of another detection system	N/A
Problems with the supply of raw materials - Problems with the supply of raw materials for the assembly of the kit due to the geopolitical situation	WP4	Medium	Low	Establishing contractual cooperation with verified suppliers	N/A
Patent restrictions- The results of patent searches will limit assay development for commercial purpose	WP4	Medium	Medium	Conducting a patent search before planning outputs	N/A
Validation failure of low-input miRNA sequencing protocol - Low miRNA inputs from	WP4	Medium	Medium	Multiple sample input types will be tested. In-house miRNA purification step can be replaced with other available	N/A

targeted body fluids may not lead to consistent sequencing results.				approaches.	
Catastrophic sample degradation/loss - Patient samples used for R&I could get destroyed in an accident (e.g., freezer malfunction).	WP4	High	Low	Prudent sample storage & logistics management of consortium members.	N/A

2 T7.3 Management of project communication tools and channels

Preparation and maintenance of communication tools will be managed according to the Communication Dissemination and Exploitation Plan (CDE Plan). CDE Plan will be part of D 6.1 Initial Training Plan and CDE Plan, due M6.

A project website **https://addit-ce.ceitec.cz/** was created at the project initiation. Its content is managed and regularly updated by the Coordinator with all partners being actively involved. Besides information on the project and the consortium, it will inform about the upcoming events, describe the past ones and it will also bring news about the project results and achievements. The content of the website will be regularly updated.

A new project logo was designed. It is visible on the project website. More versions of the logo are available below.

3 Ethics approvals from participating institutions and templates of informed consent

The approval of the Masaryk University Research Ethics Committee is a part of **Annex 1**. Any other ethical approval for MU is not necessary for the following reasons. Full-length and truncated ApoE protein variants will be expressed in Escherichia coli or mammalian cells and affinity purified for down-stream lab-based biochemical experiments. There are no ethical issues. For in vitro experiments with stem-cell-based cellular models, we will use already established induced pluripotent stem cell (iPSC) lines that were previously derived, characterized, and registered at hpscreg.eu (Raska et al., 2021a,b; Lin et al., 2018). Since no new derivation of iPSCs from patients' samples is planned, no ethical approval is currently needed.

The ethics approval and the template of the informed consent for St. Anne´s University Hospital Brno are part of **Annex 2**.

The ethics approval and the template of the informed consent for the Biomedical Research Centre of the Slovak Academy of Sciences are part of **Annex 3**.

The ethics approval for the Institute of Neuroimmunology of the Slovak Academy of Sciences (NII SAS) together with the Memory Centre (MC) are part of **Annex 4**. The ethics approval is valid for the project Harmonizácia diagnostiky demencie, longitudinálne hodnotenie neurodegenerácie a vývoj nových diagnostických testov (Harmonization of dementia diagnostics, longitudinal neurodegeneration assessment and development of new diagnostics tests), which is composed of two research projects: APVV-20-0447 - LANCRE-AD and HORIZON-WIDERA 2022 – ADDIT-CE. The approval is for NII SAS, MC, and other institutions involved in the project. Further details, including the template of the informed consent, are included in the project synopsis which was submitted to the ethical committee as the basis for the assessment. As it includes sensitive and confidential information about the project, it is not included in this public deliverable.

For none of the remaining partners, the approval is relevant as they either work with fully anonymized samples or they do not work with samples at all.

4 Annexes

Annex 1 Masaryk University Research Ethics Committee
Annex 2 The ethics approval and the template of the informed consent for St. Anne´s University Hospital Brno
Annex 3 The ethics approval and the template of the informed consent for the Biomedical Research Centre of the Slovak Academy of Sciences
Annex 4 The ethics approval for the Institute of Neuroimmunology of the Slovak Academy of Sciences and the Memory Centre