EUROPEAN RESEARCH EXECUTIVE AGENCY (REA)

REA.C – Future Society
C.3 – Widening Participation

GRANT AGREEMENT

Project 101087124 — ADDIT-CE

PREAMBLE

This **Agreement** ('the Agreement') is **between** the following parties:

on the one part,

the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and

on the other part,

1. 'the coordinator':

Masarykova univerzita (MU), PIC 999880657, established in Zerotinovo namesti 9, BRNO 601 77, Czechia,

and the following other beneficiaries, if they sign their 'accession form' (see Annex 3 and Article 40):

2. **NEUROIMUNOLOGICKY USTAV SLOVENSKEJAKADEMIA VIED (NII SAS)**, PIC 984972436, established in DUBRAVSKA CESTA 9, BRATISLAVA 84510, Slovakia,

3. **FAKULTNI NEMOCNICE U SV. ANNY V BRNE (ICRC)**, PIC 994491822, established in Pekarska 53, Brno 656 91, Czechia,

4. **CENTRUM MEMORY NO (MC)**, PIC 892489532, established in MLYNAROVICOVA 2571/21, BRATISLAVA 851 03, Slovakia,

5. **BIOVENDOR - LABORATORNI MEDICINA AS (BIOVENDOR)**, PIC 973936455, established in KARASEK 1767/1, BRNO 621 00, Czechia,

6. **BIOMEDICINSKE CENTRUM SLOVENSKEJ AKADEMIE VIED, VEREJNA VYSKUMNA INSTITUCIA (BMC SAS)**, PIC 918583890, established in DUBRAVSKA CESTA 9, BRATISLAVA 845 05, Slovakia,

7. **MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY (MH)**, PIC 999825173, established in LIMBOVA 2, BRATISLAVA 83752, Slovakia,

8. **MULTIPLEXDX S.R.O. (MDX)**, PIC 918777890, established in ILKOVICOVA 8, BRATISLAVA 841 04, Slovakia,

9. **GENETON S.R.O. (GENETON)**, PIC 951290059, established in ILKOVICOVA 8, BRATISLAVA 841 04, Slovakia,

Unless otherwise specified, references to 'beneficiary' or 'beneficiaries' include the coordinator and affiliated entities (if any).

If only one beneficiary signs the grant agreement ('mono-beneficiary grant'), all provisions referring to the 'coordinator' or the 'beneficiaries' will be considered — mutatis mutandis — as referring to the beneficiary.

The parties referred to above have agreed to enter into the Agreement.

By signing the Agreement and the accession forms, the beneficiaries accept the grant and agree to implement the action under their own responsibility and in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

The Agreement is composed of:

Preamble

Terms and Conditions (including Data Sheet)

Annex 1 Description of the action[1]

Annex 2 Estimated budget for the action

Annex 2a Additional information on unit costs and contributions (if applicable)

Annex 3 Accession forms (if applicable)[2]

Annex 3a Declaration on joint and several liability of affiliated entities (if applicable)[3]

Annex 4 Model for the financial statements

Annex 5 Specific rules (if applicable)

[1] Template published on Portal Reference Documents.
[2] Template published on Portal Reference Documents.
[3] Template published on Portal Reference Documents.

TERMS AND CONDITIONS

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DATA SHEET

1. General data

Project summary:

Project summary
More than 55 million people worldwide suffer from dementia. Alzheimer disease (AD) is the main cause of this fatal disorder, without any effective disease modifying therapy. Early diagnosis and lifestyle modifications can significantly reduce the costs of care and treatment. There is no conceptual plan implementing modern diagnostic methods in the clinical practice in Czechia and Slovakia. The interaction between universities and private sector developing molecular diagnostic tools is fragmented and lacking. Limited number of talented students are invested in applied AD-focused research. The aim of ADDIT-CE is to interlink two ecosystems in Brno and Bratislava region, embracing the full quadruple helix of innovation driving actors: excellent scientific teams from Masaryk University and Slovak Academy of Sciences, collaborating with top biotech companies: Geneton, BioVendor, and MultiplexDX. Societal actors will be represented by organisations such as Slovak and Czech Alzheimer Societies, Memory Center and Czech Brain Aging Study. The regional government will be involved via Ministry of Health Slovak Republic, and South Moravian Innovation Centre. The joined ecosystems will unite R&I activities focusing on new diagnostic methods and their applications and further interlink academia and business spheres by creating a pilot industrial PhD programme. ADDIT-CE will generate a joint cross-border strategy covering basic and applied research activities aiming on accelerating the development of new tools for preclinical AD diagnostics and lifestyle/pharmacological intervention monitoring. New cutting-edge technologies will be transferred into clinical practise. Results of ADDIT-CE will be used to develop the Slovak National Plan to Combat Dementia, to enrich the Czech National Plan for AD, and will be widely disseminated to end users and society. ADDIT-CE will join forces of the involved ecosystems to revolutionise diagnostic approaches in both countries.

Keywords:

- Cell differentiation, physiology and dynamics
- Health services, health care research
- Molecular and cellular neuroscience
- Molecular biology and interactions
- Neurological disorders (e.g. Alzheimer's disease, Huntington's disease, Parkinson's disease)
- Structural biology

Project number: 101087124

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

Project acronym: ADDIT-CE

Call: HORIZON-WIDERA-2022-ACCESS-04

Topic: HORIZON-WIDERA-2022-ACCESS-04-01

Type of action: HORIZON Coordination and Support Actions

Granting authority: European Research Executive Agency

Grant managed through EU Funding & Tenders Portal: Yes (eGrants)

Project starting date: fixed date: 1 January 2023

Project end date: 31 December 2026

Project duration: 48 months

Consortium agreement: Yes

2. Participants

List of participants:

N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
1	COO	MU	Masarykova univerzita	CZ	999880657	1 684 320.00	1 684 320.00

N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
2	BEN	NII SAS	NEUROIMUNOLOGICKY USTAV SLOVENSKEJAKADEMIA VIED	SK	984972436	823 977.50	823 977.50
2.1	AE	SALS	SLOVENSKA ALZHEIMEROVA SPOLOCNOST	SK	887301681	70 887.50	70 887.50
3	BEN	ICRC	FAKULTNI NEMOCNICE U SV. ANNY V BRNE	CZ	994491822	580 925.75	580 925.75
4	BEN	MC	CENTRUM MEMORY NO	SK	892489532	238 587.50	238 587.50
5	BEN	BIOVENDOR	BIOVENDOR - LABORATORNI MEDICINA AS	CZ	973936455	234 000.00	234 000.00
6	BEN	BMC SAS	BIOMEDICINSKE CENTRUM SLOVENSKEJ AKADEMIE VIED, VEREJNA VYSKUMNA INSTITUCIA	SK	918583890	216 212.50	216 212.50
7	BEN	MH	MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY	SK	999825173	104 012.50	104 012.50
8	BEN	MDX	MULTIPLEXDX S.R.O.	SK	918777890	716 202.50	716 202.50
9	BEN	GENETON	GENETON S.R.O.	SK	951290059	270 173.75	270 173.75
10	AP	JIC	JIC, ZAJMOVE SDRUZENI PRAVNICKCH OSOB	CZ	999780262	0.00	0.00
11	AP	CALS	CESKA ALZHEIMEROVSKA SPOLECNOST, OPS	CZ	888747466	0.00	0.00
Total						4 939 299.50	4 939 299.50

Coordinator:

– Masarykova univerzita (MU)

3. Grant

Maximum grant amount, total estimated eligible costs and contributions and funding rate:

Total eligible costs (BEN and AE)	Funding rate (%)	Maximum grant amount (Annex 2)	Maximum grant amount (award decision)
4 939 299.50	100	4 939 299.50	4 939 299.50

Grant form: Budget-based

Grant mode: Action grant

Budget categories/activity types:

- A. Personnel costs
  - A.1 Employees, A.2 Natural persons under direct contract, A.3 Seconded persons
  - A.4 SME owners and natural person beneficiaries
- B. Subcontracting costs
- C. Purchase costs
  - C.1 Travel and subsistence
  - C.2 Equipment
  - C.3 Other goods, works and services
- D. Other cost categories
  - D.2 Internally invoiced goods and services
- E. Indirect costs

Cost eligibility options:

- In-kind contributions eligible costs

- Parental leave
- Project-based supplementary payments
- Average personnel costs (unit cost according to usual cost accounting practices)
- Limitation for subcontracting
- Travel and subsistence:
  - Travel: Actual costs
  - Accommodation: Actual costs
  - Subsistence: Actual costs
- Equipment: depreciation only
- Indirect cost flat-rate: 25% of the eligible direct costs (categories A-D, except volunteers costs, subcontracting costs, financial support to third parties and exempted specific cost categories, if any)
- VAT: Yes
- Other ineligible costs

Budget flexibility: Yes (no flexibility cap)

4. Reporting, payments and recoveries

4.1 Continuous reporting (art 21)

Deliverables: see Funding & Tenders Portal Continuous Reporting tool

4.2 Periodic reporting and payments

Reporting and payment schedule (art 21, 22):

Reporting					Payments	
Reporting periods			Type	Deadline	Type	Deadline (time to pay)
RP No	Month from	Month to				
					Initial prefinancing	30 days from entry into force/10 days before starting date – whichever is the latest
1	1	15	Periodic report	60 days after end of reporting period	Interim payment	90 days from receiving periodic report
2	16	30	Periodic report	60 days after end of reporting period	Interim payment	90 days from receiving periodic report
3	31	48	Periodic report	60 days after end of reporting period	Final payment	90 days from receiving periodic report

Prefinancing payments and guarantees:

Prefinancing payment	
Type	**Amount**
Prefinancing 1 (initial)	2 617 828.74

Reporting and payment modalities (art 21, 22):

Mutual Insurance Mechanism (MIM): Yes

MIM contribution: 5% of the maximum grant amount (246 964.98), retained from the initial prefinancing

Restrictions on distribution of initial prefinancing: The prefinancing may be distributed only if the minimum number of beneficiaries set out in the call condititions (if any) have acceded to the Agreement and only to beneficiaries that have acceded.

Interim payment ceiling (if any): 90% of the maximum grant amount

Exception for revenues: Yes

No-profit rule: Yes

Late payment interest: ECB + 3.5%

Bank account for payments:

CZ4301000000000085636621

Conversion into euros: Double conversion

Reporting language: Language of the Agreement

4.3 Certificates (art 24):

Certificates on the financial statements (CFS):

Conditions:

Schedule: only at final payment, if threshold is reached

Standard threshold (beneficiary-level):

- financial statement: requested EU contribution to costs ≥ EUR 430 000.00

Special threshold for beneficiaries with a systems and process audit(see Article 24): financial statement: requested EU contribution to costs ≥ EUR 725 000.00

4.4 Recoveries (art 22)

First-line liability for recoveries:

Beneficiary termination: Beneficiary concerned

Final payment: Each beneficiary for their own debt

After final payment: Beneficiary concerned

Joint and several liability for enforced recoveries (in case of non-payment):

Individual financial responsibility: Each beneficiary is liable only for its own debts (and those of its affiliated entities, if any)

5. Consequences of non-compliance, applicable law & dispute settlement forum

Suspension and termination:

Additional suspension grounds (art 31)

Additional termination grounds (art 32)

Applicable law (art 43):

Standard applicable law regime: EU law + law of Belgium

Dispute settlement forum (art 43):

Standard dispute settlement forum:

EU beneficiaries: EU General Court + EU Court of Justice (on appeal)

Non-EU beneficiaries: Courts of Brussels, Belgium (unless an international agreement provides for the enforceability of EU court judgements)

6. Other

Specific rules (Annex 5): Yes

Standard time-limits after project end:

Confidentiality (for X years after final payment): 5

Record-keeping (for X years after final payment): 5 (or 3 for grants of not more than EUR 60 000)

Reviews (up to X years after final payment): 2

Audits (up to X years after final payment): 2

Extension of findings from other grants to this grant (no later than X years after final payment): 2

Impact evaluation (up to X years after final payment): 5 (or 3 for grants of not more than EUR 60 000)

CHAPTER 1 GENERAL

ARTICLE 1 — SUBJECT OF THE AGREEMENT

This Agreement sets out the rights and obligations and terms and conditions applicable to the grant awarded for the implementation of the action set out in Chapter 2.

ARTICLE 2 — DEFINITIONS

For the purpose of this Agreement, the following definitions apply:

Actions — The project which is being funded in the context of this Agreement.

Grant — The grant awarded in the context of this Agreement.

EU grants — Grants awarded by EU institutions, bodies, offices or agencies (including EU executive agencies, EU regulatory agencies, EDA, joint undertakings, etc.).

Participants — Entities participating in the action as beneficiaries, affiliated entities, associated partners, third parties giving in-kind contributions, subcontractors or recipients of financial support to third parties.

Beneficiaries (BEN) — The signatories of this Agreement (either directly or through an accession form).

Affiliated entities (AE) — Entities affiliated to a beneficiary within the meaning of Article 187 of EU Financial Regulation 2018/1046[4] which participate in the action with similar rights and obligations as the beneficiaries (obligation to implement action tasks and right to charge costs and claim contributions).

Associated partners (AP) — Entities which participate in the action, but without the right to charge costs or claim contributions.

Purchases — Contracts for goods, works or services needed to carry out the action (e.g. equipment, consumables and supplies) but which are not part of the action tasks (see Annex 1).

Subcontracting — Contracts for goods, works or services that are part of the action tasks (see Annex 1).

In-kind contributions — In-kind contributions within the meaning of Article 2(36) of EU Financial

[4] For the definition, see Article 187 Regulation (EU, Euratom) 2018/1046 of the European Parliament and of the Council of 18 July 2018 on the financial rules applicable to the general budget of the Union, amending Regulations (EU) No 1296/2013, (EU) No 1301/2013, (EU) No 1303/2013, (EU) No 1304/2013, (EU) No 1309/2013, (EU) No 1316/2013, (EU) No 223/2014, (EU) No 283/2014, and Decision No 541/2014/EU and repealing Regulation (EU, Euratom) No 966/2012 ('EU Financial Regulation') (OJ L 193, 30.7.2018, p. 1): "**affiliated entities** [are]:
(a) entities that form a sole beneficiary [(i.e. where an entity is formed of several entities that satisfy the criteria for being awarded a grant, including where the entity is specifically established for the purpose of implementing an action to be financed by a grant)];
(b) entities that satisfy the eligibility criteria and that do not fall within one of the situations referred to in Article 136(1) and 141(1) and that have a link with the beneficiary, in particular a legal or capital link, which is neither limited to the action nor established for the sole purpose of its implementation".

Regulation 2018/1046, i.e. non-financial resources made available free of charge by third parties.

Fraud — Fraud within the meaning of Article 3 of EU Directive 2017/1371[5] and Article 1 of the Convention on the protection of the European Communities' financial interests, drawn up by the Council Act of 26 July 1995[6], as well as any other wrongful or criminal deception intended to result in financial or personal gain.

Irregularities — Any type of breach (regulatory or contractual) which could impact the EU financial interests, including irregularities within the meaning of Article 1(2) of EU Regulation 2988/95[7].

Grave professional misconduct — Any type of unacceptable or improper behaviour in exercising one's profession, especially by employees, including grave professional misconduct within the meaning of Article 136(1)(c) of EU Financial Regulation 2018/1046.

Applicable EU, international and national law — Any legal acts or other (binding or non-binding) rules and guidance in the area concerned.

Portal — EU Funding & Tenders Portal; electronic portal and exchange system managed by the European Commission and used by itself and other EU institutions, bodies, offices or agencies for the management of their funding programmes (grants, procurements, prizes, etc.).

CHAPTER 2 ACTION

ARTICLE 3 — ACTION

The grant is awarded for the action **101087124** — **ADDIT-CE** ('action'), as described in Annex 1.

ARTICLE 4 — DURATION AND STARTING DATE

The duration and the starting date of the action are set out in the Data Sheet (see Point 1).

CHAPTER 3 GRANT

ARTICLE 5 — GRANT

5.1 Form of grant

The grant is an action grant[8] which takes the form of a budget-based mixed actual cost grant (i.e. a

[5] Directive (EU) 2017/1371 of the European Parliament and of the Council of 5 July 2017 on the fight against fraud to the Union's financial interests by means of criminal law (OJ L 198, 28.7.2017, p. 29).
[6] OJ C 316, 27.11.1995, p. 48.
[7] Council Regulation (EC, Euratom) No 2988/95 of 18 December 1995 on the protection of the European Communities financial interests (OJ L 312, 23.12.1995, p. 1).
[8] For the definition, see Article 180(2)(a) EU Financial Regulation 2018/1046: '**action grant**' means an EU grant to finance "an action intended to help achieve a Union policy objective".

grant based on actual costs incurred, but which may also include other forms of funding, such as unit costs or contributions, flat-rate costs or contributions, lump sum costs or contributions or financing not linked to costs).

5.2 Maximum grant amount

The maximum grant amount is set out in the Data Sheet (see Point 3) and in the estimated budget (Annex 2).

5.3 Funding rate

The funding rate for costs is 100% of the action's eligible costs.

Contributions are not subject to any funding rate.

5.4 Estimated budget, budget categories and forms of funding

The estimated budget for the action is set out in Annex 2.

It contains the estimated eligible costs and contributions for the action, broken down by participant and budget category.

Annex 2 also shows the types of costs and contributions (forms of funding)[9] to be used for each budget category.

If unit costs or contributions are used, the details on the calculation will be explained in Annex 2a.

5.5 Budget flexibility

The budget breakdown may be adjusted — without an amendment (see Article 39) — by transfers (between participants and budget categories), as long as this does not imply any substantive or important change to the description of the action in Annex 1.

However:

- changes to the budget category for volunteers (if used) always require an amendment
- changes to budget categories with lump sums costs or contributions (if used; including financing not linked to costs) always require an amendment
- changes to budget categories with higher funding rates or budget ceilings (if used) always require an amendment
- addition of amounts for subcontracts not provided for in Annex 1 either require an amendment or simplified approval in accordance with Article 6.2
- other changes require an amendment or simplified approval, if specifically provided for in Article 6.2
- flexibility caps: not applicable.

[9] See Article 125 EU Financial Regulation 2018/1046.

ARTICLE 6 — ELIGIBLE AND INELIGIBLE COSTS AND CONTRIBUTIONS

In order to be eligible, costs and contributions must meet the **eligibility** conditions set out in this Article.

6.1 General eligibility conditions

The **general eligibility conditions** are the following:

(a) for actual costs:

(i) they must be actually incurred by the beneficiary

(ii) they must be incurred in the period set out in Article 4 (with the exception of costs relating to the submission of the final periodic report, which may be incurred afterwards; see Article 21)

(iii) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(iv) they must be incurred in connection with the action as described in Annex 1 and necessary for its implementation

(v) they must be identifiable and verifiable, in particular recorded in the beneficiary's accounts in accordance with the accounting standards applicable in the country where the beneficiary is established and with the beneficiary's usual cost accounting practices

(vi) they must comply with the applicable national law on taxes, labour and social security and

(vii) they must be reasonable, justified and must comply with the principle of sound financial management, in particular regarding economy and efficiency

(b) for unit costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(ii) the units must:

- be actually used or produced by the beneficiary in the period set out in Article 4 (with the exception of units relating to the submission of the final periodic report, which may be used or produced afterwards; see Article 21)

- be necessary for the implementation of the action and

(iii) the number of units must be identifiable and verifiable, in particular supported by records and documentation (see Article 20)

(c) for flat-rate costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(ii) the costs or contributions to which the flat-rate is applied must:

- be eligible
- relate to the period set out in Article 4 (with the exception of costs or contributions relating to the submission of the final periodic report, which may be incurred afterwards; see Article 21)

(d) for lump sum costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(ii) the work must be properly implemented by the beneficiary in accordance with Annex 1

(iii) the deliverables/outputs must be achieved in the period set out in Article 4 (with the exception of deliverables/outputs relating to the submission of the final periodic report, which may be achieved afterwards; see Article 21)

(e) for unit, flat-rate or lump sum costs or contributions according to usual cost accounting practices (if any):

(i) they must fulfil the general eligibility conditions for the type of cost concerned

(ii) the cost accounting practices must be applied in a consistent manner, based on objective criteria, regardless of the source of funding

(f) for financing not linked to costs (if any): the results must be achieved or the conditions must be fulfilled as described in Annex 1.

In addition, for direct cost categories (e.g. personnel, travel & subsistence, subcontracting and other direct costs) only costs that are directly linked to the action implementation and can therefore be attributed to it directly are eligible. They must not include any indirect costs (i.e. costs that are only indirectly linked to the action, e.g. via cost drivers).

In-kind contributions provided by third parties free of charge may be declared as eligible direct costs by the beneficiaries which use them (under the same conditions as if they were their own, provided that they concern only direct costs and that the third parties and their in-kind contributions are set out in Annex 1 (or approved ex post in the periodic report, if their use does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants; 'simplified approval procedure').

6.2 Specific eligibility conditions for each budget category

For each budget category, the **specific eligibility conditions** are as follows:

Direct costs

A. Personnel costs

A.1 Costs for employees (or equivalent) are eligible as personnel costs if they fulfil the general eligibility conditions and are related to personnel working for the beneficiary under an employment contract (or equivalent appointing act) and assigned to the action.

They must be limited to salaries (including net payments during parental leave), social security contributions, taxes and other costs linked to the remuneration, if they arise from national law or the employment contract (or equivalent appointing act) and be calculated on the basis of the costs actually incurred, in accordance with the following method:

{daily rate for the person

multiplied by

number of day-equivalents worked on the action (rounded up or down to the nearest half-day)}.

The daily rate must be calculated as:

{annual personnel costs for the person

divided by

215}.

The number of day-equivalents declared for a person must be identifiable and verifiable (see Article 20).

The actual time spent on parental leave by a person assigned to the action may be deducted from the 215 days indicated in the above formula.

The total number of day-equivalents declared in EU grants, for a person for a year, cannot be higher than 215, minus time spent on parental leave (if any).

For personnel which receives supplementary payments for work in projects (project-based remuneration), the personnel costs must be calculated at a rate which:

- corresponds to the actual remuneration costs paid by the beneficiary for the time worked by the person in the action over the reporting period
- does not exceed the remuneration costs paid by the beneficiary for work in similar projects funded by national schemes (‘national projects reference’)
- is defined based on objective criteria allowing to determine the amount to which the person is entitled

and

- reflects the usual practice of the beneficiary to pay consistently bonuses or supplementary payments for work in projects funded by national schemes.

The national projects reference is the remuneration defined in national law, collective labour agreement or written internal rules of the beneficiary applicable to work in projects funded by national schemes.

If there is no such national law, collective labour agreement or written internal rules or if the project-based remuneration is not based on objective criteria, the national project reference will be the average

remuneration of the person in the last full calendar year covered by the reporting period, excluding remuneration paid for work in EU actions.

If the beneficiary uses average personnel costs (unit cost according to usual cost accounting practices), the personnel costs must fulfil the general eligibility conditions for such unit costs and the daily rate must be calculated:

- using the actual personnel costs recorded in the beneficiary's accounts and excluding any costs which are ineligible or already included in other budget categories; the actual personnel costs may be adjusted on the basis of budgeted or estimated elements, if they are relevant for calculating the personnel costs, reasonable and correspond to objective and verifiable information

and

- according to usual cost accounting practices which are applied in a consistent manner, based on objective criteria, regardless of the source of funding.

A.2 and **A.3 Costs for natural persons working under a direct contract** other than an employment contract and costs for **seconded persons by a third party against payment** are also eligible as personnel costs, if they are assigned to the action, fulfil the general eligibility conditions and:

(a) work under conditions similar to those of an employee (in particular regarding the way the work is organised, the tasks that are performed and the premises where they are performed) and

(b) the result of the work belongs to the beneficiary (unless agreed otherwise).

They must be calculated on the basis of a rate which corresponds to the costs actually incurred for the direct contract or secondment and must not be significantly different from those for personnel performing similar tasks under an employment contract with the beneficiary.

A.4 The work of **SME owners** for the action (i.e. owners of beneficiaries that are small and medium-sized enterprises[10] not receiving a salary) or **natural person beneficiaries** (i.e. beneficiaries that are natural persons not receiving a salary) may be declared as personnel costs, if they fulfil the general eligibility conditions and are calculated as unit costs in accordance with the method set out in Annex 2a.

B. Subcontracting costs

Subcontracting costs for the action (including related duties, taxes and charges, such as non-deductible or non-refundable value added tax (VAT)) are eligible, if they are calculated on the basis of the costs actually incurred, fulfil the general eligibility conditions and are awarded using the

[10] For the definition, see Commission Recommendation 2003/361/EC: micro, small or medium-sized enterprise (SME) are enterprises

- engaged in an economic activity, irrespective of their legal form (including, in particular, self- employed persons and family businesses engaged in craft or other activities, and partnerships or associations regularly engaged in an economic activity) and

- employing fewer than 250 persons (expressed in 'annual working units' as defined in Article 5 of the Recommendation) and which have an annual turnover not exceeding EUR 50 million, and/or an annual balance sheet total not exceeding EUR 43 million.

beneficiary's usual purchasing practices — provided these ensure subcontracts with best value for money (or if appropriate the lowest price) and that there is no conflict of interests (see Article 12).

Beneficiaries that are 'contracting authorities/entities' within the meaning of the EU Directives on public procurement must also comply with the applicable national law on public procurement.

Subcontracting may cover only a limited part of the action.

The tasks to be subcontracted and the estimated cost for each subcontract must be set out in Annex 1 and the total estimated costs of subcontracting per beneficiary must be set out in Annex 2 (or may be approved ex post in the periodic report, if the use of subcontracting does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants; 'simplified approval procedure').

C. Purchase costs

Purchase costs for the action (including related duties, taxes and charges, such as non-deductible or non-refundable value added tax (VAT)) are eligible if they fulfil the general eligibility conditions and are bought using the beneficiary's usual purchasing practices — provided these ensure purchases with best value for money (or if appropriate the lowest price) and that there is no conflict of interests (see Article 12).

Beneficiaries that are 'contracting authorities/entities' within the meaning of the EU Directives on public procurement must also comply with the applicable national law on public procurement.

C.1 Travel and subsistence

Purchases for **travel, accommodation** and **subsistence** must be calculated as follows:

- travel: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel
- accommodation: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel
- subsistence: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel .

C.2 Equipment

Purchases of **equipment, infrastructure or other assets** used for the action must be declared as depreciation costs, calculated on the basis of the costs actually incurred and written off in accordance with international accounting standards and the beneficiary's usual accounting practices.

Only the portion of the costs that corresponds to the rate of actual use for the action during the action duration can be taken into account.

Costs for **renting or leasing** equipment, infrastructure or other assets are also eligible, if they do not exceed the depreciation costs of similar equipment, infrastructure or assets and do not include any financing fees.

C.3 Other goods, works and services

Purchases of **other goods, works and services** must be calculated on the basis of the costs actually incurred.

Such goods, works and services include, for instance, consumables and supplies, promotion, dissemination, protection of results, translations, publications, certificates and financial guarantees, if required under the Agreement.

D. Other cost categories

D.2 Internally invoiced goods and services

Costs for internally invoiced goods and services directly used for the action may be declared as unit cost according to usual cost accounting practices, if and as declared eligible in the call conditions, if they fulfil the general eligibility conditions for such unit costs and the amount per unit is calculated:

- using the actual costs for the good or service recorded in the beneficiary's accounts, attributed either by direct measurement or on the basis of cost drivers, and excluding any cost which are ineligible or already included in other budget categories; the actual costs may be adjusted on the basis of budgeted or estimated elements, if they are relevant for calculating the costs, reasonable and correspond to objective and verifiable information

and

- according to usual cost accounting practices which are applied in a consistent manner, based on objective criteria, regardless of the source of funding.

'Internally invoiced goods and services' means goods or services which are provided within the beneficiary's organisation directly for the action and which the beneficiary values on the basis of its usual cost accounting practices.

This cost will not be taken into account for the indirect cost flat-rate.

Indirect costs

E. Indirect costs

Indirect costs will be reimbursed at the flat-rate of 25% of the eligible direct costs (categories A-D, except volunteers costs, subcontracting costs, financial support to third parties and exempted specific cost categories, if any).

Contributions

Not applicable

6.3 Ineligible costs and contributions

The following costs or contributions are **ineligible**:

(a) costs or contributions that do not comply with the conditions set out above (Article 6.1 and 6.2), in particular:

(i) costs related to return on capital and dividends paid by a beneficiary

(ii) debt and debt service charges

(iii) provisions for future losses or debts

(iv) interest owed

(v) currency exchange losses

(vi) bank costs charged by the beneficiary's bank for transfers from the granting authority

(vii) excessive or reckless expenditure

(viii) deductible or refundable VAT (including VAT paid by public bodies acting as public authority)

(ix) costs incurred or contributions for activities implemented during grant agreement suspension (see Article 31)

(x) in-kind contributions by third parties: not applicable

(b) costs or contributions declared under other EU grants (or grants awarded by an EU Member State, non-EU country or other body implementing the EU budget), except for the following cases:

(i) Synergy actions: not applicable

(ii) if the action grant is combined with an operating grant[11] running during the same period and the beneficiary can demonstrate that the operating grant does not cover any (direct or indirect) costs of the action grant

(c) costs or contributions for staff of a national (or regional/local) administration, for activities that are part of the administration's normal activities (i.e. not undertaken only because of the grant)

(d) costs or contributions (especially travel and subsistence) for staff or representatives of EU institutions, bodies or agencies

(e) other :

(i) country restrictions for eligible costs: not applicable

(ii) costs or contributions declared specifically ineligible in the call conditions.

6.4 Consequences of non-compliance

If a beneficiary declares costs or contributions that are ineligible, they will be rejected (see Article 27).

This may also lead to other measures described in Chapter 5.

[11] For the definition, see Article 180(2)(b) of EU Financial Regulation 2018/1046: '**operating grant**' means an EU grant to finance "the functioning of a body which has an objective forming part of and supporting an EU policy".

CHAPTER 4 GRANT IMPLEMENTATION

SECTION 1 CONSORTIUM: BENEFICIARIES, AFFILIATED ENTITIES AND OTHER PARTICIPANTS

ARTICLE 7 — BENEFICIARIES

The beneficiaries, as signatories of the Agreement, are fully responsible towards the granting authority for implementing it and for complying with all its obligations.

They must implement the Agreement to their best abilities, in good faith and in accordance with all the obligations and terms and conditions it sets out.

They must have the appropriate resources to implement the action and implement the action under their own responsibility and in accordance with Article 11. If they rely on affiliated entities or other participants (see Articles 8 and 9), they retain sole responsibility towards the granting authority and the other beneficiaries.

They are jointly responsible for the *technical* implementation of the action. If one of the beneficiaries fails to implement their part of the action, the other beneficiaries must ensure that this part is implemented by someone else (without being entitled to an increase of the maximum grant amount and subject to an amendment; see Article 39). The *financial* responsibility of each beneficiary in case of recoveries is governed by Article 22.

The beneficiaries (and their action) must remain eligible under the EU programme funding the grant for the entire duration of the action. Costs and contributions will be eligible only as long as the beneficiary and the action are eligible.

The **internal roles and responsibilities** of the beneficiaries are divided as follows:

(a) Each beneficiary must:

(i) keep information stored in the Portal Participant Register up to date (see Article 19)

(ii) inform the granting authority (and the other beneficiaries) immediately of any events or circumstances likely to affect significantly or delay the implementation of the action (see Article 19)

(iii) submit to the coordinator in good time:

- the prefinancing guarantees (if required; see Article 23)
- the financial statements and certificates on the financial statements (CFS) (if required; see Articles 21 and 24.2 and Data Sheet, Point 4.3)
- the contribution to the deliverables and technical reports (see Article 21)
- any other documents or information required by the granting authority under the Agreement

(iv) submit via the Portal data and information related to the participation of their affiliated entities.

(b) The coordinator must:

(i) monitor that the action is implemented properly (see Article 11)

(ii) act as the intermediary for all communications between the consortium and the granting authority, unless the Agreement or granting authority specifies otherwise, and in particular:

- submit the prefinancing guarantees to the granting authority (if any)
- request and review any documents or information required and verify their quality and completeness before passing them on to the granting authority
- submit the deliverables and reports to the granting authority
- inform the granting authority about the payments made to the other beneficiaries (report on the distribution of payments; if required, see Articles 22 and 32)

(iii) distribute the payments received from the granting authority to the other beneficiaries without unjustified delay (see Article 22).

The coordinator may not delegate or subcontract the above-mentioned tasks to any other beneficiary or third party (including affiliated entities).

However, coordinators which are public bodies may delegate the tasks set out in Point (b)(ii) last indent and (iii) above to entities with 'authorisation to administer' which they have created or which are controlled by or affiliated to them. In this case, the coordinator retains sole responsibility for the payments and for compliance with the obligations under the Agreement.

Moreover, coordinators which are 'sole beneficiaries'[12] (or similar, such as European research infrastructure consortia (ERICs)) may delegate the tasks set out in Point (b)(i) to (iii) above to one of their members. The coordinator retains sole responsibility for compliance with the obligations under the Agreement.

The beneficiaries must have **internal arrangements** regarding their operation and co-ordination, to ensure that the action is implemented properly.

If required by the granting authority (see Data Sheet, Point 1), these arrangements must be set out in a written **consortium agreement** between the beneficiaries, covering for instance:

- the internal organisation of the consortium
- the management of access to the Portal
- different distribution keys for the payments and financial responsibilities in case of recoveries (if any)
- additional rules on rights and obligations related to background and results (see Article 16)

[12] For the definition, see Article 187(2) EU Financial Regulation 2018/1046: "Where several entities satisfy the criteria for being awarded a grant and together form one entity, that entity may be treated as the **sole beneficiary**, including where it is specifically established for the purpose of implementing the action financed by the grant."

- settlement of internal disputes
- liability, indemnification and confidentiality arrangements between the beneficiaries.

The internal arrangements must not contain any provision contrary to this Agreement.

ARTICLE 8 — AFFILIATED ENTITIES

The following entities which are linked to a beneficiary will participate in the action as 'affiliated entities':

- **SLOVENSKA ALZHEIMEROVA SPOLOCNOST (SALS)**, PIC 887301681, linked to NEUROIMUNOLOGICKY USTAV SLOVENSKEJAKADEMIA VIED (NII SAS)

Affiliated entities can charge costs and contributions to the action under the same conditions as the beneficiaries and must implement the action tasks attributed to them in Annex 1 in accordance with Article 11.

Their costs and contributions will be included in Annex 2 and will be taken into account for the calculation of the grant.

The beneficiaries must ensure that all their obligations under this Agreement also apply to their affiliated entities.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the affiliated entities.

Breaches by affiliated entities will be handled in the same manner as breaches by beneficiaries. Recovery of undue amounts will be handled through the beneficiaries.

If the granting authority requires joint and several liability of affiliated entities (see Data Sheet, Point 4.4), they must sign the declaration set out in Annex 3a and may be held liable in case of enforced recoveries against their beneficiaries (see Article 22.2 and 22.4).

ARTICLE 9 — OTHER PARTICIPANTS INVOLVED IN THE ACTION

9.1 Associated partners

The following entities which cooperate with a beneficiary will participate in the action as 'associated partners':

- **JIC, ZAJMOVE SDRUZENI PRAVNICKCH OSOB (JIC)**, PIC 999780262
- **CESKA ALZHEIMEROVSKA SPOLECNOST, OPS (CALS)**, PIC 888747466

Associated partners must implement the action tasks attributed to them in Annex 1 in accordance with Article 11. They may not charge costs or contributions to the action and the costs for their tasks are not eligible.

The tasks must be set out in Annex 1.

The beneficiaries must ensure that their contractual obligations under Articles 11 (proper

implementation), 12 (conflict of interests), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping) also apply to the associated partners.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the associated partners.

9.2 Third parties giving in-kind contributions to the action

Other third parties may give in-kind contributions to the action (i.e. personnel, equipment, other goods, works and services, etc. which are free-of-charge) if necessary for the implementation.

Third parties giving in-kind contributions do not implement any action tasks. They may not charge costs or contributions to the action, but the costs for the in-kind contributions are eligible and may be charged by the beneficiaries which use them, under the conditions set out in Article 6. The costs will be included in Annex 2 as part of the beneficiaries' costs.

The third parties and their in-kind contributions should be set out in Annex 1.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the third parties giving in-kind contributions.

9.3 Subcontractors

Subcontractors may participate in the action, if necessary for the implementation.

Subcontractors must implement their action tasks in accordance with Article 11. The costs for the subcontracted tasks (invoiced price from the subcontractor) are eligible and may be charged by the beneficiaries, under the conditions set out in Article 6. The costs will be included in Annex 2 as part of the beneficiaries' costs.

The beneficiaries must ensure that their contractual obligations under Articles 11 (proper implementation), 12 (conflict of interest), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping) also apply to the subcontractors.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the subcontractors.

9.4 Recipients of financial support to third parties

If the action includes providing financial support to third parties (e.g. grants, prizes or similar forms of support), the beneficiaries must ensure that their contractual obligations under Articles 12 (conflict of interest), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping)also apply to the third parties receiving the support (recipients).

The beneficiaries must also ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the recipients.

ARTICLE 10 — PARTICIPANTS WITH SPECIAL STATUS

10.1 Non-EU participants

Participants which are established in a non-EU country (if any) undertake to comply with their obligations under the Agreement and:

- to respect general principles (including fundamental rights, values and ethical principles, environmental and labour standards, rules on classified information, intellectual property rights, visibility of funding and protection of personal data)

- for the submission of certificates under Article 24: to use qualified external auditors which are independent and comply with comparable standards as those set out in EU Directive 2006/43/EC[13]

- for the controls under Article 25: to allow for checks, reviews, audits and investigations (including on-the-spot checks, visits and inspections) by the bodies mentioned in that Article (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.).

Special rules on dispute settlement apply (see Data Sheet, Point 5).

10.2 Participants which are international organisations

Participants which are international organisations (IOs; if any) undertake to comply with their obligations under the Agreement and:

- to respect general principles (including fundamental rights, values and ethical principles, environmental and labour standards, rules on classified information, intellectual property rights, visibility of funding and protection of personal data)

- for the submission of certificates under Article 24: to use either independent public officers or external auditors which comply with comparable standards as those set out in EU Directive 2006/43/EC

- for the controls under Article 25: to allow for the checks, reviews, audits and investigations by the bodies mentioned in that Article, taking into account the specific agreements concluded by them and the EU (if any).

For such participants, nothing in the Agreement will be interpreted as a waiver of their privileges or immunities, as accorded by their constituent documents or international law.

Special rules on applicable law and dispute settlement apply (see Article 43 and Data Sheet, Point 5).

10.3 Pillar-assessed participants

Pillar-assessed participants (if any) may rely on their own systems, rules and procedures, in so far as they have been positively assessed and do not call into question the decision awarding the grant or breach the principle of equal treatment of applicants or beneficiaries.

[13] Directive 2006/43/EC of the European Parliament and of the Council of 17 May 2006 on statutory audits of annual accounts and consolidated accounts or similar national regulations (OJ L 157, 9.6.2006, p. 87).

'Pillar-assessment' means a review by the European Commission on the systems, rules and procedures which participants use for managing EU grants (in particular internal control system, accounting system, external audits, financing of third parties, rules on recovery and exclusion, information on recipients and protection of personal data; see Article 154 EU Financial Regulation 2018/1046).

Participants with a positive pillar assessment may rely on their own systems, rules and procedures, in particular for:

- record-keeping (Article 20): may be done in accordance with internal standards, rules and procedures
- currency conversion for financial statements (Article 21): may be done in accordance with usual accounting practices
- guarantees (Article 23): for public law bodies, prefinancing guarantees are not needed
- certificates (Article 24):
    - certificates on the financial statements (CFS): may be provided by their regular internal or external auditors and in accordance with their internal financial regulations and procedures
    - certificates on usual accounting practices (CoMUC): are not needed if those practices are covered by an ex-ante assessment

and use the following specific rules, for:

- recoveries (Article 22): in case of financial support to third parties, there will be no recovery if the participant has done everything possible to retrieve the undue amounts from the third party receiving the support (including legal proceedings) and non-recovery is not due to an error or negligence on its part
- checks, reviews, audits and investigations by the EU (Article 25): will be conducted taking into account the rules and procedures specifically agreed between them and the framework agreement (if any)
- impact evaluation (Article 26): will be conducted in accordance with the participant's internal rules and procedures and the framework agreement (if any)
- grant agreement suspension (Article 31): certain costs incurred during grant suspension are eligible (notably, minimum costs necessary for a possible resumption of the action and costs relating to contracts which were entered into before the pre-information letter was received and which could not reasonably be suspended, reallocated or terminated on legal grounds)
- grant agreement termination (Article 32): the final grant amount and final payment will be calculated taking into account also costs relating to contracts due for execution only after termination takes effect, if the contract was entered into before the pre-information letter was received and could not reasonably be terminated on legal grounds
- liability for damages (Article 33.2): the granting authority must be compensated for damage it sustains as a result of the implementation of the action or because the action was not implemented in full compliance with the Agreement only if the damage is due to an

infringement of the participant's internal rules and procedures or due to a violation of third parties' rights by the participant or one of its employees or individual for whom the employees are responsible.

Participants whose pillar assessment covers procurement and granting procedures may also do purchases, subcontracting and financial support to third parties (Article 6.2) in accordance with their internal rules and procedures for purchases, subcontracting and financial support.

Participants whose pillar assessment covers data protection rules may rely on their internal standards, rules and procedures for data protection (Article 15).

The participants may however not rely on provisions which would breach the principle of equal treatment of applicants or beneficiaries or call into question the decision awarding the grant, such as in particular:

- eligibility (Article 6)
- consortium roles and set-up (Articles 7-9)
- security and ethics (Articles 13, 14)
- IPR (including background and results, access rights and rights of use), communication, dissemination and visibility (Articles 16 and 17)
- information obligation (Article 19)
- payment, reporting and amendments (Articles 21, 22 and 39)
- rejections, reductions, suspensions and terminations (Articles 27, 28, 29-32)

If the pillar assessment was subject to remedial measures, reliance on the internal systems, rules and procedures is subject to compliance with those remedial measures.

Participants whose assessment has not yet been updated to cover (the new rules on) data protection may rely on their internal systems, rules and procedures, provided that they ensure that personal data is:

- processed lawfully, fairly and in a transparent manner in relation to the data subject
- collected for specified, explicit and legitimate purposes and not further processed in a manner that is incompatible with those purposes
- adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed
- accurate and, where necessary, kept up to date
- kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the data is processed and
- processed in a manner that ensures appropriate security of the personal data.

Participants must inform the coordinator without delay of any changes to the systems, rules and

procedures that were part of the pillar assessment. The coordinator must immediately inform the granting authority.

Pillar-assessed participants that have also concluded a framework agreement with the EU, may moreover — under the same conditions as those above (i.e. not call into question the decision awarding the grant or breach the principle of equal treatment of applicants or beneficiaries) — rely on the provisions set out in that framework agreement.

SECTION 2 RULES FOR CARRYING OUT THE ACTION

ARTICLE 11 — PROPER IMPLEMENTATION OF THE ACTION

11.1 Obligation to properly implement the action

The beneficiaries must implement the action as described in Annex 1 and in compliance with the provisions of the Agreement, the call conditions and all legal obligations under applicable EU, international and national law.

11.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 12 — CONFLICT OF INTERESTS

12.1 Conflict of interests

The beneficiaries must take all measures to prevent any situation where the impartial and objective implementation of the Agreement could be compromised for reasons involving family, emotional life, political or national affinity, economic interest or any other direct or indirect interest (‘conflict of interests’).

They must formally notify the granting authority without delay of any situation constituting or likely to lead to a conflict of interests and immediately take all the necessary steps to rectify this situation.

The granting authority may verify that the measures taken are appropriate and may require additional measures to be taken by a specified deadline.

12.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28) and the grant or the beneficiary may be terminated (see Article 32).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 13 — CONFIDENTIALITY AND SECURITY

13.1 Sensitive information

The parties must keep confidential any data, documents or other material (in any form) that is identified as sensitive in writing ('sensitive information') — during the implementation of the action and for at least until the time-limit set out in the Data Sheet (see Point 6).

If a beneficiary requests, the granting authority may agree to keep such information confidential for a longer period.

Unless otherwise agreed between the parties, they may use sensitive information only to implement the Agreement.

The beneficiaries may disclose sensitive information to their personnel or other participants involved in the action only if they:

(a) need to know it in order to implement the Agreement and

(b) are bound by an obligation of confidentiality.

The granting authority may disclose sensitive information to its staff and to other EU institutions and bodies.

It may moreover disclose sensitive information to third parties, if:

(a) this is necessary to implement the Agreement or safeguard the EU financial interests and

(b) the recipients of the information are bound by an obligation of confidentiality.

The confidentiality obligations no longer apply if:

(a) the disclosing party agrees to release the other party

(b) the information becomes publicly available, without breaching any confidentiality obligation

(c) the disclosure of the sensitive information is required by EU, international or national law.

Specific confidentiality rules (if any) are set out in Annex 5.

13.2 Classified information

The parties must handle classified information in accordance with the applicable EU, international or national law on classified information (in particular, Decision 2015/444[14] and its implementing rules).

Deliverables which contain classified information must be submitted according to special procedures agreed with the granting authority.

Action tasks involving classified information may be subcontracted only after explicit approval (in writing) from the granting authority.

Classified information may not be disclosed to any third party (including participants involved in the action implementation) without prior explicit written approval from the granting authority.

[14] Commission Decision 2015/444/EC, Euratom of 13 March 2015 on the security rules for protecting EU classified information (OJ L 72, 17.3.2015, p. 53).

Specific security rules (if any) are set out in Annex 5.

13.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 14 — ETHICS AND VALUES

14.1 Ethics

The action must be carried out in line with the highest ethical standards and the applicable EU, international and national law on ethical principles.

Specific ethics rules (if any) are set out in Annex 5.

14.2 Values

The beneficiaries must commit to and ensure the respect of basic EU values (such as respect for human dignity, freedom, democracy, equality, the rule of law and human rights, including the rights of minorities).

Specific rules on values (if any) are set out in Annex 5.

14.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 15 — DATA PROTECTION

15.1 Data processing by the granting authority

Any personal data under the Agreement will be processed under the responsibility of the data controller of the granting authority in accordance with and for the purposes set out in the Portal Privacy Statement.

For grants where the granting authority is the European Commission, an EU regulatory or executive agency, joint undertaking or other EU body, the processing will be subject to Regulation 2018/1725[15].

15.2 Data processing by the beneficiaries

[15] Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC (OJ L 295, 21.11.2018, p. 39).

The beneficiaries must process personal data under the Agreement in compliance with the applicable EU, international and national law on data protection (in particular, Regulation 2016/679[16]).

They must ensure that personal data is:

- processed lawfully, fairly and in a transparent manner in relation to the data subjects
- collected for specified, explicit and legitimate purposes and not further processed in a manner that is incompatible with those purposes
- adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed
- accurate and, where necessary, kept up to date
- kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the data is processed and
- processed in a manner that ensures appropriate security of the data.

The beneficiaries may grant their personnel access to personal data only if it is strictly necessary for implementing, managing and monitoring the Agreement. The beneficiaries must ensure that the personnel is under a confidentiality obligation.

The beneficiaries must inform the persons whose data are transferred to the granting authority and provide them with the Portal Privacy Statement.

15.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 16 — INTELLECTUAL PROPERTY RIGHTS (IPR) — BACKGROUND AND RESULTS —ACCESS RIGHTS AND RIGHTS OF USE

16.1 Background and access rights to background

The beneficiaries must give each other and the other participants access to the background identified as needed for implementing the action, subject to any specific rules in Annex 5.

'Background' means any data, know-how or information — whatever its form or nature (tangible or intangible), including any rights such as intellectual property rights — that is:

(a) held by the beneficiaries before they acceded to the Agreement and

(b) needed to implement the action or exploit the results.

[16] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC ('GDPR') (OJ L 119, 4.5.2016, p. 1).

If background is subject to rights of a third party, the beneficiary concerned must ensure that it is able to comply with its obligations under the Agreement.

16.2 Ownership of results

The granting authority does not obtain ownership of the results produced under the action.

'Results' means any tangible or intangible effect of the action, such as data, know-how or information, whatever its form or nature, whether or not it can be protected, as well as any rights attached to it, including intellectual property rights.

16.3 Rights of use of the granting authority on materials, documents and information received for policy, information, communication, dissemination and publicity purposes

The granting authority has the right to use non-sensitive information relating to the action and materials and documents received from the beneficiaries (notably summaries for publication, deliverables, as well as any other material, such as pictures or audio-visual material, in paper or electronic form) for policy, information, communication, dissemination and publicity purposes — during the action or afterwards.

The right to use the beneficiaries' materials, documents and information is granted in the form of a royalty-free, non-exclusive and irrevocable licence, which includes the following rights:

(a) **use for its own purposes** (in particular, making them available to persons working for the granting authority or any other EU service (including institutions, bodies, offices, agencies, etc.) or EU Member State institution or body; copying or reproducing them in whole or in part, in unlimited numbers; and communication through press information services)

(b) **distribution to the public** (in particular, publication as hard copies and in electronic or digital format, publication on the internet, as a downloadable or non-downloadable file, broadcasting by any channel, public display or presentation, communicating through press information services, or inclusion in widely accessible databases or indexes)

(c) **editing or redrafting** (including shortening, summarising, inserting other elements (e.g. meta-data, legends, other graphic, visual, audio or text elements), extracting parts (e.g. audio or video files), dividing into parts, use in a compilation)

(d) **translation**

(e) **storage** in paper, electronic or other form

(f) **archiving**, in line with applicable document-management rules

(g) the right to authorise **third parties** to act on its behalf or sub-license to third parties the modes of use set out in Points (b), (c), (d) and (f), if needed for the information, communication and publicity activity of the granting authority

(h) **processing**, analysing, aggregating the materials, documents and information received and **producing derivative works**.

The rights of use are granted for the whole duration of the industrial or intellectual property rights concerned.

If materials or documents are subject to moral rights or third party rights (including intellectual property rights or rights of natural persons on their image and voice), the beneficiaries must ensure that they comply with their obligations under this Agreement (in particular, by obtaining the necessary licences and authorisations from the rights holders concerned).

Where applicable, the granting authority will insert the following information:

> "© – [year] – [name of the copyright owner]. All rights reserved. Licensed to the [name of granting authority] under conditions."

16.4 Specific rules on IPR, results and background

Specific rules regarding intellectual property rights, results and background (if any) are set out in Annex 5.

16.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such a breach may also lead to other measures described in Chapter 5.

ARTICLE 17 — COMMUNICATION, DISSEMINATION AND VISIBILITY

17.1 Communication — Dissemination — Promoting the action

Unless otherwise agreed with the granting authority, the beneficiaries must promote the action and its results by providing targeted information to multiple audiences (including the media and the public), in accordance with Annex 1 and in a strategic, coherent and effective manner.

Before engaging in a communication or dissemination activity expected to have a major media impact, the beneficiaries must inform the granting authority.

17.2 Visibility — European flag and funding statement

Unless otherwise agreed with the granting authority, communication activities of the beneficiaries related to the action (including media relations, conferences, seminars, information material, such as brochures, leaflets, posters, presentations, etc., in electronic form, via traditional or social media, etc.), dissemination activities and any infrastructure, equipment, vehicles, supplies or major result funded by the grant must acknowledge EU support and display the European flag (emblem) and funding statement (translated into local languages, where appropriate):

The emblem must remain distinct and separate and cannot be modified by adding other visual marks, brands or text.

Apart from the emblem, no other visual identity or logo may be used to highlight the EU support.

When displayed in association with other logos (e.g. of beneficiaries or sponsors), the emblem must be displayed at least as prominently and visibly as the other logos.

For the purposes of their obligations under this Article, the beneficiaries may use the emblem without first obtaining approval from the granting authority. This does not, however, give them the right to exclusive use. Moreover, they may not appropriate the emblem or any similar trademark or logo, either by registration or by any other means.

17.3 Quality of information — Disclaimer

Any communication or dissemination activity related to the action must use factually accurate information.

Moreover, it must indicate the following disclaimer (translated into local languages where appropriate):

> "Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or [name of the granting authority]. Neither the European Union nor the granting authority can be held responsible for them."

17.4 Specific communication, dissemination and visibility rules

Specific communication, dissemination and visibility rules (if any) are set out in Annex 5.

17.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 18 — SPECIFIC RULES FOR CARRYING OUT THE ACTION

18.1 Specific rules for carrying out the action

Specific rules for implementing the action (if any) are set out in Annex 5.

18.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such a breach may also lead to other measures described in Chapter 5.

SECTION 3 GRANT ADMINISTRATION

ARTICLE 19 — GENERAL INFORMATION OBLIGATIONS

19.1 Information requests

The beneficiaries must provide — during the action or afterwards and in accordance with Article 7 — any information requested in order to verify eligibility of the costs or contributions declared, proper implementation of the action and compliance with the other obligations under the Agreement.

The information provided must be accurate, precise and complete and in the format requested, including electronic format.

19.2 Participant Register data updates

The beneficiaries must keep — at all times, during the action or afterwards — their information stored in the Portal Participant Register up to date, in particular, their name, address, legal representatives, legal form and organisation type.

19.3 Information about events and circumstances which impact the action

The beneficiaries must immediately inform the granting authority (and the other beneficiaries) of any of the following:

(a) **events** which are likely to affect or delay the implementation of the action or affect the EU's financial interests, in particular:

(i) changes in their legal, financial, technical, organisational or ownership situation (including changes linked to one of the exclusion grounds listed in the declaration of honour signed before grant signature)

(ii) linked action information: not applicable

(b) **circumstances** affecting:

(i) the decision to award the grant or

(ii) compliance with requirements under the Agreement.

19.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 20 — RECORD-KEEPING

20.1 Keeping records and supporting documents

The beneficiaries must — at least until the time-limit set out in the Data Sheet (see Point 6) — keep records and other supporting documents to prove the proper implementation of the action in line with the accepted standards in the respective field (if any).

In addition, the beneficiaries must — for the same period — keep the following to justify the amounts declared:

(a) for actual costs: adequate records and supporting documents to prove the costs declared (such as contracts, subcontracts, invoices and accounting records); in addition, the beneficiaries' usual accounting and internal control procedures must enable direct reconciliation between the amounts declared, the amounts recorded in their accounts and the amounts stated in the supporting documents

(b) for flat-rate costs and contributions (if any): adequate records and supporting documents to prove the eligibility of the costs or contributions to which the flat-rate is applied

(c) for the following simplified costs and contributions: the beneficiaries do not need to keep specific records on the actual costs incurred, but must keep:

  (i) for unit costs and contributions (if any): adequate records and supporting documents to prove the number of units declared

  (ii) for lump sum costs and contributions (if any): adequate records and supporting documents to prove proper implementation of the work as described in Annex 1

  (iii) for financing not linked to costs (if any): adequate records and supporting documents to prove the achievement of the results or the fulfilment of the conditions as described in Annex 1

(d) for unit, flat-rate and lump sum costs and contributions according to usual cost accounting practices (if any): the beneficiaries must keep any adequate records and supporting documents to prove that their cost accounting practices have been applied in a consistent manner, based on objective criteria, regardless of the source of funding, and that they comply with the eligibility conditions set out in Articles 6.1 and 6.2.

Moreover, the following is needed for specific budget categories:

(e) for personnel costs: time worked for the beneficiary under the action must be supported by declarations signed monthly by the person and their supervisor, unless another reliable time-record system is in place; the granting authority may accept alternative evidence supporting the time worked for the action declared, if it considers that it offers an adequate level of assurance

(f) additional record-keeping rules: not applicable

The records and supporting documents must be made available upon request (see Article 19) or in the context of checks, reviews, audits or investigations (see Article 25).

If there are on-going checks, reviews, audits, investigations, litigation or other pursuits of claims under the Agreement (including the extension of findings; see Article 25), the beneficiaries must keep these records and other supporting documentation until the end of these procedures.

The beneficiaries must keep the original documents. Digital and digitalised documents are considered originals if they are authorised by the applicable national law. The granting authority may accept non-original documents if they offer a comparable level of assurance.

20.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, costs or contributions insufficiently substantiated will be ineligible (see Article 6) and will be rejected (see Article 27), and the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 21 — REPORTING

21.1 Continuous reporting

The beneficiaries must continuously report on the progress of the action (e.g. **deliverables, milestones, outputs/outcomes, critical risks, indicators,** etc; if any), in the Portal Continuous Reporting tool and in accordance with the timing and conditions it sets out (as agreed with the granting authority).

Standardised deliverables (e.g. progress reports not linked to payments, reports on cumulative expenditure, special reports, etc; if any) must be submitted using the templates published on the Portal.

21.2 Periodic reporting: Technical reports and financial statements

In addition, the beneficiaries must provide reports to request payments, in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2):

- for additional prefinancings (if any): an **additional prefinancing report**
- for interim payments (if any) and the final payment: a **periodic report**.

The prefinancing and periodic reports include a technical and financial part.

The technical part includes an overview of the action implementation. It must be prepared using the template available in the Portal Periodic Reporting tool.

The financial part of the additional prefinancing report includes a statement on the use of the previous prefinancing payment.

The financial part of the periodic report includes:

- the financial statements (individual and consolidated; for all beneficiaries/affiliated entities)
- the explanation on the use of resources (or detailed cost reporting table, if required)
- the certificates on the financial statements (CFS) (if required; see Article 24.2 and Data Sheet, Point 4.3).

The **financial statements** must detail the eligible costs and contributions for each budget category and, for the final payment, also the revenues for the action (see Articles 6 and 22).

All eligible costs and contributions incurred should be declared, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Amounts that are not declared in the individual financial statements will not be taken into account by the granting authority.

By signing the financial statements (directly in the Portal Periodic Reporting tool), the beneficiaries confirm that:

- the information provided is complete, reliable and true
- the costs and contributions declared are eligible (see Article 6)
- the costs and contributions can be substantiated by adequate records and supporting documents (see Article 20) that will be produced upon request (see Article 19) or in the context of checks, reviews, audits and investigations (see Article 25)
- for the final periodic report: all the revenues have been declared (if required; see Article 22).

Beneficiaries will have to submit also the financial statements of their affiliated entities (if any). In case of recoveries (see Article 22), beneficiaries will be held responsible also for the financial statements of their affiliated entities.

21.3 Currency for financial statements and conversion into euros

The financial statements must be drafted in euro.

Beneficiaries with general accounts established in a currency other than the euro must convert the costs recorded in their accounts into euro, at the average of the daily exchange rates published in the C series of the *Official Journal of the European Union* (ECB website), calculated over the corresponding reporting period.

If no daily euro exchange rate is published in the *Official Journal* for the currency in question, they must be converted at the average of the monthly accounting exchange rates published on the European Commission website (InforEuro), calculated over the corresponding reporting period.

Beneficiaries with general accounts in euro must convert costs incurred in another currency into euro according to their usual accounting practices.

21.4 Reporting language

The reporting must be in the language of the Agreement, unless otherwise agreed with the granting authority (see Data Sheet, Point 4.2).

21.5 Consequences of non-compliance

If a report submitted does not comply with this Article, the granting authority may suspend the payment deadline (see Article 29) and apply other measures described in Chapter 5.

If the coordinator breaches its reporting obligations, the granting authority may terminate the grant or the coordinator's participation (see Article 32) or apply other measures described in Chapter 5.

ARTICLE 22 — PAYMENTS AND RECOVERIES — CALCULATION OF AMOUNTS DUE

22.1 Payments and payment arrangements

Payments will be made in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2).

They will be made in euro to the bank account indicated by the coordinator (see Data Sheet, Point 4.2) and must be distributed without unjustified delay (restrictions may apply to distribution of the initial prefinancing payment; see Data Sheet, Point 4.2).

Payments to this bank account will discharge the granting authority from its payment obligation.

The cost of payment transfers will be borne as follows:

- the granting authority bears the cost of transfers charged by its bank
- the beneficiary bears the cost of transfers charged by its bank
- the party causing a repetition of a transfer bears all costs of the repeated transfer.

Payments by the granting authority will be considered to have been carried out on the date when they are debited to its account.

22.2 Recoveries

Recoveries will be made, if — at beneficiary termination, final payment or afterwards — it turns out that the granting authority has paid too much and needs to recover the amounts undue.

Each beneficiary's financial responsibility in case of recovery is in principle limited to their own debt and undue amounts of their affiliated entities.

In case of enforced recoveries (see Article 22.4), affiliated entities will be held liable for repaying debts of their beneficiaries, if required by the granting authority (see Data Sheet, Point 4.4).

22.3 Amounts due

22.3.1 Prefinancing payments

The aim of the prefinancing is to provide the beneficiaries with a float.

It remains the property of the EU until the final payment.

For **initial prefinancings** (if any), the amount due, schedule and modalities are set out in the Data Sheet (see Point 4.2).

For **additional prefinancings** (if any), the amount due, schedule and modalities are also set out in the Data Sheet (see Point 4.2). However, if the statement on the use of the previous prefinancing payment shows that less than 70% was used, the amount set out in the Data Sheet will be reduced by the difference between the 70% threshold and the amount used.

The contribution to the Mutual Insurance Mechanism will be retained from the prefinancing payments (at the rate and in accordance with the modalities set out in the Data Sheet, see Point 4.2) and transferred to the Mechanism.

Prefinancing payments (or parts of them) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

22.3.2 Amount due at beneficiary termination — Recovery

In case of beneficiary termination, the granting authority will determine the provisional amount due for the beneficiary concerned. Payments (if any) will be made with the next interim or final payment.

The **amount due** will be calculated in the following step:

Step 1 — Calculation of the total accepted EU contribution

Step 1 — Calculation of the total accepted EU contribution

The granting authority will first calculate the 'accepted EU contribution' for the beneficiary for all reporting periods, by calculating the 'maximum EU contribution to costs' (applying the funding rate to the accepted costs of the beneficiary), taking into account requests for a lower contribution to costs and CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions (if any). The resulting amount is the 'total accepted EU contribution' for the beneficiary.

The **balance** is then calculated by deducting the payments received (if any; see report on the distribution of payments in Article 32), from the total accepted EU contribution:

{total accepted EU contribution for the beneficiary

minus

{prefinancing and interim payments received (if any)}}.

If the balance is **positive**, the amount will be included in the next interim or final payment to the consortium.

If the balance is **negative**, it will be **recovered** in accordance with the following procedure:

The granting authority will send a **pre-information letter** to the beneficiary concerned:

- formally notifying the intention to recover, the amount due, the amount to be recovered and the reasons why and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received), it will confirm the amount to be recovered and ask this amount to be paid to the coordinator (**confirmation letter**).

If payment is not made to the coordinator by the date specified in the confirmation letter, the granting authority may call on the Mutual Insurance Mechanism to intervene, if continuation of the action is guaranteed and the conditions set out in the rules governing the Mechanism are met.

In this case, it will send a **beneficiary recovery letter**, together with a **debit note** with the terms and date for payment.

The debit note for the beneficiary will include the amount calculated for the affiliated entities which also had to end their participation (if any).

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

The amounts will later on also be taken into account for the next interim or final payment.

22.3.3 Interim payments

Interim payments reimburse the eligible costs and contributions claimed for the implementation of the action during the reporting periods (if any).

Interim payments (if any) will be made in accordance with the schedule and modalities set out the Data Sheet (see Point 4.2).

Payment is subject to the approval of the periodic report. Its approval does not imply recognition of compliance, authenticity, completeness or correctness of its content.

The **interim payment** will be calculated by the granting authority in the following steps:

Step 1 — Calculation of the total accepted EU contribution

Step 2 — Limit to the interim payment ceiling

Step 1 — Calculation of the total accepted EU contribution

The granting authority will calculate the ‘accepted EU contribution’ for the action for the reporting period, by first calculating the ‘maximum EU contribution to costs’ (applying the funding rate to the accepted costs of each beneficiary), taking into account requests for a lower contribution to costs, and CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions from beneficiary termination (if any). The resulting amount is the 'total accepted EU contribution'.

Step 2 — Limit to the interim payment ceiling

The resulting amount is then capped to ensure that the total amount of prefinancing and interim payments (if any) does not exceed the interim payment ceiling set out in the Data Sheet (see Point 4.2).

Interim payments (or parts of them) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

22.3.4 Final payment — Final grant amount — Revenues and Profit — Recovery

The final payment (payment of the balance) reimburses the remaining part of the eligible costs and contributions claimed for the implementation of the action (if any).

The final payment will be made in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2).

Payment is subject to the approval of the final periodic report. Its approval does not imply recognition of compliance, authenticity, completeness or correctness of its content.

The **final grant amount for the action** will be calculated in the following steps:

Step 1 — Calculation of the total accepted EU contribution

Step 2 — Limit to the maximum grant amount

Step 3 — Reduction due to the no-profit rule

Step 1 — Calculation of the total accepted EU contribution

The granting authority will first calculate the 'accepted EU contribution' for the action for all reporting periods, by calculating the 'maximum EU contribution to costs' (applying the funding rate to the total accepted costs of each beneficiary), taking into account requests for a lower contribution to costs, CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions (if any). The resulting amount is the 'total accepted EU contribution'.

Step 2 — Limit to the maximum grant amount

If the resulting amount is higher than the maximum grant amount set out in Article 5.2, it will be limited to the latter.

Step 3 — Reduction due to the no-profit rule

If the no-profit rule is provided for in the Data Sheet (see Point 4.2), the grant must not produce a profit (i.e. surplus of the amount obtained following Step 2 plus the action's revenues, over the eligible costs and contributions approved by the granting authority).

'Revenue' is all income generated by the action, during its duration (see Article 4), for beneficiaries that are profit legal entities (— with the exception of income generated by the exploitation of results, which are not considered as revenues).

If there is a profit, it will be deducted in proportion to the final rate of reimbursement of the eligible costs approved by the granting authority (as compared to the amount calculated following Steps 1 and 2 minus the contributions).

The **balance** (final payment) is then calculated by deducting the total amount of prefinancing and interim payments already made (if any), from the final grant amount:

{final grant amount

minus

{prefinancing and interim payments made (if any)}}.

If the balance is **positive**, it will be **paid** to the coordinator.

The amount retained for the Mutual Insurance Mechanism (see above) will be released and **paid** to the coordinator (in accordance with the rules governing the Mechanism).

The final payment (or part of it) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

If — despite the release of the Mutual Insurance Mechanism contribution — the balance is **negative**, it will be **recovered** in accordance with the following procedure:

The granting authority will send a **pre-information letter** to the coordinator:

- formally notifying the intention to recover, the final grant amount, the amount to be recovered and the reasons why
- requesting a report on the distribution of payments to the beneficiaries within 30 days of receiving notification and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received) and the coordinator has submitted the report on the distribution of payments, it will calculate the **share of the debt per beneficiary**, by:

(a) identifying the beneficiaries for which the amount calculated as follows is negative:

{{{total accepted EU contribution for the beneficiary

divided by

total accepted EU contribution for the action}

multiplied by

final grant amount for the action},

minus

{prefinancing and interim payments received by the beneficiary (if any)}}

and

(b) dividing the debt:

{{amount calculated according to point (a) for the beneficiary concerned

divided by

the sum of the amounts calculated according to point (a) for all the beneficiaries identified according to point (a)}

multiplied by

the amount to be recovered}.

and confirm the amount to be recovered from each beneficiary concerned (**confirmation letter**), together with **debit notes** with the terms and date for payment.

The debit notes for beneficiaries will include the amounts calculated for their affiliated entities (if any).

If the coordinator has not submitted the report on the distribution of payments, the granting authority will **recover** the full amount from the coordinator (**confirmation letter** and **debit note** with the terms and date for payment).

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

22.3.5 Audit implementation after final payment — Revised final grant amount — Recovery

If — after the final payment (in particular, after checks, reviews, audits or investigations; see Article 25) — the granting authority rejects costs or contributions (see Article 27) or reduces the grant (see Article 28), it will calculate the **revised final grant amount** for the beneficiary concerned.

The **beneficiary revised final grant amount** will be calculated in the following step:

Step 1 — Calculation of the revised total accepted EU contribution

Step 1 — Calculation of the revised total accepted EU contribution

The granting authority will first calculate the ‘revised accepted EU contribution’ for the beneficiary, by calculating the ‘revised accepted costs’ and ‘revised accepted contributions’.

After that, it will take into account grant reductions (if any). The resulting 'revised total accepted EU contribution' is the beneficiary revised final grant amount.

If the revised final grant amount is lower than the beneficiary's final grant amount (i.e. its share in the final grant amount for the action), it will be **recovered** in accordance with the following procedure:

The **beneficiary final grant amount** (i.e. share in the final grant amount for the action) is calculated as follows:

{{total accepted EU contribution for the beneficiary

divided by

total accepted EU contribution for the action}

multiplied by

final grant amount for the action}.

The granting authority will send a **pre-information letter** to the beneficiary concerned:

- formally notifying the intention to recover, the amount to be recovered and the reasons why and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received), it will confirm the amount to be recovered (**confirmation letter**), together with a **debit note** with the terms and the date for payment.

Recoveries against affiliated entities (if any) will be handled through their beneficiaries.

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

22.4 Enforced recovery

If payment is not made by the date specified in the debit note, the amount due will be recovered:

(a) by offsetting the amount — without the coordinator or beneficiary's consent — against any amounts owed to the coordinator or beneficiary by the granting authority.

In exceptional circumstances, to safeguard the EU financial interests, the amount may be offset before the payment date specified in the debit note.

For grants where the granting authority is the European Commission or an EU executive agency, debts may also be offset against amounts owed by other Commission services or executive agencies.

(b) financial guarantee(s): not applicable

(c) joint and several liability of beneficiaries: not applicable

(d) by holding affiliated entities jointly and severally liable (if any, see Data Sheet, Point 4.4)

(e) by taking legal action (see Article 43) or, provided that the granting authority is the European

Commission or an EU executive agency, by adopting an enforceable decision under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 100(2) of EU Financial Regulation 2018/1046.

If the Mutual Insurance Mechanism was called on by the granting authority to intervene, recovery will be continued in the name of the Mutual Insurance Mechanism. If two debit notes were sent, the second one (in the name of the Mutual Insurance Mechanism) will be considered to replace the first one (in the name of the granting authority). Where the MIM intervened, offsetting, enforceable decisions or any other of the above-mentioned forms of enforced recovery may be used mutatis mutandis.

The amount to be recovered will be increased by **late-payment interest** at the rate set out in Article 22.5, from the day following the payment date in the debit note, up to and including the date the full payment is received.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2015/2366[17] applies.

For grants where the granting authority is an EU executive agency, enforced recovery by offsetting or enforceable decision will be done by the services of the European Commission (see also Article 43).

22.5 Consequences of non-compliance

22.5.1 If the granting authority does not pay within the payment deadlines (see above), the beneficiaries are entitled to **late-payment interest** at the rate applied by the European Central Bank (ECB) for its main refinancing operations in euros ('reference rate'), plus the rate specified in the Data Sheet (Point 4.2). The reference rate is the rate in force on the first day of the month in which the payment deadline expires, as published in the C series of the *Official Journal of the European Union*.

If the late-payment interest is lower than or equal to EUR 200, it will be paid to the coordinator only on request submitted within two months of receiving the late payment.

Late-payment interest is not due if all beneficiaries are EU Member States (including regional and local government authorities or other public bodies acting on behalf of a Member State for the purpose of this Agreement).

If payments or the payment deadline are suspended (see Articles 29 and 30), payment will not be considered as late.

Late-payment interest covers the period running from the day following the due date for payment (see above), up to and including the date of payment.

Late-payment interest is not considered for the purposes of calculating the final grant amount.

22.5.2 If the coordinator breaches any of its obligations under this Article, the grant may be reduced (see Article 29) and the grant or the coordinator may be terminated (see Article 32).

[17] Directive (EU) 2015/2366 of the European Parliament and of the Council of 25 November 2015 on payment services in the internal market, amending Directives 2002/65/EC, 2009/110/EC and 2013/36/EU and Regulation (EU) No 1093/2010, and repealing Directive 2007/64/EC (OJ L 337, 23.12.2015, p. 35).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 23 — GUARANTEES

Not applicable

ARTICLE 24 — CERTIFICATES

24.1 Operational verification report (OVR)

Not applicable

24.2 Certificate on the financial statements (CFS)

If required by the granting authority (see Data Sheet, Point 4.3), the beneficiaries must provide certificates on their financial statements (CFS), in accordance with the schedule, threshold and conditions set out in the Data Sheet.

The coordinator must submit them as part of the periodic report (see Article 21).

The certificates must be drawn up using the template published on the Portal, cover the costs declared on the basis of actual costs and costs according to usual cost accounting practices (if any), and fulfil the following conditions:

(a) be provided by a qualified approved external auditor which is independent and complies with Directive 2006/43/EC[18] (or for public bodies: by a competent independent public officer)

(b) the verification must be carried out according to the highest professional standards to ensure that the financial statements comply with the provisions under the Agreement and that the costs declared are eligible.

The certificates will not affect the granting authority's right to carry out its own checks, reviews or audits, nor preclude the European Court of Auditors (ECA), the European Public Prosecutor's Office (EPPO) or the European Anti-Fraud Office (OLAF) from using their prerogatives for audits and investigations under the Agreement (see Article 25).

If the costs (or a part of them) were already audited by the granting authority, these costs do not need to be covered by the certificate and will not be counted for calculating the threshold (if any).

24.3 Certificate on the compliance of usual cost accounting practices (CoMUC)

Not applicable

24.4 Systems and process audit (SPA)

Beneficiaries which:

[18] Directive 2006/43/EC of the European Parliament and of the Council of 17 May 2006 on statutory audits of annual accounts and consolidated accounts or similar national regulations (OJ L 157, 9.6.2006, p. 87).

- use unit, flat rate or lump sum costs or contributions according to documented (i.e. formally approved and in writing) usual costs accounting practices (if any) or

- have formalised documentation on the systems and processes for calculating their costs and contributions (i.e. formally approved and in writing), have participated in at least 150 actions under Horizon 2020 or the Euratom Research and Training Programme (2014-2018 or 2019-2020) and participate in at least 3 ongoing actions under Horizon Europe or the Euratom Research and Training Programme (2021-2025 or 2026-2027)

may apply to the granting authority for a systems and process audit (SPA).

This audit will be carried out as follows:

Step 1 – Application by the beneficiary.

Step 2 – If the application is accepted, the granting authority will carry out the systems and process audit, complemented by an audit of transactions (on a sample of the beneficiary's Horizon Europe or the Euratom Research and Training Programme financial statements).

Step 3 – The audit result will take the form of a risk assessment classification for the beneficiary: low, medium or high.

Low-risk beneficiaries will benefit from less (or less in-depth) ex-post audits (see Article 25) and a higher threshold for submitting certificates on the financial statements (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3).

24.5 Consequences of non-compliance

If a beneficiary does not submit a certificate on the financial statements (CFS) or the certificate is rejected, the accepted EU contribution to costs will be capped to reflect the CFS threshold.

If a beneficiary breaches any of its other obligations under this Article, the granting authority may apply the measures described in Chapter 5.

ARTICLE 25 — CHECKS, REVIEWS, AUDITS AND INVESTIGATIONS — EXTENSION OF FINDINGS

25.1 Granting authority checks, reviews and audits

25.1.1 Internal checks

The granting authority may — during the action or afterwards — check the proper implementation of the action and compliance with the obligations under the Agreement, including assessing costs and contributions, deliverables and reports.

25.1.2 Project reviews

The granting authority may carry out reviews on the proper implementation of the action and compliance with the obligations under the Agreement (general project reviews or specific issues reviews).

Such project reviews may be started during the implementation of the action and until the time-limit

set out in the Data Sheet (see Point 6). They will be formally notified to the coordinator or beneficiary concerned and will be considered to start on the date of the notification.

If needed, the granting authority may be assisted by independent, outside experts. If it uses outside experts, the coordinator or beneficiary concerned will be informed and have the right to object on grounds of commercial confidentiality or conflict of interest.

The coordinator or beneficiary concerned must cooperate diligently and provide — within the deadline requested — any information and data in addition to deliverables and reports already submitted (including information on the use of resources). The granting authority may request beneficiaries to provide such information to it directly. Sensitive information and documents will be treated in accordance with Article 13.

The coordinator or beneficiary concerned may be requested to participate in meetings, including with the outside experts.

For **on-the-spot visits**, the beneficiary concerned must allow access to sites and premises (including to the outside experts) and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the review findings, a **project review report** will be drawn up.

The granting authority will formally notify the project review report to the coordinator or beneficiary concerned, which has 30 days from receiving notification to make observations.

Project reviews (including project review reports) will be in the language of the Agreement.

25.1.3 Audits

The granting authority may carry out audits on the proper implementation of the action and compliance with the obligations under the Agreement.

Such audits may be started during the implementation of the action and until the time-limit set out in the Data Sheet (see Point 6). They will be formally notified to the beneficiary concerned and will be considered to start on the date of the notification.

The granting authority may use its own audit service, delegate audits to a centralised service or use external audit firms. If it uses an external firm, the beneficiary concerned will be informed and have the right to object on grounds of commercial confidentiality or conflict of interest.

The beneficiary concerned must cooperate diligently and provide — within the deadline requested — any information (including complete accounts, individual salary statements or other personal data) to verify compliance with the Agreement. Sensitive information and documents will be treated in accordance with Article 13.

For **on-the-spot** visits, the beneficiary concerned must allow access to sites and premises (including for the external audit firm) and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the audit findings, a **draft audit report** will be drawn up.

The auditors will formally notify the draft audit report to the beneficiary concerned, which has 30 days from receiving notification to make observations (contradictory audit procedure).

The **final audit report** will take into account observations by the beneficiary concerned and will be formally notified to them.

Audits (including audit reports) will be in the language of the Agreement.

25.2 European Commission checks, reviews and audits in grants of other granting authorities

Where the granting authority is not the European Commission, the latter has the same rights of checks, reviews and audits as the granting authority.

25.3 Access to records for assessing simplified forms of funding

The beneficiaries must give the European Commission access to their statutory records for the periodic assessment of simplified forms of funding which are used in EU programmes.

25.4 OLAF, EPPO and ECA audits and investigations

The following bodies may also carry out checks, reviews, audits and investigations — during the action or afterwards:

- the European Anti-Fraud Office (OLAF) under Regulations No 883/2013[19] and No 2185/96[20]
- the European Public Prosecutor's Office (EPPO) under Regulation 2017/1939
- the European Court of Auditors (ECA) under Article 287 of the Treaty on the Functioning of the EU (TFEU) and Article 257 of EU Financial Regulation 2018/1046.

If requested by these bodies, the beneficiary concerned must provide full, accurate and complete information in the format requested (including complete accounts, individual salary statements or other personal data, including in electronic format) and allow access to sites and premises for on-the-spot visits or inspections — as provided for under these Regulations.

To this end, the beneficiary concerned must keep all relevant information relating to the action, at least until the time-limit set out in the Data Sheet (Point 6) and, in any case, until any ongoing checks, reviews, audits, investigations, litigation or other pursuits of claims have been concluded.

25.5 Consequences of checks, reviews, audits and investigations — Extension of results of reviews, audits or investigations

[19] Regulation (EU, Euratom) No 883/2013 of the European Parliament and of the Council of 11 September 2013 concerning investigations conducted by the European Anti-Fraud Office (OLAF) and repealing Regulation (EC) No 1073/1999 of the European Parliament and of the Council and Council Regulation (Euratom) No 1074/1999 (OJ L 248, 18/09/2013, p. 1).

[20] Council Regulation (Euratom, EC) No 2185/1996 of 11 November 1996 concerning on-the-spot checks and inspections carried out by the Commission in order to protect the European Communities' financial interests against fraud and other irregularities (OJ L 292, 15/11/1996, p. 2).

25.5.1 Consequences of checks, reviews, audits and investigations in this grant

Findings in checks, reviews, audits or investigations carried out in the context of this grant may lead to rejections (see Article 27), grant reduction (see Article 28) or other measures described in Chapter 5.

Rejections or grant reductions after the final payment will lead to a revised final grant amount (see Article 22).

Findings in checks, reviews, audits or investigations during the action implementation may lead to a request for amendment (see Article 39), to change the description of the action set out in Annex 1.

Checks, reviews, audits or investigations that find systemic or recurrent errors, irregularities, fraud or breach of obligations in any EU grant may also lead to consequences in other EU grants awarded under similar conditions (‘extension to other grants’).

Moreover, findings arising from an OLAF or EPPO investigation may lead to criminal prosecution under national law.

25.5.2 Extension from other grants

Results of checks, reviews, audits or investigations in other grants may be extended to this grant, if:

(a) the beneficiary concerned is found, in other EU grants awarded under similar conditions, to have committed systemic or recurrent errors, irregularities, fraud or breach of obligations that have a material impact on this grant and

(b) those findings are formally notified to the beneficiary concerned — together with the list of grants affected by the findings — within the time-limit for audits set out in the Data Sheet (see Point 6).

The granting authority will formally notify the beneficiary concerned of the intention to extend the findings and the list of grants affected.

If the extension concerns **rejections of costs or contributions**: the notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings

(b) the request to submit revised financial statements for all grants affected

(c) the correction rate for extrapolation, established on the basis of the systemic or recurrent errors, to calculate the amounts to be rejected, if the beneficiary concerned:

(i) considers that the submission of revised financial statements is not possible or practicable or

(ii) does not submit revised financial statements.

If the extension concerns **grant reductions**: the notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings and

(b) the **correction rate for extrapolation**, established on the basis of the systemic or recurrent errors and the principle of proportionality.

The beneficiary concerned has **60 days** from receiving notification to submit observations, revised financial statements or to propose a duly substantiated **alternative correction method/rate**.

On the basis of this, the granting authority will analyse the impact and decide on the implementation (i.e. start rejection or grant reduction procedures, either on the basis of the revised financial statements or the announced/alternative method/rate or a mix of those; see Articles 27 and 28).

25.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, costs or contributions insufficiently substantiated will be ineligible (see Article 6) and will be rejected (see Article 27), and the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 26 — IMPACT EVALUATIONS

26.1 Impact evaluation

The granting authority may carry out impact evaluations of the action, measured against the objectives and indicators of the EU programme funding the grant.

Such evaluations may be started during implementation of the action and until the time-limit set out in the Data Sheet (see Point 6). They will be formally notified to the coordinator or beneficiaries and will be considered to start on the date of the notification.

If needed, the granting authority may be assisted by independent outside experts.

The coordinator or beneficiaries must provide any information relevant to evaluate the impact of the action, including information in electronic format.

26.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the granting authority may apply the measures described in Chapter 5.

CHAPTER 5 CONSEQUENCES OF NON-COMPLIANCE

SECTION 1 REJECTIONS AND GRANT REDUCTION

ARTICLE 27 — REJECTION OF COSTS AND CONTRIBUTIONS

27.1 Conditions

The granting authority will — at beneficiary termination, interim payment, final payment or afterwards — reject any costs or contributions which are ineligible (see Article 6), in particular following checks, reviews, audits or investigations (see Article 25).

The rejection may also be based on the extension of findings from other grants to this grant (see Article 25).

Ineligible costs or contributions will be rejected.

27.2 Procedure

If the rejection does not lead to a recovery, the granting authority will formally notify the coordinator or beneficiary concerned of the rejection, the amounts and the reasons why. The coordinator or beneficiary concerned may — within 30 days of receiving notification — submit observations if it disagrees with the rejection (payment review procedure).

If the rejection leads to a recovery, the granting authority will follow the contradictory procedure with pre-information letter set out in Article 22.

27.3 Effects

If the granting authority rejects costs or contributions, it will deduct them from the costs or contributions declared and then calculate the amount due (and, if needed, make a recovery; see Article 22).

ARTICLE 28 — GRANT REDUCTION

28.1 Conditions

The granting authority may — at beneficiary termination, final payment or afterwards — reduce the grant for a beneficiary, if:

(a) the beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) the beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (see Article 25).

The amount of the reduction will be calculated for each beneficiary concerned and proportionate to the seriousness and the duration of the errors, irregularities or fraud or breach of obligations, by applying an individual reduction rate to their accepted EU contribution.

28.2 Procedure

If the grant reduction does not lead to a recovery, the granting authority will formally notify the coordinator or beneficiary concerned of the reduction, the amount to be reduced and the reasons why.

The coordinator or beneficiary concerned may — within 30 days of receiving notification — submit observations if it disagrees with the reduction (payment review procedure).

If the grant reduction leads to a recovery, the granting authority will follow the contradictory procedure with pre-information letter set out in Article 22.

28.3 Effects

If the granting authority reduces the grant, it will deduct the reduction and then calculate the amount due (and, if needed, make a recovery; see Article 22).

SECTION 2 SUSPENSION AND TERMINATION

ARTICLE 29 — PAYMENT DEADLINE SUSPENSION

29.1 Conditions

The granting authority may — at any moment — suspend the payment deadline if a payment cannot be processed because:

(a) the required report (see Article 21) has not been submitted or is not complete or additional information is needed

(b) there are doubts about the amount to be paid (e.g. ongoing audit extension procedure, queries about eligibility, need for a grant reduction, etc.) and additional checks, reviews, audits or investigations are necessary, or

(c) there are other issues affecting the EU financial interests.

29.2 Procedure

The granting authority will formally notify the coordinator of the suspension and the reasons why.

The suspension will **take effect** the day the notification is sent.

If the conditions for suspending the payment deadline are no longer met, the suspension will be **lifted** — and the remaining time to pay (see Data Sheet, Point 4.2) will resume.

If the suspension exceeds two months, the coordinator may request the granting authority to confirm if the suspension will continue.

If the payment deadline has been suspended due to the non-compliance of the report and the revised report is not submitted (or was submitted but is also rejected), the granting authority may also terminate the grant or the participation of the coordinator (see Article 32).

ARTICLE 30 — PAYMENT SUSPENSION

30.1 Conditions

The granting authority may — at any moment — suspend payments, in whole or in part for one or more beneficiaries, if:

(a) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed or is suspected of having committed:

(i) substantial errors, irregularities or fraud or

(ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant.

If payments are suspended for one or more beneficiaries, the granting authority will make partial payment(s) for the part(s) not suspended. If suspension concerns the final payment, the payment (or recovery) of the remaining amount after suspension is lifted will be considered to be the payment that closes the action.

30.2 Procedure

Before suspending payments, the granting authority will send a **pre-information letter** to the beneficiary concerned:

- formally notifying the intention to suspend payments and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the observations it has received, it will confirm the suspension (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

At the end of the suspension procedure, the granting authority will also inform the coordinator.

The suspension will **take effect** the day after the confirmation notification is sent.

If the conditions for resuming payments are met, the suspension will be **lifted**. The granting authority will formally notify the beneficiary concerned (and the coordinator) and set the suspension end date.

During the suspension, no prefinancing will be paid to the beneficiaries concerned. For interim payments, the periodic reports for all reporting periods except the last one (see Article 21) must not contain any financial statements from the beneficiary concerned (or its affiliated entities). The coordinator must include them in the next periodic report after the suspension is lifted or — if suspension is not lifted before the end of the action — in the last periodic report.

ARTICLE 31 — GRANT AGREEMENT SUSPENSION

31.1 Consortium-requested GA suspension

31.1.1 Conditions and procedure

The beneficiaries may request the suspension of the grant or any part of it, if exceptional circumstances — in particular *force majeure* (see Article 35) — make implementation impossible or excessively difficult.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the date the suspension takes effect; this date may be before the date of the submission of the amendment request and
- the expected date of resumption.

The suspension will **take effect** on the day specified in the amendment.

Once circumstances allow for implementation to resume, the coordinator must immediately request another **amendment** of the Agreement to set the suspension end date, the resumption date (one day after suspension end date), extend the duration and make other changes necessary to adapt the action to the new situation (see Article 39) — unless the grant has been terminated (see Article 32). The suspension will be **lifted** with effect from the suspension end date set out in the amendment. This date may be before the date of the submission of the amendment request.

During the suspension, no prefinancing will be paid. Costs incurred or contributions for activities implemented during grant suspension are not eligible (see Article 6.3).

31.2 EU-initiated GA suspension

31.2.1 Conditions

The granting authority may suspend the grant or any part of it, if:

(a) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed or is suspected of having committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant

(c) other:

  (i) linked action issues: not applicable

  (ii) the action has lost its scientific or technological relevance, for EIC Accelerator actions: the action has lost its economic relevance, for challenge-based EIC Pathfinder actions

and Horizon Europe Missions: the action has lost its relevance as part of the Portfolio for which it has been initially selected

31.2.2 Procedure

Before suspending the grant, the granting authority will send a **pre-information letter** to the coordinator:

- formally notifying the intention to suspend the grant and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the observations it has received, it will confirm the suspension (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

The suspension will **take effect** the day after the confirmation notification is sent (or on a later date specified in the notification).

Once the conditions for resuming implementation of the action are met, the granting authority will formally notify the coordinator a **lifting of suspension letter**, in which it will set the suspension end date and invite the coordinator to request an amendment of the Agreement to set the resumption date (one day after suspension end date), extend the duration and make other changes necessary to adapt the action to the new situation (see Article 39) — unless the grant has been terminated (see Article 32). The suspension will be **lifted** with effect from the suspension end date set out in the lifting of suspension letter. This date may be before the date on which the letter is sent.

During the suspension, no prefinancing will be paid. Costs incurred or contributions for activities implemented during suspension are not eligible (see Article 6.3).

The beneficiaries may not claim damages due to suspension by the granting authority (see Article 33).

Grant suspension does not affect the granting authority's right to terminate the grant or a beneficiary (see Article 32) or reduce the grant (see Article 28).

ARTICLE 32 — GRANT AGREEMENT OR BENEFICIARY TERMINATION

32.1 Consortium-requested GA termination

32.1.1 Conditions and procedure

The beneficiaries may request the termination of the grant.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the date the consortium ends work on the action ('end of work date') and
- the date the termination takes effect ('termination date'); this date must be after the date of the submission of the amendment request.

The termination will **take effect** on the termination date specified in the amendment.

If no reasons are given or if the granting authority considers the reasons do not justify termination, it may consider the grant terminated improperly.

32.1.2 Effects

The coordinator must — within 60 days from when termination takes effect — submit a **periodic report** (for the open reporting period until termination).

The granting authority will calculate the final grant amount and final payment on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before the end of work date (see Article 22). Costs relating to contracts due for execution only after the end of work are not eligible.

If the granting authority does not receive the report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/contributions if no periodic report was ever approved).

Improper termination may lead to a grant reduction (see Article 28).

After termination, the beneficiaries' obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

32.2 Consortium-requested beneficiary termination

32.2.1 Conditions and procedure

The coordinator may request the termination of the participation of one or more beneficiaries, on request of the beneficiary concerned or on behalf of the other beneficiaries.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the opinion of the beneficiary concerned (or proof that this opinion has been requested in writing)
- the date the beneficiary ends work on the action ('end of work date')
- the date the termination takes effect ('termination date'); this date must be after the date of the submission of the amendment request.

If the termination concerns the coordinator and is done without its agreement, the amendment request must be submitted by another beneficiary (acting on behalf of the consortium).

The termination will **take effect** on the termination date specified in the amendment.

If no information is given or if the granting authority considers that the reasons do not justify termination, it may consider the beneficiary to have been terminated improperly.

32.2.2 Effects

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a **report on the distribution of payments** to the beneficiary concerned

(ii) a **termination report** from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, the financial statement, the explanation on the use of resources, and, if applicable, the certificate on the financial statement (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3)

(iii) a second **request for amendment** (see Article 39) with other amendments needed (e.g. reallocation of the tasks and the estimated budget of the terminated beneficiary; addition of a new beneficiary to replace the terminated beneficiary; change of coordinator, etc.).

The granting authority will calculate the amount due to the beneficiary on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before the end of work date (see Article 22). Costs relating to contracts due for execution only after the end of work are not eligible.

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 21).

If the granting authority does not receive the termination report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/ contributions if no periodic report was ever approved).

If the granting authority does not receive the report on the distribution of payments within the deadline, it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that
- the beneficiary concerned must not repay any amount to the coordinator.

If the second request for amendment is accepted by the granting authority, the Agreement is **amended** to introduce the necessary changes (see Article 39).

If the second request for amendment is rejected by the granting authority (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the grant may be terminated (see Article 32).

Improper termination may lead to a reduction of the grant (see Article 31) or grant termination (see Article 32).

After termination, the concerned beneficiary's obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

32.3 EU-initiated GA or beneficiary termination

32.3.1 Conditions

The granting authority may terminate the grant or the participation of one or more beneficiaries, if:

(a) one or more beneficiaries do not accede to the Agreement (see Article 40)

(b) a change to the action or the legal, financial, technical, organisational or ownership situation of a beneficiary is likely to substantially affect the implementation of the action or calls into question the decision to award the grant (including changes linked to one of the exclusion grounds listed in the declaration of honour)

(c) following termination of one or more beneficiaries, the necessary changes to the Agreement (and their impact on the action) would call into question the decision awarding the grant or breach the principle of equal treatment of applicants

(d) implementation of the action has become impossible or the changes necessary for its continuation would call into question the decision awarding the grant or breach the principle of equal treatment of applicants

(e) a beneficiary (or person with unlimited liability for its debts) is subject to bankruptcy proceedings or similar (including insolvency, winding-up, administration by a liquidator or court, arrangement with creditors, suspension of business activities, etc.)

(f) a beneficiary (or person with unlimited liability for its debts) is in breach of social security or tax obligations

(g) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has been found guilty of grave professional misconduct

(h) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed fraud, corruption, or is involved in a criminal organisation, money laundering, terrorism-related crimes (including terrorism financing), child labour or human trafficking

(i) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) was created under a different jurisdiction with the intent to circumvent fiscal, social or other legal obligations in the country of origin (or created another entity with this purpose)

(j) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.)

(k) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (extension of findings from other grants to this grant; see Article 25)

(l) despite a specific request by the granting authority, a beneficiary does not request — through the coordinator — an amendment to the Agreement to end the participation of one of its affiliated entities or associated partners that is in one of the situations under points (d), (f), (e), (g), (h), (i) or (j) and to reallocate its tasks, or

(m) other:

(i) linked action issues: not applicable

(ii) the action has lost its scientific or technological relevance, for EIC Accelerator actions: the action has lost its economic relevance, for challenge-based EIC Pathfinder actions and Horizon Europe Missions: the action has lost its relevance as part of the Portfolio for which it has been initially selected

32.3.2 Procedure

Before terminating the grant or participation of one or more beneficiaries, the granting authority will send **a pre-information letter** to the coordinator or beneficiary concerned:

- formally notifying the intention to terminate and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the observations it has received, it will confirm the termination and the date it will take effect (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

For beneficiary terminations, the granting authority will — at the end of the procedure — also inform the coordinator.

The termination will **take effect** the day after the confirmation notification is sent (or on a later date specified in the notification; 'termination date').

32.3.3 Effects

(a) for **GA termination**:

The coordinator must — within 60 days from when termination takes effect — submit a **periodic report** (for the last open reporting period until termination).

The granting authority will calculate the final grant amount and final payment on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before termination takes effect (see Article 22). Costs relating to contracts due for execution only after termination are not eligible.

If the grant is terminated for breach of the obligation to submit reports, the coordinator may not submit any report after termination.

If the granting authority does not receive the report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/contributions if no periodic report was ever approved).

Termination does not affect the granting authority's right to reduce the grant (see Article 28) or to impose administrative sanctions (see Article 34).

The beneficiaries may not claim damages due to termination by the granting authority (see Article 33).

After termination, the beneficiaries' obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

(b) for **beneficiary termination**:

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a **report on the distribution of payments** to the beneficiary concerned

(ii) a **termination report** from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, the financial statement, the explanation on the use of resources, and, if applicable, the certificate on the financial statement (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3)

(iii) a **request for amendment** (see Article 39) with any amendments needed (e.g. reallocation of the tasks and the estimated budget of the terminated beneficiary; addition of a new beneficiary to replace the terminated beneficiary; change of coordinator, etc.).

The granting authority will calculate the amount due to the beneficiary on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before termination takes effect (see Article 22). Costs relating to contracts due for execution only after termination are not eligible.

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 21).

If the granting authority does not receive the termination report within the deadline, only costs and contributions included in an approved periodic report will be taken into account (no costs/ contributions if no periodic report was ever approved).

If the granting authority does not receive the report on the distribution of payments within the deadline, it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that
- the beneficiary concerned must not repay any amount to the coordinator.

If the request for amendment is accepted by the granting authority, the Agreement is **amended** to introduce the necessary changes (see Article 39).

If the request for amendment is rejected by the granting authority (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the grant may be terminated (see Article 32).

After termination, the concerned beneficiary's obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

SECTION 3 OTHER CONSEQUENCES: DAMAGES AND ADMINISTRATIVE SANCTIONS

ARTICLE 33 — DAMAGES

33.1 Liability of the granting authority

The granting authority cannot be held liable for any damage caused to the beneficiaries or to third parties as a consequence of the implementation of the Agreement, including for gross negligence.

The granting authority cannot be held liable for any damage caused by any of the beneficiaries or other participants involved in the action, as a consequence of the implementation of the Agreement.

33.2 Liability of the beneficiaries

The beneficiaries must compensate the granting authority for any damage it sustains as a result of the implementation of the action or because the action was not implemented in full compliance with the Agreement, provided that it was caused by gross negligence or wilful act.

The liability does not extend to indirect or consequential losses or similar damage (such as loss of profit, loss of revenue or loss of contracts), provided such damage was not caused by wilful act or by a breach of confidentiality.

ARTICLE 34 — ADMINISTRATIVE SANCTIONS AND OTHER MEASURES

Nothing in this Agreement may be construed as preventing the adoption of administrative sanctions (i.e. exclusion from EU award procedures and/or financial penalties) or other public law measures, in addition or as an alternative to the contractual measures provided under this Agreement (see, for instance, Articles 135 to 145 EU Financial Regulation 2018/1046 and Articles 4 and 7 of Regulation 2988/95[21]).

SECTION 4 FORCE MAJEURE

ARTICLE 35 — FORCE MAJEURE

A party prevented by force majeure from fulfilling its obligations under the Agreement cannot be considered in breach of them.

'Force majeure' means any situation or event that:

- prevents either party from fulfilling their obligations under the Agreement,

[21] Council Regulation (EC, Euratom) No 2988/95 of 18 December 1995 on the protection of the European Communities financial interests (OJ L 312, 23.12.1995, p. 1).

- was unforeseeable, exceptional situation and beyond the parties' control,
- was not due to error or negligence on their part (or on the part of other participants involved in the action), and
- proves to be inevitable in spite of exercising all due diligence.

Any situation constituting force majeure must be formally notified to the other party without delay, stating the nature, likely duration and foreseeable effects.

The parties must immediately take all the necessary steps to limit any damage due to force majeure and do their best to resume implementation of the action as soon as possible.

CHAPTER 6 FINAL PROVISIONS

ARTICLE 36 — COMMUNICATION BETWEEN THE PARTIES

36.1 Forms and means of communication — Electronic management

EU grants are managed fully electronically through the EU Funding & Tenders Portal ('Portal').

All communications must be made electronically through the Portal, in accordance with the Portal Terms and Conditions and using the forms and templates provided there (except if explicitly instructed otherwise by the granting authority).

Communications must be made in writing and clearly identify the grant agreement (project number and acronym).

Communications must be made by persons authorised according to the Portal Terms and Conditions. For naming the authorised persons, each beneficiary must have designated — before the signature of this Agreement — a 'legal entity appointed representative (LEAR)'. The role and tasks of the LEAR are stipulated in their appointment letter (see Portal Terms and Conditions).

If the electronic exchange system is temporarily unavailable, instructions will be given on the Portal.

36.2 Date of communication

The sending date for communications made through the Portal will be the date and time of sending, as indicated by the time logs.

The receiving date for communications made through the Portal will be the date and time the communication is accessed, as indicated by the time logs. Formal notifications that have not been accessed within 10 days after sending, will be considered to have been accessed (see Portal Terms and Conditions).

If a communication is exceptionally made on paper (by e-mail or postal service), general principles apply (i.e. date of sending/receipt). Formal notifications by registered post with proof of delivery will be considered to have been received either on the delivery date registered by the postal service or the deadline for collection at the post office.

If the electronic exchange system is temporarily unavailable, the sending party cannot be considered in breach of its obligation to send a communication within a specified deadline.

36.3 Addresses for communication

The Portal can be accessed via the Europa website.

The address for paper communications to the granting authority (if exceptionally allowed) is the official mailing address indicated on its website.

For beneficiaries, it is the legal address specified in the Portal Participant Register.

ARTICLE 37 — INTERPRETATION OF THE AGREEMENT

The provisions in the Data Sheet take precedence over the rest of the Terms and Conditions of the Agreement.

Annex 5 takes precedence over the Terms and Conditions; the Terms and Conditions take precedence over the Annexes other than Annex 5.

Annex 2 takes precedence over Annex 1.

ARTICLE 38 — CALCULATION OF PERIODS AND DEADLINES

In accordance with Regulation No 1182/71[22], periods expressed in days, months or years are calculated from the moment the triggering event occurs.

The day during which that event occurs is not considered as falling within the period.

'Days' means calendar days, not working days.

ARTICLE 39 — AMENDMENTS

39.1 Conditions

The Agreement may be amended, unless the amendment entails changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

Amendments may be requested by any of the parties.

39.2 Procedure

The party requesting an amendment must submit a request for amendment signed directly in the Portal Amendment tool.

The coordinator submits and receives requests for amendment on behalf of the beneficiaries (see Annex 3). If a change of coordinator is requested without its agreement, the submission must be done by another beneficiary (acting on behalf of the other beneficiaries).

[22] Regulation (EEC, Euratom) No 1182/71 of the Council of 3 June 1971 determining the rules applicable to periods, dates and time-limits (OJ L 124, 8/6/1971, p. 1).

The request for amendment must include:

- the reasons why
- the appropriate supporting documents and
- for a change of coordinator without its agreement: the opinion of the coordinator (or proof that this opinion has been requested in writing).

The granting authority may request additional information.

If the party receiving the request agrees, it must sign the amendment in the tool within 45 days of receiving notification (or any additional information the granting authority has requested). If it does not agree, it must formally notify its disagreement within the same deadline. The deadline may be extended, if necessary for the assessment of the request. If no notification is received within the deadline, the request is considered to have been rejected.

An amendment **enters into force** on the day of the signature of the receiving party.

An amendment **takes effect** on the date of entry into force or other date specified in the amendment.

ARTICLE 40 — ACCESSION AND ADDITION OF NEW BENEFICIARIES

40.1 Accession of the beneficiaries mentioned in the Preamble

The beneficiaries which are not coordinator must accede to the grant by signing the accession form (see Annex 3) directly in the Portal Grant Preparation tool, within 30 days after the entry into force of the Agreement (see Article 44).

They will assume the rights and obligations under the Agreement with effect from the date of its entry into force (see Article 44).

If a beneficiary does not accede to the grant within the above deadline, the coordinator must — within 30 days — request an amendment (see Article 39) to terminate the beneficiary and make any changes necessary to ensure proper implementation of the action. This does not affect the granting authority's right to terminate the grant (see Article 32).

40.2 Addition of new beneficiaries

In justified cases, the beneficiaries may request the addition of a new beneficiary.

For this purpose, the coordinator must submit a request for amendment in accordance with Article 39. It must include an accession form (see Annex 3) signed by the new beneficiary directly in the Portal Amendment tool.

New beneficiaries will assume the rights and obligations under the Agreement with effect from the date of their accession specified in the accession form (see Annex 3).

Additions are also possible in mono-beneficiary grants.

ARTICLE 41 — TRANSFER OF THE AGREEMENT

In justified cases, the beneficiary of a mono-beneficiary grant may request the transfer of the grant to a new beneficiary, provided that this would not call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

The beneficiary must submit a request for **amendment** (see Article 39), with

- the reasons why
- the accession form (see Annex 3) signed by the new beneficiary directly in the Portal Amendment tool and
- additional supporting documents (if required by the granting authority).

The new beneficiary will assume the rights and obligations under the Agreement with effect from the date of accession specified in the accession form (see Annex 3).

ARTICLE 42 — ASSIGNMENTS OF CLAIMS FOR PAYMENT AGAINST THE GRANTING AUTHORITY

The beneficiaries may not assign any of their claims for payment against the granting authority to any third party, except if expressly approved in writing by the granting authority on the basis of a reasoned, written request by the coordinator (on behalf of the beneficiary concerned).

If the granting authority has not accepted the assignment or if the terms of it are not observed, the assignment will have no effect on it.

In no circumstances will an assignment release the beneficiaries from their obligations towards the granting authority.

ARTICLE 43 — APPLICABLE LAW AND SETTLEMENT OF DISPUTES

43.1 Applicable law

The Agreement is governed by the applicable EU law, supplemented if necessary by the law of Belgium.

Special rules may apply for beneficiaries which are international organisations (if any; see Data Sheet, Point 5).

43.2 Dispute settlement

If a dispute concerns the interpretation, application or validity of the Agreement, the parties must bring action before the EU General Court — or, on appeal, the EU Court of Justice — under Article 272 of the Treaty on the Functioning of the EU (TFEU).

For non-EU beneficiaries (if any), such disputes must be brought before the courts of Brussels, Belgium — unless an international agreement provides for the enforceability of EU court judgements.

For beneficiaries with arbitration as special dispute settlement forum (if any; see Data Sheet, Point 5), the dispute will — in the absence of an amicable settlement — be settled in accordance with the Rules for Arbitration published on the Portal.

If a dispute concerns administrative sanctions, offsetting or an enforceable decision under Article 299 TFEU (see Articles 22 and 34), the beneficiaries must bring action before the General Court — or, on appeal, the Court of Justice — under Article 263 TFEU.

For grants where the granting authority is an EU executive agency (see Preamble), actions against offsetting and enforceable decisions must be brought against the European Commission (not against the granting authority; see also Article 22).

ARTICLE 44 — ENTRY INTO FORCE

The Agreement will enter into force on the day of signature by the granting authority or the coordinator, depending on which is later.

SIGNATURES

For the coordinator

Lukas Palko with ECAS id n002s2hh signed in the Participant Portal on 10/11/2022 at 15:16:42 (transaction id SigId-71634-g6nuHogKtTuAnHre7i7ghk4wxgzfpwky2cgRssqkNJExIeFSKKBlbZmAzzTEBasFyVm3aSFDSzqQZ4GGFodBPie-rS0vSrmBGYCYOonzu9chxJ-9t8JRlSI8Iuqszh4jMiPtefrSlENW0mJeFQ2Wg8CECFP2miGb0hqGIJpAu9SQLJgAKM1D9TMnxHXO58a4poMDy). Timestamp by third party at 2022.11.10 15:16:48 CET

For the granting authority

Signed by Ales FIALA with ECAS id fialaal as an authorised representative on 10-11-2022 16:36:35 (transaction id SigId-73777-im8dcjHopwDTlZMbzYzp6OPA72eZ2whhMa0bFMRiErYefrq259XZPcJLBZ2FSwdfHpncrl34ewIDqRJnculpNf-rS0vSrmBGYCYOonzu9chxJ-ZQPzVi04yd75Yi4IBD0hsbpYOBtkACQ57rp0uczu6kZKJLEcT6KozL4jqHitcIDp9UbeTST7NzXmwbJ5V2Tqb2O)
2022.11.10 16:36:38 CET

ANNEX 1

Horizon Europe (HORIZON)

Description of the action (DoA)

Part A

Part B

DESCRIPTION OF THE ACTION (PART A)

COVER PAGE

Part A of the Description of the Action (DoA) must be completed directly on the Portal Grant Preparation screens.

PROJECT *Grant Preparation (General Information screen) — Enter the info.*	
Project number:	101087124
Project name:	Alzheimer's Disease Diagnostics Innovation and Translation to Clinical Practice in Central Europe
Project acronym:	ADDIT-CE
Call:	HORIZON-WIDERA-2022-ACCESS-04
Topic:	HORIZON-WIDERA-2022-ACCESS-04-01
Type of action:	HORIZON-CSA
Service:	REA/C/03
Project starting date:	fixed date: 1 January 2023
Project duration:	48 months

TABLE OF CONTENTS

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PROJECT SUMMARY

Project summary

Grant Preparation (General Information screen) — Provide an overall description of your project (including context and overall objectives, planned activities and main achievements, and expected results and impacts (on target groups, change procedures, capacities, innovation etc)). This summary should give readers a clear idea of what your project is about.

Use the project summary from your proposal.

More than 55 million people worldwide suffer from dementia. Alzheimer disease (AD) is the main cause of this fatal disorder, without any effective disease modifying therapy. Early diagnosis and lifestyle modifications can significantly reduce the costs of care and treatment. There is no conceptual plan implementing modern diagnostic methods in the clinical practice in Czechia and Slovakia. The interaction between universities and private sector developing molecular diagnostic tools is fragmented and lacking. Limited number of talented students are invested in applied AD-focused research. The aim of ADDIT-CE is to interlink two ecosystems in Brno and Bratislava region, embracing the full quadruple helix of innovation driving actors: excellent scientific teams from Masaryk University and Slovak Academy of Sciences, collaborating with top biotech companies: Geneton, BioVendor, and MultiplexDX. Societal actors will be represented by organisations such as Slovak and Czech Alzheimer Societies, Memory Center and Czech Brain Aging Study. The regional government will be involved via Ministry of Health Slovak Republic, and South Moravian Innovation Centre. The joined ecosystems will unite R&I activities focusing on new diagnostic methods and their applications and further interlink academia and business spheres by creating a pilot industrial PhD programme. ADDIT-CE will generate a joint cross-border strategy covering basic and applied research activities aiming on accelerating the development of new tools for preclinical AD diagnostics and lifestyle/pharmacological intervention monitoring. New cutting-edge technologies will be transferred into clinical practise. Results of ADDIT-CE will be used to develop the Slovak National Plan to Combat Dementia, to enrich the Czech National Plan for AD, and will be widely disseminated to end users and society. ADDIT-CE will join forces of the involved ecosystems to revolutionise diagnostic approaches in both countries.

LIST OF PARTICIPANTS

PARTICIPANTS

Grant Preparation (Beneficiaries screen) — Enter the info.

Number	Role	Short name	Legal name	Country	PIC
1	COO	MU	Masarykova univerzita	CZ	999880657
2	BEN	NII SAS	NEUROIMUNOLOGICKY USTAV SLOVENSKEJAKADEMIA VIED	SK	984972436
2.1	AE	SALS	SLOVENSKA ALZHEIMEROVA SPOLOCNOST	SK	887301681
3	BEN	ICRC	FAKULTNI NEMOCNICE U SV. ANNY V BRNE	CZ	994491822
4	BEN	MC	CENTRUM MEMORY NO	SK	892489532
5	BEN	BIOVENDOR	BIOVENDOR - LABORATORNI MEDICINA AS	CZ	973936455
6	BEN	BMC SAS	BIOMEDICINSKE CENTRUM SLOVENSKEJ AKADEMIE VIED, VEREJNA VYSKUMNA INSTITUCIA	SK	918583890
7	BEN	MH	MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY	SK	999825173
8	BEN	MDX	MULTIPLEXDX S.R.O.	SK	918777890
9	BEN	GENETON	GENETON S.R.O.	SK	951290059

PARTICIPANTS

Grant Preparation (Beneficiaries screen) — Enter the info.

Number	Role	Short name	Legal name	Country	PIC
10	AP	JIC	JIC, ZAJMOVE SDRUZENI PRAVNICKCH OSOB	CZ	999780262
11	AP	CALS	CESKA ALZHEIMEROVSKA SPOLECNOST, OPS	CZ	888747466

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LIST OF WORK PACKAGES

Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
WP1	Development of Joint Cross-border R&I Strategy	1 - MU	117.46	1	48	D1.1 – Report on Research and Exploitation Potential and Market Analysis D1.2 – Preliminary Joint R&I Strategy D1.3 – Final Joint R&I Strategy and Report on Business/User Networking D1.4 – Evaluation Report by the EAB
WP2	Concepts, Designs, and Infrastructure Pre-Plans	8 - MDX	79.38	13	48	D2.1 – Final Research Plans and Findings of Feasibility Studies
WP3	Pathway to Long-Term Sustainability	5 - BIOVENDOR	43.52	13	48	D3.1 – Final Investment Plans and Findings of Patentability Studies D3.2 – Technology Transfer Framework
WP4	Development of new diagnostic assays for AD progression	2 - NII SAS	218.60	1	46	D4.1 – Tau biomarker identification in CFS and blood D4.2 – Optimized protocol of the purfication and selective phosphorylation of selected Tau fragments prepared recombinantly and Molecular basis of ApoE oligomerization and aggregation D4.3 – Novel tau species in the CSF and blood and in the medium of iPSCs and Tau assay development D4.4 – Assigned solution NMR spectra of the selected Tau fragments D4.5 – Structural analyses of the selected tau biomarkers and validations of assays and new biomarkers

Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
						D4.6 – Validation of low input microRNA sequencing protocol D4.7 – Identification and validation of microRNA biomarkers for AD
WP5	Engagement of End Users	3 - ICRC	254.76	1	48	D5.1 – Report on the AD cohorts D5.2 – Harmonisation of recruitment and diagnostics method and Report on Non-pharmacological Interventions D5.3 – Plan of the Communication Campaign D5.4 – Summary of the Communication Campaign
WP6	Creating A Culture of Innovation	1 - MU	174.32	1	48	D6.1 – Initial Training Plan and CDE Plan D6.2 – Interim Training and CDE Report and Plan D6.3 – Final Training Report and Scientific Report on Industrial PhDs, CDE Plan for post-project period
WP7	Project Governance, Management and Ethics	1 - MU	107.52	1	48	D7.1 – Data Management Plan D7.2 – Quality Plan, Ethics Requirements and Project Visual Identity, Website and Social Media

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Work package WP1 – Development of Joint Cross-border R&I Strategy

Work Package Number	WP1	Lead Beneficiary	1. MU
Work Package Name	Development of Joint Cross-border R&I Strategy		
Start Month	1	End Month	48

Objectives
- Identification of R&I needs and gaps - Developing Joint Cross-Border R&I Strategy for the implementation of a new diagnostics framework of AD in the CZ-SK region - Integration of regional and national policy making bodies into the R&I development in the region - Laying down the foundation for a long-term sustainability of the joint ecosystem

Description
WP1 builds on the identification of research and innovation needs and gaps in the joint ecosystems to develop a joint cross-border Research and Innovation Strategy for the emerging CZ-SK R&I ecosystem. T1.1 - Identification of R&I Needs and Gaps (NII SAS, MU, JIC, MH, GENETON, BioVendor, MDX, BMC SAS, M1- M12) The potential for synergic AD diagnostics research and innovation-driven collaboration will be investigated between the research and business partners. Gaps in the exploitation mechanisms in the region will be identified by JIC and MH. A market analysis mapping out the industry's potential for the valorisation of project's results will be prepared by the industrial partners. T1.2– Development of Joint Cross-Border R&I Strategy (MU, NII SAS, JIC, BioVendor, GENETON, BMC SAS, MDX, MH, M13-M48) All project partners will collaborate on and formulate the Joint Cross-Border R&I Strategy for the modernisation of AD diagnostics in the CZ-SK region. The Strategy will address the R&I needs and gaps identified in T1.1 and provide a roadmap towards not only scientific excellence, but also the transformation of the region into a robust and sustainable innovation hub with all its actors (research, industry, policy makers and societal) fully immersed in collaboration and equally benefiting from the results. T1.3 – Establishing of External Advisory Board (MU, NII SAS, JIC, MH, MDX M25–M36) A supporting mechanism in the form of an External Advisory Board will be put into place to ensure high quality and long-term sustainability of the Strategy. The members will evaluate the draft of the Strategy during a weeklong meeting in Brno; their recommendations will be observed for the finalisation of the Strategy. The EAB will seat renowned scientists invited by MU and NII SAS, as well as representatives of government and funding agencies in CZ and SK invited by JIC and Slovak Ministry of Health. T1.4 - Fostering cross-border business-academia linkages (JIC, MU, NII SAS, GENETON, BioVendor, MDX M25–M42) Two tailor-made brokerage events will be organised by JIC (in the 3rd and 4th year of the project) bringing together project partners and companies from the field of AD diagnostics and therapy as an opportunity to forge new academia-business partnerships and collaborations. T1.5 – Creating a Network of Potential Users (JIC, MU, NII SAS, GENETON, MH, BioVendor, MDX M25-M48) JIC and MH will support the consortium in identifying potentially suitable company partners that may be interested in collaboration/application of the research results; the researchers involved in the project will have the opportunity to create new industry and end-user contact on workshops and conferences with industry participation. The established network will be integrated into the emerging joint R&I ecosystem and applied during the implementation phase of the joint R&I Strategy after the project end.

Work package WP2 – Concepts, Designs, and Infrastructure Pre-Plans

Work Package Number	WP2	Lead Beneficiary	8. MDX

Work Package Name	Concepts, Designs, and Infrastructure Pre-Plans		
Start Month	13	End Month	48

Objectives
- Drafting of joint international and inter-sectoral project proposals in line with the Joint R&I Strategy - Design of an epidemiologic study for the Slovak National Program - Provide the ecosystem with cutting-edge infrastructure for the implementation phase

Description
WP2 will be elaborated parallelly with T1.2, proposing an array of projects in line with the joint R&I Strategy. In the design phase, we will evaluate the available infrastructure and identify possible needs for large infrastructure investments. Synergy with the regional and national strategies for the R&I infrastructure development will be sought through the involvement of policy makers in the project. T2.1 – Design of joint research proposals (NII SAS, MU, BioVendor, GENETON, MDX, BMC SAS, MH, M13-M48) Collaborating research teams and their business partners will conceptualise and design joint research proposals, international and inter-sectoral, including the specifications for the necessary infrastructure. (i.e. an epidemiologic study for the Slovak National Program against dementia will be designed) T2.2– Tracking of Technology Development (MDX, BioVendor, GENETON, MU, NII SAS, M13–M48) Technology development during the time between planning and purchase of equipment may result in significant opportunities for adoption of new technologies that will keep us on the frontiers of excellent research. The Steering Committee will hold discussions during the annual meetings on focusing the infrastructure evaluations on cuttingedge technologies. T2.3 - Feasibility studies (MU, NII SAS, M25-M48) This task will deliver the feasibility and proof-of-concept studies for the major R&I investments identified and specified in T2.1.

Work package WP3 – Pathway to Long-Term Sustainability

Work Package Number	WP3	Lead Beneficiary	5. BIOVENDOR
Work Package Name	Pathway to Long-Term Sustainability		
Start Month	13	End Month	48

Objectives
- To mobilise funds necessary for a successful implementation of the Joint R&I Strategy - Establishment of an efficient technology transfer framework in the joint R&I ecosystem

Description
WP3 will prepare action and investment plans corresponding to the task T2.1. T3.1 – Development of Investment Plans (Biovendor, MU, NII SAS, GENETON, MDX M13–M48) Investment plans stemming from the demands of the planned research projects integrated into the Joint R&I Strategy will be elaborated parallelly with the task T2.1 and will reflect the results of T2.1. The research institutions will be the main drivers in applying for competitive public funding. T3.2 – Stabilisation of technology transfer framework (JIC, MU, NII SAS, GENETON, Biovendor, MDX M25-M36) We will utilise the expertise of the JIC in this field to raise awareness and proficiency in technology transfer amongst the scientific community. A ‘handbook’ describing a clearly defined framework will be compiled to lower the current barrier of obstacles in transferring scientific discoveries into practice. T3.3 - Identifying commercialisation potential (MDX, Biovendor, GENETON, MU, NII SAS, JIC, M37–M48)

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The innovation potential of viable project designs will be evaluated. Patentability studies will be carried out for selected innovative ideas to maximise the valorisation potential of the results.

Work package WP4 – Development of new diagnostic assays for AD progression

Work Package Number	WP4	Lead Beneficiary	2. NII SAS
Work Package Name	Development of new diagnostic assays for AD progression		
Start Month	1	End Month	46

Objectives

- to identify the nature and the structural and interaction properties of new tau and ApoE biomarkers in body fluids that may better reflect the progression of Alzheimer´s disease
- to develop a research-based diagnostic assay to monitor the concentration of selected biomarkers

Description

In WP4, we will develop research-based assay to analyse specific tau and APOE biomarker in body fluids.

Task 4.1. Identification of tau species in CSF and blood of AD patients, and in the medium of iPSCs derived neuronal models from AD (NII SAS, ICRC, MC M1-M36)
We will analyse tau species in cerebrospinal fluid and blood of AD patients and age-matched control subjects by mass spectrometry and in the medium from cultured iPSCs, that will be differentiated into 2D neurons or 3D cerebral organoids. Tau proteins, mostly truncated, will be isolated by protein chromatography or immunopurification with tau-specific antibodies. Then, high-resolution mass spectrometry (HR-MS/MS) will primarily serve for exploratory screening for tau protein truncation and phosphorylation. Subsequently, selected reaction monitoring (SRM) assays will target specific tau species for higher sensitivity and precise quantification.

Task 4.2. Structural properties of the monomeric form of Tau variants (MU, NII SAS, BioVendor, M4-M46)
Tau variants identified in previous Task 4.1 as potentially relevant in AD pathology will be cloned in suitable expression vectors. For phosphorylated tau variants we will prepare the corresponding recombinant form either by applying of selected kinases or by applying the extended genetic code technology if only 1-2 pSer should be incorporated into the particular site. Another tested approach within BioVendor company will be the expression in mammalian cell lines. Tau variants aimed for NMR analysis will be expressed in minimal M9 media containing the appropriate source of isotopes. The purity and level of the isotopes labelling will be checked by mass spectrometry. The structural ensembles of selected Tau variants in the monomeric form will be generated by combining the solution NMR spectroscopy and molecular dynamics (MD) simulations.

Task 4.3. Interaction properties of the monomeric form of Tau variants (MU, NII SAS, M13-M46)
The binding sites of the antibodies generated by NII using the relevant Tau variants (determined in T4.1-2) will be mapped by epitope peptide ELISA (NII SAS). In the next step, the assigned NMR spectra will be applied in determination of precise binding epitopes. NMR determination of the binding epitope we have already successfully applied for another microtubule associated protein (Map2c) - homologous to the Tau protein (MU). Tau-antibody complexes will be characterized by biophysical methods (binding affinity and stoichiometry) and by X-ray crystallography (structure) (NII SAS, MU).

Task 4.4. Production of biomarkers on organoid cultures (MU, M7-M46)
Synthetic tau fibrils will be used to induce potential biomarkers ex vivo. Screening of different topologies of Tau fibrils at the different conditions will be performed by AFM and negative staining EM. We will use in-situ cryoelectron tomography to visualize the structural architecture of tau neurofibrils within iPSC-derived neurons or organoids (from Task 4.1). We will evaluate how the presence of tau fibrils influences the stability of microtubules and how it affects the intracellular trafficking and membranes. The cryo-ET technique will allow for unique insight into the relationships between initial Tau misfolding, the formation of neurofibrils, pathology propagation, subsequent cytotoxicity on the level of individual neurons and production of candidate biomarker species.

Task 4.5. Development of the research-based assay (NII SAS, ICRC, MU, MC, M13-M46)
Based on the selection of specific tau peptides and structural analyses we will propose the antigens for immunization. Based on the length of peptides we can conjugate them on carrier protein in order to be immunogenic. Mice will be

immunized for several months to produce specific antibodies recognizing the target. We will test several combinations of antibodies with the highest affinity either on ELISA or digital ELISA (Quanterix) platforms. Generation of antibodies with higher affinity/selectivity will be accomplished by display techniques (NII SAS) and by in silico approach (MU). Recombinant expression of antibodies will be dome in mammalian cells (NII). We will perform analytical validation to estimate the quantitative performance of an assay, including sensitivity, specificity, accuracy, precision, detection limit, range and limits of quantitation and other analytical parameters using the CSF and blood samples. The research-based assay will be further clinically validated using samples from AD patients, age-matched controls and patients suffering from other neurodegenerative diseases.

Task 4.6. Exploring the structural organization and multimerization potential of ApoE proteins (MU, BioVendor, ICRC, M1-M24)
We will clone genes coding for the most prevalent ApoE isoforms (ApoE2, ApoE3 and Apo4) into corresponding expression vectors for their recombinant production in bacterial and mammalian cells. Special attention will be devoted to producing ApoE in mammalian expression system that provides native-like post-translational modifications. Recombinantly produced ApoE proteins will be purified to a high homogeneity through affinity and size-exclusion chromatography. Molecular structures of well-characterized ApoE protein specimens will be determined by X-ray crystallography. The newly solved high-resolution crystal structures will be fitted into lowto-medium resolution structures simultaneously determined by small-angle X-ray scattering (SAXS) and/or cryoelectron microscopy, which will help to clarify the structural organization and multimerization potential of ApoE
proteins.

Task 4.7. Characterization and detection of aggregated ApoE species as diagnostic biomarkers (MU, BioVendor, ICRC, MC, M18-M46)
We will study aggregation potential of ApoE isoforms in in vitro assays using Fourier transform infrared (FTIR) spectroscopy, differential scanning fluorimetry (DSF) and dynamic light scattering (DLS). We will design, construct and purify a new set of single-point mutants and truncated variants of ApoE proteins, which will be inspired by molecular structures determined in Task 4.2, and will be key to delineate the aggregation mechanism of ApoE proteins. The identified ApoE proteinopathy-associated species will be characterized in CSF and blood of AD patients and age-matched control subjects by immunodetection techniques for their potential as new biomarkers in AD diagnostics (BioVendor).

Task 4.8: Development of a novel miRNA-seq protocol for low RNA input samples (MDX, M1–M22)
We will develop a miRNA-seq protocol for low input RNA samples such as CSF/blood with three innovations: 1) novel fluorescently labeled 3'-seq. adapters circumvent the use of hazardous radioactivity and intercalating dyes, allowing precise gel purification of ligation products. 2) chemically modified adapters that prevent adapter dimers, a common problem in low input samples. 3) random nucleotides placed into adapters to mitigate miRNA sequencing biases.

Task 4.9: Identification of miRNA biomarkers in CSF/blood and validation in AD-derived patient tissues (MDX, M22–M46)
We will analyze novel miRNA biomarkers in CSF/blood of AD patients and age-matched controls as well as cerebral organoids (see Task 4.1 and 4.4) by miRNA sequencing. To identify top candidates, we will conduct in silico analyses to identify differentially expressed miRNAs targeting Tau variants (Task 4.1), ApoE proteins (Tasks 4.6 and 4.7), and signaling pathways implicated in AD. We will validate miRNA biomarkers by conducting microRNA fluorescent in situ hybridization using our novel hybridization chain reaction technology in cerebral organoids of AD patients and age-matched controls. We will also verify colocalization with proteins implicated in AD.

Work package WP5 – Engagement of End Users

Work Package Number	WP5	**Lead Beneficiary**	3. ICRC
Work Package Name	Engagement of End Users		
Start Month	1	**End Month**	48

Objectives
- To directly involve end users in the process of valorisation of research results - To enrich existing AD cohorts with early stages dementia patients and MCI in Brno and Bratislava regions

- To streamline the processes of sample and data collection from patients and to harmonise the recruitment and diagnostic work in both countries
- To design activities based on non-pharmacological interventions for validation of biomarkers detection
- To launch a large-scale communication campaign designed to involve the society and end users in the development of the Joint R&I Strategy.

Description
WP5 focuses on the societal actors of the joint ecosystem - patients, their families, GPs, clinical specialists, and specialised AD diagnostic centres. Their involvement in both current and future research in the field of AD diagnostics is crucial for a sustainable implementation of the developed Strategy. Task 5.1. Recruiting patients to existing cohorts in Brno and Bratislava (ICRC, MC, NII SAS, BMC SAS, GENETON M1–M36) New participants will be recruited to the CBAS cohort. A harmonised protocol for clinical evaluation will be implemented for the Memory Centre cohort. Memory Centre will use the expertise of CBAS to enrich and update their recruitment and evaluation processes. GENETON will be testing mutations on AD related genes (ApoE, APP, PS1, PS2, tau). Task 5.2. Standardisation of sample collection procedures, (ICRC, MC, M4–M48) Sample collection methodology will be updated for MC to streamline the clinical work of both centres. The personnel of MC will use internships and job shadowing to familiarise themselves with best practices. In total, 16 person-weeks of personnel exchanges are planned. Task 5.3 Non-pharmacological interventions (BMC SAS, ICRC, MC, NII SAS, MDX M25–M48) Using the expertise of the Centre for Physical Activity and Clinical Research Unit at BMC SAS, new nonpharmacological intervention based on physical activity will be designed for at risk subjects from both CBAS and Memory Center Bratislava cohorts. The impact of physical exercise on cognitive state, markers of neurodegeneration and newly identified biomarkers in this project will be studied. Task 5.4 Communication campaign towards end-users and society (ICRC, MC, CALS, SALS, BMC SAS, NII SAS, MDX M1-M48) Two separate campaigns (lectures and workshops, discussions and questionnaires) will be prepared: one targeting GPs, healthcare workers and social care workers (using the contacts and expertise of CBAS and MC) and one targeting the general public (at-risk population, families of AD patients, etc.). These will serve to communicate the project and its results, involve end-users in the development and implementation of Joint AD Diagnostics Strategy, and improve the current level of awareness about the symptoms and early diagnostics of AD amongst the general public. The campaigns will consider the gender aspect of AD diagnostics, namely with respect to the persistent social gender bias in AD diagnostics.

Work package WP6 – Creating A Culture of Innovation

Work Package Number	WP6	**Lead Beneficiary**	1. MU
Work Package Name	Creating A Culture of Innovation		
Start Month	1	**End Month**	48

Objectives
- Capitalise on the shared expertise through mutual mentoring of students and junior researchers - Increase relevance of PhD training on partnered institutions through direct involvement of industry in student research - Support drive towards entrepreneurship and innovation through trainings in entrepreneurship skills - Raise awareness of the project and of early-stage AD diagnostics as a whole - Inspire scientific discussion on non-pharmacological treatment of AD primarily in preclinical/early stages - Raise interest of young generation in AD diagnostics and its role in prevention and treatment

Description
T6.1 – Enriching the expertise and know-how (MU, NII SAS, M1-M48)

Members of the research groups involved in the project will have direct access to the expertise of both collaborating institutions and their respective international contacts, sharing their knowledge through invited lectures (4/year). PIs from MU and NII will be involved in the supervision of PhD theses elaborated under the project. The students will have access (through mobility support) to intensive 1-week hands-on trainings on relevant techniques at both the research and business partners. 4 person-weeks/year of trainings are planned.

T6.2 – Industrial PhDs (MU, NII SAS, Biovendor, GENETON, MDX, M1–M48)
4 students will be recruited into joint projects with industrial partners (PhD thesis co-supervised by industrial partner, collaboration with business partner on a research project). Towards the end of the project, the students will be required to compile a final scientific report on their project (either finished PhD thesis or a baseline).

T6.3– Soft Skills Training Program (JIC, MU, NII SAS, MDX M6–M46)
Training sessions delivered by a specialist in the relevant field will be delivered 1-2times/year (6 in total) on the following topics: leadership skills and communication, grant application writing, project management and teamwork, entrepreneurship and IPR protection, and time management and work-life balance.

T6.4 - Dissemination of results towards stakeholder groups (MU, NII SAS, BMC SAS, Biovendor, GENETON, MDX M3-M48)
Support of Gold Open Access in publications, fostering participation of PIs, post-docs and students on international conferences. Detailed CDE Plan will be created and regularly updated, describing the CDE strategy towards different stakeholder groups (scientific, industry, society etc.)

T6.5 - Thematic Summer School and Workshops (MU, NII SAS, BMC SAS, GENETON, MDX M5-M46)
2 thematic Summer Schools will be organised (5 days, at least 60 participants and 10 speakers). Gender balance of invited speakers will be considered. The Consortium will co-organise the semi-annual AD workshops in the CR.

T6.6 - Events Targeting the Broader Community (MU, NII SAS, BMC SAS, ICRC M4 - M48)
The consortium will co-organise and participate in events described in Section 2.2.1. In addition, further communication and dissemination options will be sought and exploited during the project lifetime

Work package WP7 – Project Governance, Management and Ethics

Work Package Number	WP7	**Lead Beneficiary**	1. MU
Work Package Name	Project Governance, Management and Ethics		
Start Month	1	**End Month**	48

Objectives

- Provide general strategic and operational management, including the CDE management and risk management
- Manage liaisons with the European Commission and ensure quality and timeliness of deliverables
- Conduct day-to-day administrative and financial management of the project
- Establish a long-term management framework for the operation of the joint ecosystem
- Ensuring the proper observation of ethics issues and following the principles of ethical research

Description

T7.1 – Project Management, Administrative and Financial Reporting (MU, all, timespan M1–M48)
Interfacing with the European Commission, decision making coordination, Data Management plan, updates and internal communication tools. Coordination of interim and final financial and technical reporting.

T7.2 – Quality and Risk Management (MU, all, timespan M1–M48)
Continuous quality management and risk monitoring and assessment. Coordination of risk mitigating measures.

T7.3 – Management of project communication tools and channels (MU, all, M1–M48)
Preparation and maintaining of communication tools according to CDE Plan. Creation of project visual identity.

T7.4 – Strategic Steering of the Joint Ecosystem (MU, all, timespan M1–M48)
Annual meetings of Steering Committee, assessing the project implementation.

T7.5 - Ethics Management (MU, timespan M1-M6)
This task ensures the preparation and submission of deliverables on Ethics issues – Protection of personal data, Informed consent of human participation in research, etc.

STAFF EFFORT

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	WP6	WP7	Total Person-Months
1 - MU	39.10	24.90	14.00	130.20		100.80	26.40	335.40
2 - NII SAS	32.10	30.00	11.00	43.92	30.40	20.40	19.20	187.02
2.1 - SALS					9.60		2.40	12.00
3 - ICRC	9.60			21.20	99.00	17.60	4.80	152.20
4 - MC				4.80	67.20		14.40	86.40
5 - BIOVENDOR	4.80	4.80	7.20	9.60		4.80	4.80	36.00
6 - BMC SAS	4.80	3.60			19.20	14.40	14.40	56.40
7 - MH	6.00	3.60					4.80	14.40
8 - MDX	9.00	9.44	5.56	8.88	10.38	5.06	5.76	54.08
9 - GENETON	3.06	3.04	2.16		9.38	4.06	5.76	27.46
10 - JIC	9.00		3.60			7.20	2.40	22.20
11 - CALS					9.60		2.40	12.00
Total Person-Months	117.46	79.38	43.52	218.60	254.76	174.32	107.52	995.56

LIST OF DELIVERABLES

Deliverables

Grant Preparation (Deliverables screen) — Enter the info.

The labels used mean:

Public — fully open (⚠ automatically posted online)
Sensitive — limited under the conditions of the Grant Agreement
EU classified —RESTREINT-UE/EU-RESTRICTED, CONFIDENTIEL-UE/EU-CONFIDENTIAL, SECRET-UE/EU-SECRET under Decision 2015/444

Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D1.1	Report on Research and Exploitation Potential and Market Analysis	WP1	2 - NII SAS	R — Document, report	SEN - Sensitive	12
D1.2	Preliminary Joint R&I Strategy	WP1	1 - MU	R — Document, report	SEN - Sensitive	18
D1.3	Final Joint R&I Strategy and Report on Business/User Networking	WP1	1 - MU	R — Document, report	SEN - Sensitive	48
D1.4	Evaluation Report by the EAB	WP1	1 - MU	R — Document, report	SEN - Sensitive	36
D2.1	Final Research Plans and Findings of Feasibility Studies	WP2	2 - NII SAS	R — Document, report	SEN - Sensitive	48
D3.1	Final Investment Plans and Findings of Patentability Studies	WP3	5 - BIOVENDOR	R — Document, report	SEN - Sensitive	48
D3.2	Technology Transfer Framework	WP3	1 - MU	R — Document, report	SEN - Sensitive	36
D4.1	Tau biomarker identification in CFS and blood	WP4	2 - NII SAS	R — Document, report	SEN - Sensitive	12
D4.2	Optimized protocol of the purfication and selective phosphorylation of selected Tau fragments prepared recombinantly and Molecular basis of ApoE oligomerization and aggregation	WP4	1 - MU	R — Document, report	SEN - Sensitive	24

Deliverables

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D4.3	Novel tau species in the CSF and blood and in the medium of iPSCs and Tau assay development	WP4	2 - NII SAS	R — Document, report	SEN - Sensitive	36
D4.4	Assigned solution NMR spectra of the selected Tau fragments	WP4	1 - MU	R — Document, report	SEN - Sensitive	32
D4.5	Structural analyses of the selected tau biomarkers and validations of assays and new biomarkers	WP4	1 - MU	R — Document, report	SEN - Sensitive	46
D4.6	Validation of low input microRNA sequencing protocol	WP4	8 - MDX	R — Document, report	SEN - Sensitive	22
D4.7	Identification and validation of microRNA biomarkers for AD	WP4	8 - MDX	R — Document, report	SEN - Sensitive	46
D5.1	Report on the AD cohorts	WP5	3 - ICRC	R — Document, report	SEN - Sensitive	36
D5.2	Harmonisation of recruitment and diagnostics method and Report on Non-pharmacological Interventions	WP5	3 - ICRC	R — Document, report	SEN - Sensitive	48
D5.3	Plan of the Communication Campaign	WP5	3 - ICRC	R — Document, report	PU - Public	12
D5.4	Summary of the Communication Campaign	WP5	3 - ICRC	R — Document, report	PU - Public	48
D6.1	Initial Training Plan and CDE Plan	WP6	1 - MU	R — Document, report	PU - Public	6
D6.2	Interim Training and CDE Report and Plan	WP6	1 - MU	R — Document, report	PU - Public	24

Deliverables

Grant Preparation (Deliverables screen) — Enter the info.

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D6.3	Final Training Report and Scientific Report on Industrial PhDs, CDE Plan for post-project period	WP6	1 - MU	R — Document, report	PU - Public	48
D7.1	Data Management Plan	WP7	1 - MU	DMP — Data Management Plan	PU - Public	6
D7.2	Quality Plan, Ethics Requirements and Project Visual Identity, Website and Social Media	WP7	1 - MU	R — Document, report	PU - Public	2

Deliverable D1.1 – Report on Research and Exploitation Potential and Market Analysis

Deliverable Number	D1.1	**Lead Beneficiary**	2. NII SAS
Deliverable Name	Report on Research and Exploitation Potential and Market Analysis		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	12	**Work Package No**	WP1

Description
summary of the results of T1.1.

Deliverable D1.2 – Preliminary Joint R&I Strategy

Deliverable Number	D1.2	**Lead Beneficiary**	1. MU
Deliverable Name	Preliminary Joint R&I Strategy		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	18	**Work Package No**	WP1

Description
Preliminary plans for Task 1.3.

Deliverable D1.3 – Final Joint R&I Strategy and Report on Business/User Networking

Deliverable Number	D1.3	**Lead Beneficiary**	1. MU
Deliverable Name	Final Joint R&I Strategy and Report on Business/User Networking		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	48	**Work Package No**	WP1

Description
Results of the Tasks 1.3. and 1.5. The draft version of Joint Research Strategy will be presented for evaluation to the EAB in M36.

Deliverable D1.4 – Evaluation Report by the EAB

Deliverable Number	D1.4	**Lead Beneficiary**	1. MU
Deliverable Name	Evaluation Report by the EAB		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP1

Description
Results of evaluation of the drafted Strategy.

Deliverable D2.1 – Final Research Plans and Findings of Feasibility Studies

Deliverable Number	D2.1	**Lead Beneficiary**	2. NII SAS
Deliverable Name	Final Research Plans and Findings of Feasibility Studies		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	48	**Work Package No**	WP2

Description
Final designs of research projects for the post-project period. Report on the results of the Task 2.3. The working versions of the research plans will be evaluated in M36 by the EAB.

Deliverable D3.1 – Final Investment Plans and Findings of Patentability Studies

Deliverable Number	D3.1	**Lead Beneficiary**	5. BIOVENDOR
Deliverable Name	Final Investment Plans and Findings of Patentability Studies		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	48	**Work Package No**	WP3

Description
Final plans of investments for the post-project period. A draft version in M36 will be evaluated by the EAB. Report on the results of the T3.3.

Deliverable D3.2 – Technology Transfer Framework

Deliverable Number	D3.2	**Lead Beneficiary**	1. MU
Deliverable Name	Technology Transfer Framework		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP3

Description
Description of best practices for technology transfer, tailored for the regional specifics of the project consortium.

Deliverable D4.1 – Tau biomarker identification in CFS and blood

Deliverable Number	D4.1	**Lead Beneficiary**	2. NII SAS
Deliverable Name	Tau biomarker identification in CFS and blood		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	12	**Work Package No**	WP4

Description
Description of analytical strategy leading to novel tau identification.

Associated with document Ref. Ares(2022)7738099 - 09/11/2022

Deliverable D4.2 – Optimized protocol of the purfication and selective phosphorylation of selected Tau fragments prepared recombinantly and Molecular basis of ApoE oligomerization and aggregation

Deliverable Number	D4.2	**Lead Beneficiary**	1. MU
Deliverable Name	Optimized protocol of the purfication and selective phosphorylation of selected Tau fragments prepared recombinantly and Molecular basis of ApoE oligomerization and aggregation		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	24	**Work Package No**	WP4

Description
Special attention will be given to the yield of the purified proteins and purity of the prepared proteins (T4.2). Description of the molecular mechanism of pathological aggregation of ApoE proteins. (T4.6)

Deliverable D4.3 – Novel tau species in the CSF and blood and in the medium of iPSCs and Tau assay development

Deliverable Number	D4.3	**Lead Beneficiary**	2. NII SAS
Deliverable Name	Novel tau species in the CSF and blood and in the medium of iPSCs and Tau assay development		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP4

Description
Report on the novel Tau biomarkers identified in the CSF and blood. Assay development targeting selected tau biomarkers.

Deliverable D4.4 – Assigned solution NMR spectra of the selected Tau fragments

Deliverable Number	D4.4	**Lead Beneficiary**	1. MU
Deliverable Name	Assigned solution NMR spectra of the selected Tau fragments		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	32	**Work Package No**	WP4

Description
NUS-NMR approaches will be applied for the assignment.

Deliverable D4.5 – Structural analyses of the selected tau biomarkers and validations of assays and new biomarkers

Deliverable Number	D4.5	**Lead Beneficiary**	1. MU
Deliverable Name	Structural analyses of the selected tau biomarkers and validations of assays and new biomarkers		

Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	46	**Work Package No**	WP4

Description
Structural analyses of selected tau biomarkers identified in the CSF and iPSCs medium. Results from validation of analytic aspect of the assay as well as its diagnostic accuracy. Results from immuno-characterization of pathological ApoE species and assays development.

Deliverable D4.6 – Validation of low input microRNA sequencing protocol

Deliverable Number	D4.6	**Lead Beneficiary**	8. MDX
Deliverable Name	Validation of low input microRNA sequencing protocol		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	22	**Work Package No**	WP4

Description
Characterization of miRNA sequencing protocol that can analyze miRNA in 1 ng total RNA input for CSF/blood.

Deliverable D4.7 – Identification and validation of microRNA biomarkers for AD

Deliverable Number	D4.7	**Lead Beneficiary**	8. MDX
Deliverable Name	Identification and validation of microRNA biomarkers for AD		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	46	**Work Package No**	WP4

Description
Report on novel miRNA biomarkers identified in CSF/blood of AD patients and cerebral organoids. Results from validation of miRNA biomarkers using miRNA-FISH combined with protein co-detection.

Deliverable D5.1 – Report on the AD cohorts

Deliverable Number	D5.1	**Lead Beneficiary**	3. ICRC
Deliverable Name	Report on the AD cohorts		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	36	**Work Package No**	WP5

Description
New clinically well-defined subjects (controls, SCD, MCI, AD) will be recruited using categorical A/T/N biomarker classification system.

Deliverable D5.2 – Harmonisation of recruitment and diagnostics method and Report on Non-pharmacological Interventions

Deliverable Number	D5.2	**Lead Beneficiary**	3. ICRC
Deliverable Name	Harmonisation of recruitment and diagnostics method and Report on Non-pharmacological Interventions		
Type	R — Document, report	**Dissemination Level**	SEN - Sensitive
Due Date (month)	48	**Work Package No**	WP5

Description
Report on the results of the task T5.2 and T5.3.

Deliverable D5.3 – Plan of the Communication Campaign

Deliverable Number	D5.3	**Lead Beneficiary**	3. ICRC
Deliverable Name	Plan of the Communication Campaign		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP5

Description
A detailed plan for the Task T5.4.

Deliverable D5.4 – Summary of the Communication Campaign

Deliverable Number	D5.4	**Lead Beneficiary**	3. ICRC
Deliverable Name	Summary of the Communication Campaign		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	48	**Work Package No**	WP5

Description
A follow-up report on the Task T5.4.

Deliverable D6.1 – Initial Training Plan and CDE Plan

Deliverable Number	D6.1	**Lead Beneficiary**	1. MU
Deliverable Name	Initial Training Plan and CDE Plan		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	6	**Work Package No**	WP6

Description
Action plan of training activities for the 1st year of the project, (planned speakers/coaches, topics/fields of trainings, trainees for internships, and outline for industrial PhD projects).

Definition of CDE measures and action plan of CDE activities for the project.

Deliverable D6.2 – Interim Training and CDE Report and Plan

Deliverable Number	D6.2	**Lead Beneficiary**	1. MU
Deliverable Name	Interim Training and CDE Report and Plan		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	24	**Work Package No**	WP6

Description
Report on the training and CDE activities of the previous period. Evaluation of the strategies and Plan for the upcoming period.

Deliverable D6.3 – Final Training Report and Scientific Report on Industrial PhDs, CDE Plan for post-project period

Deliverable Number	D6.3	**Lead Beneficiary**	1. MU
Deliverable Name	Final Training Report and Scientific Report on Industrial PhDs, CDE Plan for post-project period		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	48	**Work Package No**	WP6

Description
Report on the training and CDE activities of the previous period and updated action plan for the following/post project period. Results of the Task 6.2 (summary of publications, published theses).

Deliverable D7.1 – Data Management Plan

Deliverable Number	D7.1	**Lead Beneficiary**	1. MU
Deliverable Name	Data Management Plan		
Type	DMP — Data Management Plan	**Dissemination Level**	PU - Public
Due Date (month)	6	**Work Package No**	WP7

Description
Detailed guidelines of the treatment of all types of data associated with the project utilising the Horizon Europe best practices on data management.

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

Deliverable Number	D7.2	**Lead Beneficiary**	1. MU

Deliverable Name	Quality Plan, Ethics Requirements and Project Visual Identity, Website and Social Media		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	2	**Work Package No**	WP7

Description
Summary of set-up related to T7.2 and T7.3. Ethics approvals from participating institutions and templates of informed consent.

Associated with document Ref. Ares(2022)7738099 - 09/11/2022

LIST OF MILESTONES

Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
1	R&I Needs and Gaps Analyzed	WP1	2-NII SAS	D1.1	12
2	External Advisory Board Established	WP1	1-MU	D1.5	36
3	Joint R&I Strategy Finalised	WP1	1-MU	D1.4	48
4	Brokerage Events Organised	WP1	-	D6.3	42
5	First batches of recombinantly prepared selected Tau fragments	WP4	1-MU	D4.1	12
6	Knowledge on the molecular mechanism of ApoE aggregation	WP4	1-MU	D4.2	24
7	Novel tau biomarkers in CSF and blood	WP4	2-NII SAS	D4.3	30
8	Structural characterization of Tau fragments	WP4	1-MU	D4.5	32
9	Structural characterization of fibrils formed by selected Tau fragments	WP4	1-MU	D4.5	42
10	Determined binding epitopes of selected proteins and antibodies within the selected Tau fragments	WP4	2-NII SAS	D4.5	46
11	Tau assay	WP4	2-NII SAS	D4.5	46
12	Completion of miRNA sequencing protocol	WP4	8-MDX	D4.6	22
13	Characterization of biomarker panel for AD	WP4	8-MDX	D4.7	46
14	AD Cohorts Recruitment	WP5	3-ICRC	D5.1	36
15	Communication Campaign Plan Adopted	WP5	3-ICRC	D5.3	12
16	Industrial PhDs Recruited	WP6	2-NII SAS	D6.1	6

Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
17	Training Plan Completed	WP6	1-MU	D6.3	46
18	Industrial PhDs Completed	WP6	2-NII SAS	D6.3	46
19	2 Summer schools organised	WP6	2-NII SAS	D6.2, D6.3	46
20	8 Project Workshops organised	WP6	1-MU	D6.3	48

LIST OF CRITICAL RISKS

Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
1	Internal rules and processes of the partnered institutions can be incompatible, making the implementation (i.e. job shadowing, hands-on internships etc.) inefficient.	WP7, WP3, WP6, WP4	(i) Possible incompatibilities will be presumed and resolved within the Consortium Agreement prior the project period. (ii) PM will be monitoring possible conflicts that might occur during the implementation of the project and will ensure their timely handling.
2	PI from an academic institution will leave during the project, causing discontinuity of research, training, and strategy development.	WP1, WP2, WP6, WP4	All PIs 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 PI to take over.
3	Business partner will leave the project by external forces (i.e. economic decline).	WP1, WP2, WP3, WP6, WP4	Due to the war in Ukraine, the economy of the Central Europe can become more vulnerable in this decade. Therefore, all companies will focus either on enlargement of product portfolio or by more intensive collaboration with pharma partners to mitigate the risk of economic decline.
4	Rise of new epidemics resulting in state-	WP6, WP5	All partners already have vast experience with online spaces for networking and

Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
	wide lockdowns and border closures, blocking dissemination and training vectors.		dissemination. If need arises, we are able to convert workshops, lectures, discussions etc. in online format.
5	Low interest of civil society in the project, resulting in an inefficient communication campaign.	WP5	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.
6	Deterioration of economy (spiralling inflation) raising the cost of services and materials above planned budget.	WP7, WP6, WP4	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.

PROJECT REVIEWS

Project Reviews

Grant Preparation (Reviews screen) — Enter the info.

Review No	Timing (month)	Location	Comments
RV1	18	TBC	online or face to face depending on the situation
RV2	33	TBC	online or face to face depending on the situation
RV3	48	TBC	online or face to face depending on the situation

History of changes

Page/Section	Nature of change and reason
Part A – page numbers refer to the submitted proposal (file: Proposal-SEP-210822210.pdf)	
List of participants (page 5 part A, page 1 part B)	Participant 4/AXON NEUROSCIENCE removed. All subsequent partners renumbered. Participant 9/GENETON added.
List of work packages (page 18 part B)	The lead participant of WP4 – AXON replaced by NII SAS. The lead participant of WP2 replaced by MDX and the lead of WP3 replaced by BioVendor. These changes reflect the removal of AXON from the project and the heightened role of business partners in the consortium following the evaluation comments.
Work packages description – WP2, Task T2.2 (page 20 part B)	NII SAS will identify and adopt new technologies (proteomics) for this project. MDX will identify and adopt new mRNA technologies for this project. GENETON will identify and adopt new genomic sequencing technologies for this project. The lead of this task is MDX.
Work packages description – WP3, Task T3.1 (page 20 part B)	MU will be replaced by BioVendor as a leader on this task, utilising the company's long-standing success in collaborative research and securing project investment.
Work packages description – WP3, Task T3.2 (page 20 part B)	MU will be replaced by JIC as a leader on this task, utilising the established position of JIC in the technology transfer scene in the South Moravian Region.
Work packages description – WP3, Task T3.3 (page 20 part B)	AXON will be replaced by MDX as a leader of this task. The innovation potential of viable project designs will be evaluated by MDX. Patentability studies will be performed together with BIOVENDOR and JIC.
Work packages description – WP4 (pages 21 + 22 part B)	AXON will be replaced by NII SAS as a leader of this WP. AXON experts from the field are employed by the Institute, therefore all activities will be realised according to the plans. AXON provides monoclonal antibodies against tau to NII SAS. The ELISA assays will be performed by NII SAS. The assay will be developed and validated by NII SAS.
WP5, T5.1 (page 23 part B)	AXON was responsible for fluid biomarker analyses of patients suffering from dementia. NII SAS has long lasting expertise in this field so this can be easily transferred to the Institute.
WP6, T6.3 (page 24 part B)	MDX will cooperate on soft skills education instead of AXON.
Work packages description – WP6, T6.4 (page 24 part B)	Since NII SAS will realise all scientific activities planned by AXON, it will be also responsible for dissemination of results to scientific community. MDX will be responsible for business fair and industrial conferences.
All Work Packages	Personnel effort per participant adjusted to reflect the change in project consortium.
List of deliverables (pages 26+27 part B)	DLVs D1.1 a D1.2 grouped (M12). D1.4, D1.5 and D1.7 grouped in M48. D2.1, D2.2 and D2.3 grouped in M48. D3.1, D3.2 and D3.4 grouped in M48. D4.2, D4.3 and D4.4 grouped in M24. D4.5 and D4.7 grouped in M36. D4.8, D4.9, D4.10 and D4.11 grouped in M46. D5.2 and D5.3 grouped in M48. D6.1 and D6.5 grouped in M6. D6.2 and D6.6 grouped in M24. D6.3, D6.4 and D6.7 grouped in M48. D7.1 moved to M6. D7.2, D7.4 and D7.9 grouped in M2. D7.3 and D7.5–8 removed due to being superfluous.
List of milestones (page 27 part B)	Removed milestones in WP7 as they are excessive.
Summary of staff effort (page 28 part B)	Table adjusted to reflect the change in project consortium. Personnel effort of AXON distributed between NII, MDX and GENETON in accordance with the relocated tasks.

Part B of the DoA – page numbers refer to the Annex 1 part B of the DoA	
Throughout the text	Removed mentions of AXON. Added description of roles of GENETON. Unified short names of participants to correspond to DoA part A.
Page 4	Updated graphics of consortium.
Page 14, section Gender balance	Added a line confirming that all partners requiring GEP already have it.
Page 17	Updated the budget breakdown per participant graphics.
Page 17	Updated Gantt chart to reflect the grouped deliverables.
Section 3.2, page 20-21	Description of partner AXON removed. Added description of partner GENETON. The entire section moved to correct the structure of the document (after Tables 3.1).
Table 3.1g, page 18	Subcontracting cost of 1000 EUR from participant 1/MU removed. The acquiring of new project partner GENETON, able to carry out genomic sequencing, the consortium no longer needs to subcontract this task.
Page 18	Added a line clearly stating no subcontracting and no third-party contribution.
Tables 3.1h, pages 18-20	Justification of costs for partner AXON removed. GENETON justification of costs table added. Updated the tables for NII SAS and MDX to reflect the new distribution of work following the change in consortium.
Tables 3.1h, pages 18-20	Corrected the sums and information for partners MU, MDX, and GENETON.
Tables 3.1h, pages 18-20	For partners 2.1/SALS, 4/MC, 5/Biovendor, 6/BMC SAS and 8/MDX, small amounts of OWGS have been moved under Remaining Purchase Costs without justification, as they fall under 15% of personnel costs.
Tables 3.1h, pages 18-20	Replaced “recruitment costs” with “cost of enriching AD patient cohorts” for partner 4/MC. Clarified justification for OWGS for partner 9/GENETON.
Table 3.1i, page 20	Added clarification of internally invoiced costs.
Ethics self-assessment	Added as Section 4.
Section 5 added	Consortium reply and clarifications to shortcomings identified in evaluation.

1. Excellence

Dementia is recognized by the World Health Organization as a public health priority. Globally, an estimated 57 million people were living with dementia in 2019 and this figure is expected to triple to 153 million in 2050[1]. The total costs have already reached 1 trillion USD[2]. As the population ages, the number progressively increases, as currently no effective disease modifying therapy exists. Dementia covers a diverse assortment of disorders with various biological causes. The most numerous amongst them is Alzheimer's disease. Dementia affects memory and other cognitive functions as well as social abilities. These symptoms interfere with patients' activities of everyday life. The modern diagnostics of dementia rely on diagnostic biomarkers - mainly modern PET, CSF or blood biomarkers.[3]

Alzheimer's disease is the main cause for disabilities in later life in Europe. The estimated prevalence of AD and other dementias in Czech Republic is 192 748, while in Slovakia 77 185. Population ageing is expected to lead to increases in projected dementia cases.[1]

	Estimated number of dementia cases		Percentage change
	2019	**2050**	
Slovakia	77 185	163 037	111%
Czech Republic	192 748	379 742	97%

There is still very high number of undiagnosed and misdiagnosed patients. In addition, the majority of patients are diagnosed in the later stages of the disease (moderate-to-severe) where the possibilities for non-pharmacologic intervention vanish. Missed and delayed dementia diagnosis may lead to an increase of patient and caregiver burden.[4] This increases an economic burden in both countries since the estimated total annual cost per person with dementia in Europe is on average €32,506.73.[5]

Currently, there is no conceptual plan which would implement the modern diagnostic approaches able of an early AD detection into the clinical practice in Czechia and Slovakia. Multiple molecular diagnostic tests are running exclusively on the research base. Although, the Czech government accepted the "National Action Plan for Alzheimer's disease and similar diseases", which runs from 2020 to 2030, it does not include novel diagnostic strategies which may help to diagnose the disease in early stages. In contrast, Slovakia belongs to a very few European countries which do not yet possess a National Plan to combat dementia.

The interaction between universities and private sectors leading to the development of molecular diagnostic tools is fragmented and not properly organised. Limited number of talented students are interested in an intensive industry-academia collaboration. Although there are networks encompassing university and academic institutions collaborating on AD research projects, private biotech companies usually do not take part in these networks.

Strong linkages between science and business constitute a tone of the main competitive success factors for R&I performance in more advanced regions of the EU, but these links are under-developed in Czech and Slovak republics (Central Europe). A report on the risk analysis prepared for the updated RIS3 strategy[6] for the region mentions low level of entrepreneurship amongst students and absolvents caused by insufficient support of personal growth, which brings on unsatisfactory exploitation of local human potential. Another existing barrier is a systematically dysfunctional relationship between universities and companies and mutual deficiency in readiness for cooperation, including a persistent gap between academic and industry research.

The main aim of ADDIT-CE is to create two inter-linked ecosystems in Central Europe, one in South Moravia (CZ) and one in Bratislava region (SK), which will encompass the whole quadruple helix of innovation driving actors: excellent scientific teams from Masaryk University and Slovak Academy of Sciences will collaborate with private biotech companies BioVendor Geneton s r.o. and MultiplexDX. The societal actors will be represented by Czech and Slovak Alzheimer Societies, Centrum Memory (SK) and Czech Brain Aging Study. The regional government will be involved through Ministry of Health Slovak Republic, which organises clinical research and supports talented researchers, and South Moravian Innovation Centre (JIC), a publicly funded agency supporting entrepreneurship in South Moravia (see also Section 3.2).

The ecosystems will create a **joint cross-border R&I Strategy** which will unite R&I activities focusing on new AD diagnostic methods and their applications, perform academia-industry collaborative research on identification of

1) Nichols E., Lancet Public Health. 2022, 7(2): e105–e125
2) Prince M, Wimo A, Guerchet M, Gemma-Claire A., London: Alzheimer's Disease International; 2015.
3) Jack CR Jr et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. 2018, 14(4):535-562
4) Bradford A et al., Alzheimer Dis Assoc Disord. 2009 Oct–Dec; 23(4): 306–314
5) Cantarero-Prieto D, et al., Dementia (London). 2020, 19(8):2637-2657
6) https://www.mpo.cz/assets/en/business/ris3-strategy/2022/1/National-RIS3-Strategy_2.pdf

novel biomarkers reflecting the progression of the disease, which can be used in early diagnostics and as efficacy biomarkers for non-pharmacological therapy, foster a culture of innovation by jointly organising a wide array of supporting activities for students and prospective innovators, and further interlink academia and business spheres by creating a pilot programme of industrial PhD positions for talented students from both regions.

ADDIT-CE will generate new collaborative research project proposals in the field of AD diagnostics, mobilise private capital, competitive national and international funding for development of research infrastructures, transfer new cutting-edge technologies into the clinical practice, and accelerate the development of new diagnostic tools for AD diagnostics which will bring on new business opportunities especially for SMEs. In addition, we plan to disseminate knowledge on the modern concept of the AD diagnosis to general practitioners, clinical specialists and professional caretakers, and organise a communication campaign to inform public about the opportunity to identify AD in early stages of the disease. The project will join forces of all actors of the involved ecosystems to revolutionise the diagnostic approaches in both countries.

Pertinence to the Work Programme: Excellence Hubs are part of the European Excellence Initiative focusing on innovation by allowing R&I ecosystems in widening countries to team up and create better linkages between academia, business, government and society. In this respect, ADDIT-CE will foster a real place-based innovation culture in two regions closely interconnected geographically, economically, historically and culturally. The **Strategic Agenda** of ADDIT-CE is **fully aligned with RIS3 priorities in both involved countries**, namely:

- Healthcare and advanced medicine (Smart specialisation strategy area of the Czech National RIS3),
- Healthy Society specialisation domain of the Slovak National RIS3.

ADDIT-CE will contribute to the RIS3 design to interlink competitive, economically and socially important and promising sectors with research capacities and key technologies that have been identified based on an analysis of the countries' technological specialisations.

1.1 Objectives

Project objective:

Connecting two existing R&I ecosystems in Brno (South Moravia) and Bratislava regions with a joint cross-border Strategy to modernise Alzheimer's Disease diagnostics approaches and transfer them into clinical practice with the involvement of all innovation driving actors: academic, industry, government and society.

Specific objectives for the project related to the overall intensification of academia-business relations in the field of applied AD research and the strengthening of the involvement of governmental and societal actors on the strategic AD-focused research and innovation development in the region include:

(1) Creating an excellent knowledge base enabling the development of new AD-diagnostic tools.

By sharing our expertise from basic and clinical neuroscience between the two regions and further enhancing it by knowledge exchange networking with top neuroscience experts outside the consortium, we will speed up the development of new diagnostic tools for AD and harmonise the processes of molecular diagnostics across the border. The rise in excellence will be verified by a measurable performance indicator – a **300% increase of high-quality publications** in major peer-reviewed journals in the field of AD diagnostic research, affiliated to ADDIT-CE academia partners, when compared to the 4-year pre-project period (2019-2022).

(2) Stimulating interaction between academic and private sector developing AD-diagnostic assays.

Through the ADDIT-CE collaborative research project (WP4), proposing further collaborations with industry on brokerage events (WP1), and launching a pilot programme of industrial PhD to bring together academic and industry-based research (WP6), we will contribute to the expected call outcome – strengthened linkages between science and business. The fulfilment of this objective will be verified by the following performance indicators – **at least 4 academia-industry collaborative projects (2 from each ecosystem)** in line with the joint **Strategy**, and **4 industrial doctorates finalised** immediately after the project.

(3) Developing common plans for R&I development and infrastructure investments.

The successful implementation of ADDIT-CE will result in the mobilisation of regional, national and international funding as well as private and venture capital. The Joint Strategy will feature pilot R&I projects (WP2) in the field of AD diagnostics aligned with the regional innovation strategies for smart specialisation (RIS3). The rise in excellence, innovation potential and collaboration opportunities will bring about an increase in success rate of attracting competitive funding and private capital (WP3). This increase can be quantified with the following indicators: a) above threshold evaluation of at least **10 new project proposals** during the project; b) international grants awarded to the consortium partners in the total of at least 3 Mio EUR in the year following the project; c) **20% increase in private and venture capital** when compared to the pre-project period (2019-2022).

(4) Joining forces of private and academic research to identify new tau protein, apolipoprotein E (ApoE) and miRNA biomarkers for AD, modernise the standard of AD diagnostics, and validate it for clinical use.

This specific objective is fully in line with the proposed **Joint R&I Strategy** of ADDIT-CE to modernise AD-diagnostics in CZ and SK. We aim to move from the old-fashioned NINCDS-ADRDA diagnostic criteria based solely on purely clinical evaluation to the NIA-AA clinical criteria with biomarker support and/or IWG criteria where clinical and biomarker features must be present for diagnosis. Therefore, we plan to integrate biomarkers from body fluids (blood, CSF) and imaging into diagnostic algorithm. We will focus on new strategies to identify innovative tau, ApoE species and miRNAs to better reflect the course of the disease and increase the chance of early diagnosis. The diagnostic potency of selected candidates will be validated through testing in the existing AD cohorts in both countries. This way, the proposed diagnostic assays for determination of biomarkers will be introduced directly into the clinical practice, which contributes to the expected outcome of the call – uptake of innovative technologies. The achieving of this objective will be verified by fulfilling the project's milestones in WP4 and publication of results.

(5) Validating selective biomarkers as efficacy readout for non-pharmacological therapy.

The assays and biomarkers developed in WP4 will be used to monitor the efficacy of the non-pharmacology therapy (such as memory training, mental and social stimulation, and physical exercise programs) on the cohorts recruited in both regions following the international standards (WP5). This will directly involve regional societal actors and end users (patients and clinical specialists) in ADDIT-CE, corresponding with the Destination impact – greater involvement of regional actors in R&I processes. The achieving of this objective will be verified by the publication of results.

(6) Harmonising cohorts of AD patients in Czech and Slovak republics.

Currently, there are two independent AD cohorts, one in Memory Centre, Bratislava, and the Czech Brain Aging Study which is a part of the International Clinical Research Centre, St. Anne's University Hospital in Brno. They use different diagnostic approaches. Thus, we aim to coordinate the processes and the diagnostic tools between both clinical centres to build a fully harmonised Czech-Slovak AD cohort (WP5), aided by the easy understanding between Czech and Slovak languages. We will expand the present databases on the patient cohorts with further state-of-the-art methods and conduct a public information and outreach campaign to recruit patients into our longitudinal observation cohorts. Through these efforts, we will secure a steady stream of high-quality samples for biomarkers validation and elevate the uptake of modern AD diagnostic methods used at the clinical centres. At least 100 participants will be recruited or re-screened in CBAS and 50 in Memory Center.

(7) Improve connections between general practitioners, psychiatrists, neurologists, neuropsychologists, healthcare professionals and family caretakers.

The aim is to empower general practitioners to take an active role in dementia diagnosis; start dementia diagnosis pathway already during first patient contact and to connect them to the clinical centres. We will prepare the concept of a nation-wide epidemiological study on AD to gather the necessary data, implement more efficient patient handling to save resources, and the time of healthcare professionals, patients, and both professional and family caregivers. This activity (WP5, WP6) will be endorsed by governmental and societal partners of ADDIT-CE and we aim to implement the results into the emerging National Plan Against Dementia in Slovakia.

1.2 Coordination and/or support measures and methodology

The ADDIT-CE project is comprised from a bundle of activities designed to achieve the project objectives. The CZ-SK network built within the joint ecosystem will create a mass of concentrated knowledge and know-how to overcome the gaps and tackle the obstacles of R&I development and achieve the **objective 1** by maximising the potential for nucleation and growth of innovative ideas. The students and junior researchers will be trained to cover state-of-art methodologies of AD diagnostics research (described in section 3.2) through participation in the research project. Their expertise will be elevated by hands-on trainings in methods and techniques employed at the business partners, as well as through lectures by invited renowned experts in the field (4x/year), which will also offer opportunities for new collaborations.

Research group leaders will build on their synergic links to branch out the collaborative potential beyond the CZ-SK region. They will identify relevant conferences to meet prospective partners for scientific collaboration as well as partners for consortia for future research proposals. We expect an active participation (invited lecture, oral) to at least 4 conferences/year. Research group leaders will also monitor existing international networks (i.e., COST actions) and strive to join those in which they can contribute to the expected impact of the network, in turn building the international reputation of the CZ-SK region.

To ensure the highest degree of **excellence and openness** of R&I activities in the emerging hub, the developed Strategy will be independently evaluated (M36) by an External Advisory Board (EAB) consisting of world-renown experts in the field, experts from industry, and representatives of policy making bodies both in CZ and SK. This will ensure that the developed Strategy will be fully aligned with the national and regional RIS, will have a continuous support for its implementation phase after the project end, and gains **credibility** (through independent evaluation) in line with the principles of Open Science.

Multiple activities are planned to stimulate interaction between academic and private sector (**objective 2**). By synergizing research and development capacities of academic and industrial partners within both ecosystems we will boost modern comprehensive diagnostics of AD by a discovery of new **tau protein, ApoE and miRNA candidate biomarkers (objective 4)**, validated on clinical samples and prepared towards clinical development. The original innovative approach will consist in targeted development of diagnostic assays for the biomarkers with thoroughly characterised origin, molecular identity and 3D structure. A close collaboration will be established between research teams from three faculties of MU (CEITEC MU, Faculty of Sciences, Faculty of Medicine), two institutes of Slovak Academy of Sciences and three biotechnological companies, MultiplexDX, Geneton and BioVendor, on the exploration of new biomarkers of AD.

Particular attention will be given on tau fragments of various length and position, containing multiple post-translational modifications and on APOE fragments and aggregates. In the case of **tau protein**, new biomarkers will be derived from two complementary approaches: (i) discovery of new tau species directly from patient body fluids obtained from clinical cohort samples, validated on organoid models and (ii) structural knowledge-based selection of the hot-spots on tau species, the most appropriate for detection. This approach would have the potential to generate a qualitatively new level of more specific, more sensitive and more selective tau biomarkers. All this process can be fuelled by more than thirty-year long experience of tau research present in NII SAS. As the tau is disordered protein, detailed structural analysis of new tau diagnostic species will be performed at MU by applying solution NMR, which is the method of choice for this type of analysis and of which the MU team pioneered the methodological developments and their applications for microtubule associated proteins, including the Tau protein.[7]

Highly innovative will be the use of **ApoE as an AD protein biomarker**. MU in collaboration with BioVendor will be focussed on structural characterization of diagnostic forms of ApoE protein, with a particular attention to its multimerization. Hybridoma technology (NII SAS) will serve for generation of new biomarker specific antibodies, whose affinities will be further increased experimentally and *in silico*. Finally, for the discovery phase of candidate biomarkers will be necessary to embark on development of a sufficiently sensitive bioassays (NII SAS, BioVendor). To complement protein biomarkers, a panel of **miRNA biomarkers** will be identified as well (MultiplexDX).

As a part of the **accompanying measures** in view of creating a culture of innovation in the joint ecosystem, we will provide the students and researchers of the partnering institutions with new skills beneficial to their career development through international and inter-sectoral mobility. Four **Industrial PhD students** (2 in CZ, 2 in SK) will be supported by ADDIT-CE as a pilot project for this activity, which is one of the most effective ways to strengthen the academic and business sector. The students will spend the majority of their research in industry-based environment, and their theses will be co-supervised by the industry experts. After the project, the Industrial PhD programme will be continued under the patronage of the business partners.

7) Zapletal et al., Biophysical journal, 118 (7), 2020, pp. 1621-1633

To create common plans for R&I development in the field of AD applied research (**objective 3**), PIs of the research project will discuss ideas and formulate personnel requirements for future **collaborative projects** during various opportunities provided by the dissemination and networking activities. Synergies in research will be built through bilateral interactions between jointly working teams to share know-how and technical expertise. The plans for future research projects will branch out from the current research project, will react to the newest developments in the field of AD diagnostics, and will be in line with the Strategy developed in T1.2. For example, we have already identified the need for a large-scale **epidemiologic study** to be carried out in SK, which will tie into the plan to prepare the National program against dementia in collaboration with the Slovak Ministry of Health (MH).

To secure the **financial resources** needed to implement the Strategy through the joint research projects and activities, the ADDIT-CE project will foster interplay between academic and business actors on both regional and national level (through planned brokerage events) and establish an efficient technology transfer framework in the joint R&I ecosystem.

Parallelly with the design of joint intersectoral research projects (WP2), we will prepare investment plans for these projects, mobilising the funds from ERDF, national funding providers, venture capital, and collaborating private businesses (WP3). To maximise the commercial exploitation of research results, we will establish a clear and efficient **technology transfer** framework within the joint R&I ecosystem. JIC will provide its expertise and experience with fostering innovation ecosystems and exploit its vast database of contacts in the business/industrial sphere. Patentability studies will be carried out for selected prospective innovative ideas. In case of a positive result, the foundation of a spin-off will be considered. In this activity, JIC will provide its long-standing expertise in stimulation of innovative entrepreneurship in the region. This will result in the creation of new jobs and new exploitation revenues. Similar role will play the Institute of Research and Development (IRD) of MH on the Slovak ecosystem.

To maximise the cross-border collaboration, the **societal actors** in the individual ecosystems will need to harmonise their activities. In Czech Republic exists one running longitudinal study of AD patients (Czech Brain Aging Study[8]) ran under ICRC at two major hospitals in Brno and Prague, whereas in Slovakia a similar effort is being undertaken at the Memory Centre (MC) in Bratislava. As of now, the AD diagnostics methods used in Slovakia and Czech Republic differ - MC assessment is focused on cognitive testing; while CBAS uses also neurologic testing, multimodal 3T MRI evaluation, genetic evaluation, and laboratory analysis. To achieve **objective 6** and harmonise these two centres, MC's diagnostics procedures will be updated using the CBAS experience ("learning by doing") through regular internships and job shadowing between MC and ICRC. Procedures in sample collection from clinically well-defined subjects (newly recruited + the follow up controls) will be harmonised between centres. Collaboratively, MC and ICRC will devise new procedures for testing new biomarker assays and comparing them with existing clinical data. Business partner Geneton will also participate on this task, where we plan to use their expertise in genomic sequencing to verify a key exclusion criterion for the clinical trials on non-pharmacological therapy, the presence of causative mutations on APP, PS1, PS2 and tau genes which drive familial forms of Alzheimer's dementia and Fronto-temporal dementia.

In Bratislava region, new participants with MCI will be recruited for a non-pharmacological intervention study, based on the complex lifestyle modification. Recruitment and screening will be performed by Memory Centre, in close collaboration with BMC SAS. Using the expertise of the Centre of Physical Activity Research (CPA) of BMC SAS, and data from CBAS life-style questionnaires and interventions, effective non-pharmacological intervention based on the supervised multicomponent exercise training combined with nutrition counselling and mindfulness practices will be designed for at risk subjects from both CBAS and MC cohorts. The multicomponent exercise training has been designed and implemented over the course of more than 4 years at the CPA BMC SAS and proved to be effective in enhancing and maintaining cognitive, motor, and metabolic functions in the elderly, including individuals with MCI. The efficacy of the non-pharmacological therapy will be verified by newly identified biomarkers, which will serve as a validation mechanism for these biomarkers and facilitate the achievement of **objective 5**.

For a successful implementation of the **Strategy** on the regional and national scale, the endorsement and support of **society** is crucial. Alzheimer's Disease Research will always possess a considerable **socio-humanistic** aspect. To broadly communicate our research and innovation efforts to the group of end users and society, we will use the networks of Czech and Slovak Alzheimer Societies (CAS and SAS) to prepare and implement a large-scale communication campaign to engage the target groups in debate about AD early diagnostics, raise awareness about AD diagnostics and non-pharmacological treatment, and **destigmatise the perception of AD** in society. This way, we will improve the connections between societal actors in AD diagnostics and achieve the **objective 7**.

[8]) Sheardova K. et al., BMJ Open, 9(12), e030379

In Czechia, the CAS will be the main driving force behind communication and dissemination of ADDIT-CE to end users, mainly professional caretakers and general practitioners, through articles, info days, online lectures, flyers and newsletters. General public will be addressed through online campaign on social networks and in news outlets (video, articles) to both spread awareness about ADDIT-CE and recruit new subjects for clinical studies of AD patients. Professional caretakers will be addressed on the annual conference Prague Gerontologic Days.

In Slovakia, the SAS will consolidate their network of 70 info points in Slovakia to lay down the foundation for their communication campaign. Over the next two years, 8 major regional contact points will host a series of debates and open lectures targeting society and end users on the topics covered in this project. Two conferences targeting the same audiences will be held in the last year, hosting invited speakers both internal and external to the consortium and communicating the results of the ADDIT-CE project.

Accompanying measures will ensure that the project and its results are **openly** communicated and disseminated to the scientific community, industry stakeholders, societal actors, policy makers, and end users. Building of joint CZ-SK AD diagnostics research network will be also facilitated through semi-annual workshops and two dedicated international summer schools (see section 2.2.1).

To address the broader community of societal actors and the general public, we will participate in many established public events (annual Open Days, Brain awareness week, Alzheimer Disease's Day) as well as organise dedicated communication outlets. The aim is to spark the debate about early-stage AD diagnostics, enhance the engagement of the society in the R&I ecosystem, and bring young minds into the AD diagnostic research. More details on the accompanying measures are listed in Section 2.2.1.

Data Management and Open Access Policy

The Data Management Plan will be prepared as a distinct deliverable (D7.1) and provide detailed guidelines of the treatment of primary and secondary research data and other data associated with the project in line with the FAIR principles - a set of guiding principles to make data **findable, accessible, interoperable and reusable.** This includes definition of standards, secure storage, and exploitation. The expected types of data and metadata produced include raw data gathered as part of the WP4 and documents associated with the project execution. The secure storage and management of the primary research data is the responsibility of the individual research teams complying with the rules set by EC, Consortium Agreement, and their institutions. In this respect, each involved institution provides back-up server space to secure intactness and contingency of the primary data and is responsible for maintaining a database of related metadata. To promote the **Open Research** the collaborating teams will make these data available on established subject-related or general (i.e. ZENODO) repositories. All research partners have an extensive track-record in **open access publishing**. The direct scientific results of the research activity in ADDIT-CE (WP4) will be made available to public immediately upon publishing. We envision the publication of at least 8 jointly authored articles in peer reviewed Q1 journals through the project's lifetime; these will be published using the "gold" open access option. For further scientific dissemination, we will seek publication in open access journals. All project partners fully support open and free access to information. MU (the coordinator) was the first Czech university to sign the Berlin declaration in 2010, and since 2020 implements the 'Open Science Strategy at MUNI' project setting up a comprehensive and clear institutional strategy for open science.

Organisation structure, decision making, and risk management

The organisational structure and decision-making mechanisms are related to the complexity and scale of the project. Horizontally, the project partners convene by electing one or more representatives (in case of MU – 3 SC members representing the 3 departments involved in the project) for each partner into the strategic decision-making body – the **Steering Committee**. SC meetings will be held annually via teleconference or in person during the AD Workshops. In M36, the SC meeting will convene with the External Advisory Board (EAB) meeting (see 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 towards application and development of new interaction topics in the joint ecosystem between Brno and Bratislava regions.

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 Offices or Project Management Offices at partners 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.

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 following steps: (1) Risk identification and characterisation, (2) Risk evaluation (qualitative and quantitative), (3) Risk prioritisation, (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 activity Reports. The PM is also responsible for the creation of internal communication tools and the maintaining 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 programme rules. The meetings of Project Management Team (PC, PM, WP leaders) will be organised quarterly via teleconference.

Ethical aspects of research:

ADDIT-CE project, including its embedded research project (WP4) and its methodology, has been approved by the Ethical Committee of the MU. The usability of identified biomarkers will be tested on samples from patients undergoing non-pharmacological therapeutic intervention. We will use samples of blood serum, plasma, and CSF from participants of an already running longitudinal study Czech Brain Aging Study (CBAS), and a Slovak cohort of AD patients in Memory Center Bratislava. Samples from AD patients, age-matched controls, and patients suffering from other neurodegenerative diseases will be used for this purpose.

The collection of human biological material consists of the collection of approximately 20 ml of blood, which is then sent for laboratory testing to determine blood counts and biochemical substances whose abnormalities may contribute to memory disorders, some of which will be used to determine biomarkers of neurodegeneration. In some cases, it is necessary to perform a lumbar puncture to exclude inflammatory, metabolic or vascular disease of the brain, especially in symptomatic patients where this procedure is warranted. This examination may also help to confirm an atypical course of Alzheimer's disease or other neurodegenerative diseases. The sample collected during this kind of LP is smaller than during standard LP and doesn't pose any additional risk to patients other than a temporary slight headache (in less than 5% of patients). During the research, individual cells or proteins may be isolated from clinical samples No interference with genetic information or genetic analysis will be performed on the samples.

Protection of personal data:

The blood and CSF samples will first be anonymised and, without personal data, anonymously coded, will be handed over for further processing to the researchers of the project consortium members. All samples will be available for scientific analysis only under an identification code without any personal data. Identification codes will be maintained in respective databases to which only Kateřina Sheard, MD, (Head of the CBAS study) and Iliana Királyová, MD (Memory Center) will have access.

Potential impact:

There is no danger of environmental damage in consequence of this research. This project will not cause any negative effects on the population (i.e. stigmatisation of a particular social group, adverse consequences, etc.). On the contrary, we aim to significantly improve the outlook on quality of life for the population endangered by age-related neurodegenerative diseases.

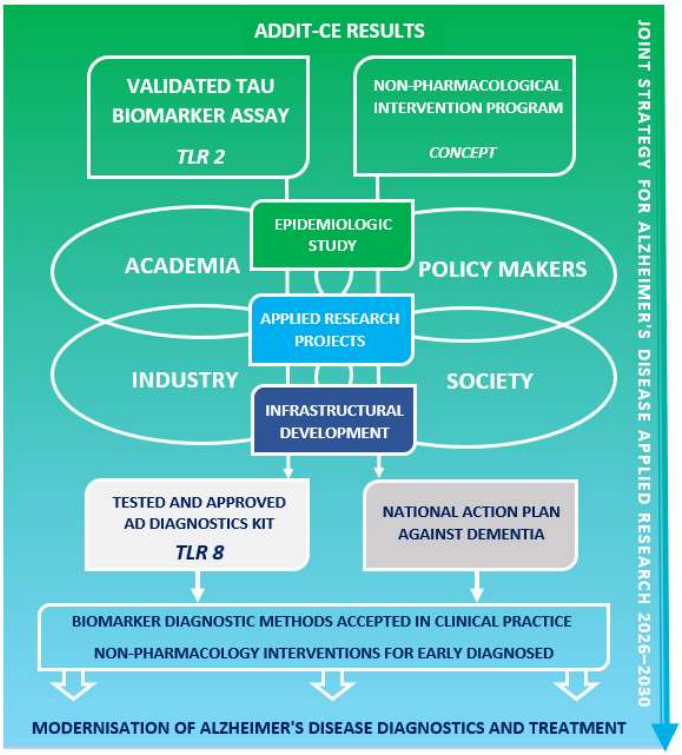
Special attention will be paid to **gender aspects** of AD diagnostics, which include the differences in longevity, biological differences, and traditionally gendered social roles and opportunities. About two thirds of persons diagnosed with AD dementia are women.[9] The life expectancy for women is longer than for men, and age is the greatest risk factor for AD dementia. There is evidence that women exhibit faster rate of cognitive deterioration and of brain atrophy, as well as faster tau accumulation then men.[10,11] Possible explanations include sex-specific risk profiles, and differing interactions between risk factors and AD hallmarks for men and women which are especially significant for women. Such evidence might be of high relevance and requires attention in clinical practice and clinical trials. However, sex and gender differences are currently seldom appreciated; importantly, consideration of sex and gender differences is not currently a focus in the design and analysis of clinical trials for AD. In the research part of this project, we aim to monitor the effect of gender on cognitive performance and molecular biomarkers in patients.

9) Alzheimer's Association: 2017. Alzheimer's disease facts and figures. Alzheimers Dement 2017; 13:325–373
10) Ferretti et al.: Eur J Neurol . 2020 Jun;27 (6): 928-943
11) Smith R. et al. The accumulation rate of tau aggregates is higher in females and younger amyloid-positive subjects. Brain. 2020

2. Impact

2.1 Project's pathways towards impact

The project will lead to the creation of two interlinked ecosystems in the Central Europe (Moravian and Bratislava regions) allowing to generate innovative approaches for future molecular diagnostics of Alzheimer's dementia. The ecosystems will interconnect private biotech companies (BioVendor Geneton and MultiplexDX) with academic institutions (Masaryk University in Brno and Slovak Academy of Sciences) to accelerate the research of new diagnostics assays for AD, to attract young talented PhD students, to translate novel scientific knowledge into the clinical practice and to increase public interest in the early stages of dementia which might be the target of disease modifying therapy in future.



The project stimulates long term joint R&I strategies with special emphasis on the biomarker development projects and will lead to the strategic plans for future collaboration with leading experts from the field. It is based on long-standing experience of biotech companies with the development and commercialization of diagnostic assays. Involvement of research institutions into the projects on AD biomarkers enrich the technological and intellectual aspects of the project and can generate new ideas leading to the innovative approaches in AD diagnostics. Future projects will stem from the findings generated by this consortium and can move the development of diagnostic tools into the next stage. For the biotech companies, participating on the project will bring new business opportunities. In long term, the Strategy will produce a portfolio of collaborative projects that will build R&I capacities in Widening countries of Czechia and Slovakia enabling them to advance to the competitive edge at European and international level, contributing to the WIDERA **Destination #1 – Improved access to excellence**.

The project will function as poles of attraction for talents who will be selected from the best students from involved universities. They will perform both basic and applied research activities, run small projects under supervision of the leaders from the Masaryk University and Slovak Academy of Sciences, and participate on projects running in the biotech companies. One of the key aspects of the project is the transfer of skills pertinent to private sector to the academic ground. Regular workshops will be organised to develop entrepreneurial skills, which allow to translate ideas into the products. The leaders from the companies will teach scientists and students how to realise the concept of applied research into the product development. Further, the project can attract young talents who want to lead risky projects in the biotech environment. This will prevent brain drain and bridge inter-sectoral barriers, directly contributing to the WIDERA **Destination #2 – Attracting and mobilising the best talents**.

The **target groups** that would benefit from the project:

- **patients, their families, and professional caregivers** – rapid transfer of knowledge into the clinical practice will improve the diagnostic accuracy, we will realise campaigns to inform people to come to the clinics in early stage of the disease (currently in both countries dementia is considered to be a normal part of ageing and thus patients come to the clinics in very late stages of the disease)
- **clinicians** – we will apply the modern diagnostic tools into the clinical practice, which will allow medical specialists to diagnose the disease in early stages and better monitor the disease progression,
- **scientists** from universities and academic institutions – it's a great opportunity for them to participate on applied research which may have direct clinical outcome, in both countries the phase between research and successful innovation (Valley of death) represents the main obstacle in the transfer of basic research ideas into the biotech product (either drug or diagnostic tool)
- **biotech companies** - participating on the project will bring new business opportunities through enrichment of their product portfolio and gaining new applied research contacts in the academic sphere.
- **talented students** – the students in the ecosystems can participate on applied research directly in the biotech companies, profit from the extensive training activities and kickstart their entrepreneurial career paths.

The outcomes and impacts of the project:

Scientific impact – the project will generate new strategy for development of innovative diagnostic assays for AD based on the knowledge of the structure of selected biomarkers. This approach is until now rarely used to generate diagnostic tools. In Slovakia, AXON Neurosciences R&D was the first company which developed new sensitive diagnostic immuno-assay to detect pT217 tau species. The majority of researchers involved in this development is currently employed at NII SAS and AXON is ready to support the project by providing their monoclonal antibodies against tau to NII. AXON experts on assay development are employed in the NII SAS, so they will perform this task. They published three papers[12] on biomarker development, we plan to increase the number of published papers on biomarker research up to ***eight research papers*** per four years.

Economic impact – implementation of molecular diagnostic into the clinical practice can improve diagnostic accuracy, thus patients will be treated based on proper diagnosis and thus therapy can be effective, which will lead to the lower rate of hospitalization. Health economic analyses indicate that biomarker analysis (e.g. CSF) effectively reduces expenses. This is attributable to the fact that using only clinical criteria to diagnose AD leads to false-positive diagnoses in roughly 30% of cases. Such patients would receive treatments intended for AD that don't benefit them, but accrue costs; furthermore, they would burden diagnostic capacities and undergo multiple diagnostic procedures until the correct diagnosis is reached[13]. Thus, utilising biomarkers to arrive at the correct diagnosis right away ***reduces costs by as much as 58%.*** [14]

Technological impact – we will use new technology of digital ELISA for clinical practice in two selected clinical centres and prepare strategies how to offer our knowledge to other centres in both countries. We plan to develop ***two research-based diagnostic assays*** which will target tau or ApoE protein species. We will use phage or ribosomal display to increase the affinity of the antibodies used for assay development. Cutting-edge methodologies and instrumentation in biomolecular NMR spectroscopy and cryo-electron microscopy and tomography will be applied to obtain detailed structural information about the target proteins.

Societal impact – the project increases awareness in the general population about the early stages of the disease and the presence of modifiable dementia risk and protective factors. Through our networks, we will spread current knowledge on AD across the countries to attract the attention of the general public. We plan to organise ***four major events on Alzheimer´s disease international*** day and ***four events on the Brain awareness week for general public***.

The project may bring profit for circa 80 000 patients in Slovakia and 160 000 patients in Czech Republic, which is 1.5 % of the population. In addition, the objectives of the projects can positively influence life of the same number of caregivers, mostly family members.

Potential barriers

- there is a **strong competition** in the development of the new diagnostic assays. Several academic institutions, biotech and pharma companies are developing new generation of diagnostic assays most focused on the blood and cerebrospinal fluid (CFS). Currently, there are three CSF biomarkers widely used for biological diagnosis; total tau, phospho-tau T181 and amyloid β42. There are some new biomarkers available in the blood as well; phospho-tau T181, T217 and amyloid β42 or β40 or its ratio. The main limitation of currently used or newly developed biomarkers is that they do not reflect progression of the disease. The only marker reflecting the progression of the disease is neurofilament light in the blood, which is not disease specific. By using deepened knowledge about the conformational changes of the studied proteins from the physiological to the pathological forms over course of the AD progress, we can increase the specificity and sensitivity of the assay.
- there is still a **partial reluctance** to use the molecular biomarkers for clinical practice in both Czech Republic and Slovakia. The diagnosis relies mostly on clinical presentation combined with MRI, which does not represent the current trends in AD diagnostics. In order to implement the use of the molecular biomarkers into the clinical practice, they have to be reimbursed by health insurance companies. This might be a potential barrier, which can be overcome by involvement of the Ministry of Health into the project.
- in central Europe, general population and many GPs consider dementia as a feature of ageing, not a disease entity. This causes missed and delayed dementia diagnosis leading to lost opportunities for treatment and increases patient and caregiver burden. This **general view on dementia** may represent the potential barrier for the project.

12) (1) McMurray L et al., CS Chem Neurosci. 2021, 12(11):1885-1893;
(2) Hanes J. et al., Neurology. 2020, 95(22):e3026-e3035;
(3) Novak P. et al., Nat Aging 2021, 521–534.
13) Kerpershoek, L., et al., BMC Health Serv Res, 2016. **16**(1): p. 423
14) Valcarcel-Nazco, C., et al., J Alzheimers Dis, 2014. **42**(3): p. 777-88.

Therefore, we will take special emphasis on dissemination of information on current trends in AD diagnostics throughout the general population and we will organise workshops for GPs. These activities will organise ICRC, MC, NII, and the Czech and Slovak Alzheimer´s societies. In Slovakia, the education of GPs will be orchestrated by Ministry of Health.

2.2 Measures to maximise impact – Communication, dissemination and exploitation (CDE)

2.2.1 - Dissemination and exploitation of results

Dissemination activities are a key part of the project, as they enhance visibility and recognition of the joint ecosystems, raise public awareness of excellent science, increase the interest and involvement of business sphere and policy makers, and contribute to the impact and exploitation potential of research outcomes. CDE activities of ADDIT-CE address full range of potential users from all parts of the quadruple helix of innovation driving actors. The consortium will prepare a detailed CDE Plan (WP6, D6.5) on a basis of a draft plan described below. It will include description of open access policy and the designation of intellectual property rights. The effectivity of the plan will be evaluated on biannual basis.

Dissemination to scientific community: All PIs involved have extensive track record of publications and conference/workshop presentations. which both serve as prime means for dissemination to the scientific community. As the scientific community itself is the principal evaluator of the quality and reputation of peer scientists and research institutions, joint publications in high profile journals will directly contribute to gaining recognition to the interlinked ecosystems. Presenting our results on impactful conferences will provide us with personal contacts outside the ecosystems and open new networking channels for collaboration on high-gain research projects, which will improve our capability to gain competitive research funding. Specifically, possible research and grant-proposal partners will be approached during brokerage events, semi-annually on workshops gathering the AD research community in CZ and SK, and individually through personal communication.

Dissemination to industry and business stakeholders will involve the following activities: direct communication at industry fairs and exhibition booths at conferences, using the established business contacts of our industry partners BioVendor Geneton and MultiplexDX; invitation of relevant industry representatives to ADDIT-CE brokerage events organised in 3rd and 4th year of the project; and local dissemination via partnered JIC in Brno and IRD MH in Bratislava, creating awareness among regional SMEs on the expertise and capabilities within the project consortium.

Communication and Dissemination to young minds: To ensure the sustainability of the developed **Strategy**, the ADDIT-CE project must invest in the future of research and innovation – Masters and high school students. We will present the attractiveness and importance of AD diagnostics research during Open Days, excursions, online lectures, and communication campaign through social media. A possibility to work on bachelor or master thesis related to the research conducted by the consortium will be offered to students of the involved research institutions. A pilot program of **industrial PhD** will be launched in both ecosystems, where the doctoral theses will be co-supervised by an industry expert, a significant part of the students' time will be spent in the industrial sphere and with the students' doctoral theses directly contributing to ADDIT-CE research outcomes. Next, students will be invited to attend the lectures given by visiting scientists as a part of enhancing the overall expertise of the consortium, and two dedicated Summer Schools on AD research-related topics, targeting about 60 students each, will be organised in the 1st and 4th year of the project.

Communication and Dissemination to policy makers: ADDIT-CE is already firmly integrated into regional policy making bodies via its partners and will seek further attention of authorities and policy influencers with the aim to increase the awareness about modern AD research, non-pharmacological interventions, and the importance of early diagnostic. Governmental representatives will be invited to the kick-off meeting, press conferences and round-table discussions. Through our partnership with the Slovak Ministry of Health, results of ADDIT-CE will be incorporated into the prepared National Action Plan for Dementia. Through its Czech equivalent, we will address the policy makers involved in its implementation.

Communication and Dissemination to end-users, societal stakeholders, and general public: The specific impact of early diagnostic of AD on society is one of ADDIT-CE's highest priorities, and we have dedicated a separate work package (WP5) to directly involve and address the main groups of the end users of AD research results: specialists at diagnostic clinics, patients, their families, professional caretakers, and general practitioners. Through a concerted effort of societal actors involved in ADDIT-CE – Czech Brain Aging Study, Memory Center Bratislava, and the

Czech and Slovak Alzheimer Societies – we will map out and consolidate the network of end-users and launch a targeted campaign through info points, newsletters, videos, podcasts, discussions, questionnaires, workshops and established conferences (Prague Gerontology days). Most of these channels will also address general public, further spreading awareness about the project outcomes and increase the project impact.

Exploitation of results: The direct goal of ADDIT-CE is the joint cross-border R&I Strategy to modernise AD diagnostic methods in the interlinked ecosystems. The Strategy will include excellent research proposals which will mobilise competitive funding. The involvement of business partners in ADDIT-CE research will lead to direct commercialisation of results. Through the future research proposals, new products and methodologies will be potentially developed, commercialised via existing or new spin-off companies. All consortium members have local structures in place that aid in all aspects of spin off company founding and commercial exploitation of IPR.

Measures to be implemented after the end of the project: In the final update of the CDE Plan, we will evaluate the efficiency of each dissemination channel; the most efficient throughout the project course will be used in the post-project period. The activities will be oriented on the continuation of project effort to enhance the visibility of ADDIT-CE (papers, conferences) and extension of scientific and business networks. Dissemination will continue towards students to form a human resource basis of appropriately educated and motivated young people for local research and industry, and towards end users and government/society stakeholders to ensure broad understanding and support for the implementation phase of the Strategy.

The consortium plans to use communication/dissemination channels described in the following table:

Measures	Description	Indicator	Scientific Community	Business and Industry	Students and young minds	Policy Makers	End Users, Societal Actors
Project website	Information on project activities, press-kit	statistics	x	x	x	x	x
Social media	LinkedIn, Twitter, Instagram, YouTube…	engagement	x	x	x	x	x
Publicity materials	Flyers, newsletters, posters, brochures	No. of copies		x	x	x	x
Conference/Workshop presentations	Presentation of ADDIT-CE research	No. of presentations	x	x			x
Partnered channels	National contact points, technology incubators, innovation centres	No. of presentations		x		x	
Summer Schools	External lectors and participants	No. of participants	x	x	x		
Training activities	Lectures, courses, hands-on trainings	No. of participants	x		x		x
Project workshops	External lectors and participants	No. of participants	x	x	x		x
Popularisation events	Researchers' Night, Open Days, etc.	No. of activities			x	x	x
Partnered websites for end-users	Podcasts, videos, e-newsletters	engagement				x	x
Scientific publications	High-profile journals, open access	No. of articles	x	x			
Public media	PR, popularisation activities	No. of outputs			x	x	x

The WP6 leader will coordinate all CDE actions organised by different partners, with the exception of the targeted end-user campaign, which will be organised by the T5.4 leader. The following principles will be applied in the course of the project: a) The **EC support** will be acknowledged regarding all the project outcomes following the EC guidelines and rules. b) The **dissemination of associated research outputs** is performed upon consent of involved research teams. The dissemination details including the exact rules will be part of the Consortium Agreement.

2.2.2 - Knowledge management and protection

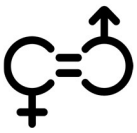
The Consortium Agreement will contain clauses codifying IPR issues and its preparation will be assisted by the Centrum of Technology Transfer MU and its legal department. The IPR strategy of the project consortium will follow the rules adopted by the European Commission, the best practice of IPR protection

published by the EC and the internal rules of all the partners involved in the consortium. It will be codified in the Consortium Agreement (CA) to protect the IP generated within the project, minimise potential risk and eliminate possible conflicts raised by IPR issues. The CA will also define the pre-existing background, regulate the conditions of joint ownership of foreground, detail the dissemination procedures in case a commercial interest will be protected, and specify the obligations of partners regarding to foreground availability under fair and reasonable conditions. The CA will be aligned with EU guidelines.

The key principles of the IPR strategy are as follows:

Each partner is and remains the sole owner of its intellectual property rights over its background. The background needed for the project realisation will be defined in the specific Annex of the Consortium Agreement. Every partner will be entitled to describe its own pre-existing background. The foreground will be owned by the project partner who will generate the foreground. If it is not possible to determine the exact share of generated intellectual property rights (more partners participated in the foreground), the parties will have the joint ownership of such foreground according to the pro rata effort invested by each partner. Every joint foreground consisting in a joint patent or patent application needs to be specified in a joint ownership agreement prior to any application.

Gender balance of the research team



ADDIT-CE is committed to upholding the principles of gender equality in all project activities. The team of PIs from all involved institutions is properly balanced. Gender balance will be maintained throughout the project in PhD recruiting processes, invitations of external lecturers to project events (invited lectures, project workshops and Summer Schools) and the nominations of experts for the External Advisory Board.

All partners requiring Gender Equality Plan (GEP) under the HORIZON EUROPE programme rules have a GEP in place and published on their respective institutions' websites.

SPECIFIC NEEDS

What are the specific needs that triggered this project?

1. The definition of AD in living people has moved from a syndromal to a biological construct. Thus, current diagnostic concept is based on clinical evaluation supported by fluid or imaging biomarkers. Currently, this has not been applied into the clinical practice in Czech Republic and Slovakia so far. This concept is used for research purpose only, thus a limited patients and caregivers can benefit from it.
2. The development of AD diagnostic assays in Central Europe is not competitive with Western Europe due to fragmented and disorganised biomarker research.
3. Slovakia is one out of five countries in European union without National plan to combat Alzheimer´s disease.
4. Precise epidemiological studies on various forms of dementia (prevalence, incidence, direct and indirect costs) have not been realised in both Czech and Slovak republics in the last decade.
5. The are no networks or hubs consisted of biotech companies and academic institutions focusing on the Alzheimer´s disease research, which would have the power to support the national medical sectors.
6. Industrial PhD students do not participate on the product driven research in AD field.

D & E & C MEASURES

What dissemination, exploitation and communication measures will you apply to the results?

1. **Exploitation:** New diagnostic algorithm reflecting the clinico-biological concept of dementia.
   Dissemination towards the clinicians and GPs: regularly organised workshops, lectures and symposia.
   Communication towards citizens: communication campaigns (media, social media, web pages, Alzheimer's disease day, Brain awareness week).
2. **Exploitation of the new product:** Research based diagnostic assay for monitoring of Alzheimer´s disease progression.
   Dissemination to the scientific community and industry: Participating at conferences, symposia; open access publishing, brokerage events with industry partners.
   Communication towards citizens: medialisation of the results through media (interviews, articles).
3. **Exploitation:** integrated ecosystems encompassing health-care institutions, clinical centres, research institutions, biotech companies and governmental bodies.
   Dissemination towards the medical and scientific community: regularly organised meetings and workshops.
   Communication towards citizens: medialisation of the current research and innovation efforts through media and social media
4. **Exploitation:** Industrial PhD students participating on applied research projects.
   Dissemination towards the universities: Meetings with students at the universities, organising seminars on biomarker research, summer schools.
   Communication towards citizens: interviews with industrial students on social media.

EXPECTED RESULTS

What do you expect to generate by the end of the project?

1. **New diagnostic algorithm reflecting clinico-biological nature of Alzheimer's dementia:** Wide-scale incorporation of biomarkers into AD diagnostics will be coordinated in cooperation with policy making actors.
2. **Research based diagnostic assay:** The assay will be based on state-of-the-art technology and will allow to monitor disease progression and efficiency of non-pharmacological intervention programs.

3. **Slovak national plan – Slovakia against dementia:** In collaboration with Ministry of Health Slovak Republic, the project will lay plans for this strategic document.
4. **The concept of epidemiological study:** First mass-scale study of this kind in both CZ and SK.
5. **Biotech-academic research platform in Moravian and Bratislava regions:** Strongly linked business-academia platform with a wider network of contacts on national and European scale
6. **Four Industrial PhD students trained.**

TARGET GROUPS

Who will use or further up-take the results of the project? Who will benefit from the results of the project?

Clinicians: neurologists, psychiatrists, GPs will apply new concept of AD diagnostics into the clinical practice.

Scientific community: Focus of academic expertise and industrial know-how will generate novel ideas, publish new data and bring opportunities for infrastructural development through successful projects.

Students will have the opportunity to join Industrial PhD programme, gaining unique experience and opportunities in applied research and career growth.

Patients and family caregivers will benefit from early diagnostics of dementia and non-pharmacological intervention programs.

Social care professionals will be educated in novel trends in understanding of dementia.

Pharma and biotech companies will participate on the diagnostic assay development.

OUTCOMES

What change do you expect to see after successful dissemination and exploitation of project results to the target group(s)?

Early diagnostics of dementia: New diagnostic concept will be used to diagnose early/preclinical stages of the disease. Thus, clinicians can better manage the therapy of patients (including non-pharmacological interventions which have more pronounced effect in early stages of the disease).

Biotech-academia research hubs: strong inclusion of local companies into AD research project; new professional skills for students.

IMPACTS

What are the expected wider scientific, economic and societal effects of the project contributing to the expected impacts outlined in the respective destination in the work programme?

Scientific: Bridging of the gap between academia- and industry-based research; prevention of the brain drain; growth of the research excellence in the region to catch up with Advanced countries

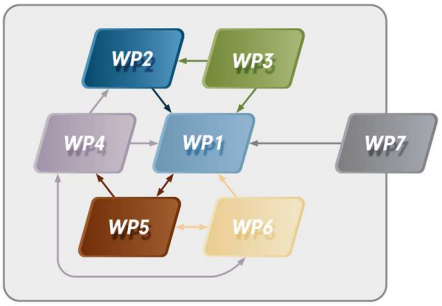
Economic: Mobilisation of national, international, private and venture funds into the R&I development of the region, creation of new spin-offs and jobs through the exploitation of AD diagnostics research results.

Societal: Patients in the preclinical/early stages of dementia better respond to the pharmacological and non-pharmacological therapy and thus can slow down the disease progression. Early diagnosis can prolong healthy life and reduce direct and indirect costs by reducing the number of hospitalizations. The society will be prepared for future disease-modifying therapeutics which relay on the biomarker proved diagnosis.

3. Quality and efficiency of the implementation

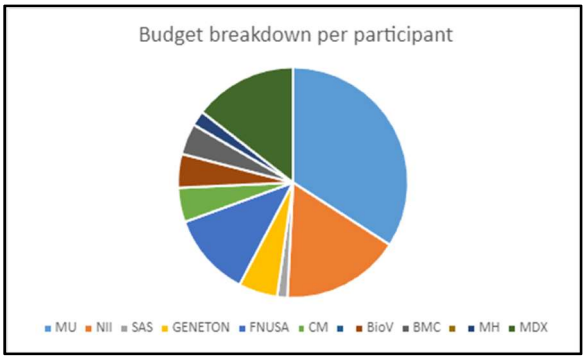
3.1 Work plan and resources

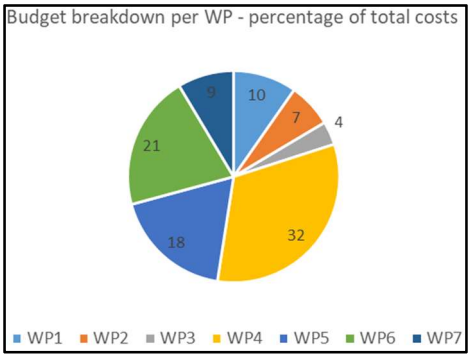
The proposed work plan includes seven work packages (WPs) necessary to fulfil the objectives of ADDIT-CE. The individual WPs and their mutual interactions are depicted in the PERT diagram on the right and are further defined in the descriptions of the WPs.



Resources to be committed:

ADDIT-CE has prepared a well-balanced budget. The distribution of person months among WPs and project partners (see Tab. 3.1a) corresponds to above detailed project activities.





Timing of the work packages and their components (Gantt chart):

TASK	Start Date	End date	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
Development of Joint Cross-Border R&I Strategy														M																								M						M						M
T1.1	M1	M12												D																																			
T1.2	M13	M48																		D																													D
T1.3	M25	M36																																			D											
T1.4	M25	M42																																														
T1.5	M25	M48																																														D
Concepts, Designs, and Infrastructure Pre-Plans																																															
T2.1	M13	M48																																														D
T2.2	M13	M48																																														
T2.3	M25	M48																																														D
Pathway to long-term sustainability																																														
T3.1	M13	M48																																														D
T3.2	M25	M36																																				D											
T3.3	M37	M48																																														D
New Diagnostic Assays for AD Progression														M											M						M			M			M						M					
T4.1	M1	M36												D																								D											
T4.2	M4	M46																								D																						D
T4.3	M13	M46																																D														D
T4.4	M7	M46																																														D
T4.5	M13	M46																																				D											D
T4.6	M1	M24																								D																						
T4.7	M18	M46																																														D
T4.8	M1	M22																						D																							
T4.9	M22	M46																																														D
Engagement of end-users														M																							M											
T5.1	M1	M36																																			D											
T5.2	M4	M48																																														D
T5.3	M25	M48																																														D
T5.4	M1	M48												D																																		D
Creating a culture of innovation							M																																							M	M
T6.1	M1	M48					D																			D																						D
T6.2	M1	M48																																														D
T6.3	M7	M46																																														
T6.4	M3	M48					D																			D																						D
T6.5	M5	M46																																														
T6.6	M4	M48																																														
Project Governance, Management and Ethics																																															
T7.1	M1	M48					D																																									
T7.2	M1	M48	D																																													
T7.3	M1	M48	D																																													
T7.4	M1	M48																																														
T7.5	M1	M6	D																																													

There are no subcontracting costs planned for this project. No third-party contribution is foreseen for this project.

Table 3.1h: 'Purchase costs' items (travel and subsistence, equipment and other goods, works and services)

Participant Number/Short Name 1/MU		
	Cost (€)	**Justification**
Travel and subsistence	**109354**	2400€ Management meetings + AD workshops (3persons; 2/year; 2 days), 32500€ SK summer school – students (50 students; 5 days), 12500€ CZ summer school – lecturers (10 persons; 5 days) 5160€ hands-on trainings (2/year; 5 days), 10400€ travel cost of invited lecturers in WP6 (4/year; 2 days), 18800€ travel cost of External Advisory Board (8 members/5 days), 27594€ Conferences (Structural Biology, Biophysics and Computational Chemistry – 14 person-events; 5 days)
Other goods, works and services (OGWS)	71112	Materials for molecular biology, protein biochemistry and purification
	47800	30000€ Organisation costs (rental, catering, PR) of AD workshops (2/year; 2 days; 50 participants) + 17800€ CZ summer school (100 participants, 5 days)
	46667	material for cell cultivation, growth factors and surface proteins
	45000	isotopes and spin labels for NMR experiments, kinases, chemicals
	35000	liquid chromatography columns, grids for EM, consumable chemicals
	33700	16000 € Open access, 7700€ conference fees, 10000€ CFS
	26585	Public events + communication campaign consumables, website, graphics
	22222	chemicals for RNA+DNA isolation, reversion transcript and PCR
	20000	antibodies for imunoblot, ELISA kits
	20000	transfections kits, siRNA, resctriction enzymes, cloning kits
Remaining purchase costs (<15% of pers. Costs)	50389	
Total	**527829**	

Participant Number/Short Name: 2/NII SAS		
	Cost (€)	**Justification**
Travel and subsistence	43316	850€ Management meetings (1/year; 2 days), 1360€ AD workshops (2/year; 2 days), 12500€ summer school – lecturers (10 persons/5 days), 2580€ hands-on trainings (1/year; 5 days), 10400€ invited lecturers for WP6 (4/year; 2 days), 15626€ conferences AAIC, EBSA, ECM meetings (8 person/events; 5 days)
OGWS	85000	recombinant protein expression and purification (ExpiCHO medium, affinity columns, labware);
	32000	crystallisation screening materials
	35400	Hybridoma technology consumables (plastics, tissue culture media, chemicals) + antibodies; Proteomics consumables (columns, solvents, enzymes, etc.), assay development consumables (SIMOA, magnetic beads, heterophylic blockers, peptides, chromatography columns)
	17900	3000€ Open access, 2400€ conference fees, 4000€ feasibility studies, 8500€ CFS
	15500	Summer school organisation (rental, catering, PR – 100 students, 5 days)
	6886	SW+HW for structure determination from diffraction data
Remaining purchase costs	0	
Total	236002	

Participant Number/Short Name 2.1/SALS		
	Cost (€)	**Justification**
Travel and subsistence	2210	850€ project meetings (1/year; 2 days), 1360€ AD workshops (2/year; 2 days)
OGWS	5500	5500€ Communication (end users) campaign
Remaining purchase costs	1000	
Total	8710	

Participant Number/Short Name 3/ICRC		
	Cost (€)	**Justification**
Travel and subsistence	22850	16890€ Travel to international conferences (AAIC congress, USA, Europe – 8 person-events, 5 days), 800€ travel to AD workshops and SC meetings (2/year, 2 days), 5160€ travel for jobshadowing-mentoring with MC (4 persons, 5 days)

OGWS	44560	Materials for sample collection and processing (Kvadruplet Euroimmune, Accelerometers)
	18900	3000€ Open access costs, 2400€ conference fees, 6500€ communication campaign for end users, 7000€ CFS
Remaining costs	0	
Total	86310	

Participant Number/Short Name 4/MC		
	Cost (€)	**Justification**
Travel and subsistence	7370	850€ project meetings (1/year; 2 days), 1360€ AD workshops (2/year; 2 days), 5160€ travel for jobshadowing-mentoring with ICRC (4 persons, 5 days)
OGWS	3000	3000€ costs of enrichment of AD patient cohort (WP5) – questionnaires, entry examination consumables
Remaining purchase costs	3500	
Total	13870	

Participant Number/Short Name 5/BIOVENDOR		
	Cost (€)	**Justification**
Travel and subsistence	5800	800€ Management meetings (1/year; 2 days), 5000€ conferences (3 personevents, 5 days)
OGWS	20000	Cell culture media, supplements, consumables
	15000	Immunoassays, antibodies, antigens, consumables
	15000	DNA and RNA isolation, cloning, PCR
	5400	2400€ Conference fees, 3000€ patentability studies
Remaining purchase costs	1000	
Total	62200	

Participant Number/Short Name: 6/BMC SAS		
	Cost (€)	**Justification**
Travel and subsistence	10790	850€ project meetings (1/year; 2 days), 1360€ AD workshops (2/year; 2 days), 2580€ hands-on trainings (1/year; 5 days), 6000€ international conferences (3 person-events; 5 days)
OGWS	39000	Short-and long-term non-pharmacological intervention programs, workshops
	5000	3000€ Open access, 2000€ conference fees
Remaining purchase costs	3500	
Total	58290	

Participant Number/Short Name 7/MH		
	Cost (€)	**Justification**
Travel and subsistence	2210	850€ project meetings (1/year; 2 days), 1360€ AD workshops (2/year; 2 days)
OGWS	1000	Communication and Dissemination cost – design and print of C-D materials
Remaining purchase costs	0	
Total	3210	

Participant Number/Short Name 8/MDX		
	Cost (€)	**Justification**
Travel and subsistence	35245	850€ project meetings (1/year; 2 days), 1360€ AD workshops (2/year; 2 days), 3035€ participation to summer schools (2x5 days), 30000€ conferences and brokerage events (15 person-events; 5 days)
OGWS	80000	Consumables and chemistry for RNA sequencing (library preparation kits, chemistry for RNA Seq adapters and RNA FISH probes, plasticware, glassware)
	61700	3000€ Open access, 5000€ conference fees, 35700€ organisation cost of brokerage events (2 events, 3 days, 50 participants each – rental, catering, PR), 6000€ organisation costs of soft skill courses (6 events, 30 participants each), 3000€ patentability studies, 9000€ CFS
Remaining purchase costs	1000	
Total	177945	

Participant Number/Short Name 9/GENETON		
	Cost (€)	**Justification**
Travel and subsistence	4000	850€ project meetings (1/year; 2 days), 1360€ AD workshops (2/year; 2 days), 1790€ travel to brokerage events (2x3 days, 2 persons)
OGWS	15000	Consumables and chemistry for genome sequencing
	13500	10500€ Costs of WP6 activities (€2500 dissemination consumables – design and print of materials; €8000 consumables for hands-on training of students), 3000€ Open access fees
Remaining purchase costs	0	
Total	32500	

Participants JIC and CALS are Associated Partners and do not claim any costs.

Table 3.1i: 'Other costs categories' items (e.g. internally invoiced goods and services)

Internally invoiced goods and services		
	Cost (€)	**Justification**
6/BMC SAS	32000	Core Facility Services – Testing of physical fitness, motor and cognitive functions performed before and after the intervention, and every year as part of the long-term intervention programme developed in WP5.
3/ICRC	22222	Core Facility Services – Biostatistics CF (data services – management of AD patients' data in WP5).
1/MU	22000	Core Facility Services – use of CEITEC CF (biomolecular NMR spectroscopy; cryoEM and tomography; Proteomics; Biomolecular interaction and crystallization; Nanobiotechnology) for WP4.

3.2 Capacity of participants and consortium as a whole

The coordination institution – MASARYK UNIVERSITY is the second-largest University in Czech Republic. The MU has extensive experience in management of different R&I projects, EU Structural Funds, and both partner and coordinator role in the EU Framework Programme projects (MSCA, Health, ERC, Spreading Excellence and Widening Participation). CEITEC MU is one of the largest research institutes with state-of-the-art research infrastructure for integrative structural biology in Central Europe providing outstanding conditions for basic and applied research, especially in the area of life sciences.

In this project, research teams from three different faculties of MU are involved (CEITEC-MU, Faculty of Science, Faculty of Medicine), possessing the synergic expertise necessary to develop the research base for molecular AD diagnostics tools and train students in the areas of applied neuroscience research. CEITEC-MU team will provide an outstanding expertise in non-uniformly sampled NMR approaches combined with the computational approaches to the structural and interaction characterization of Tau variants in their monomeric state and fibril state. It will be further extended by Cryo-EM tomography, able to characterise the impact of pathological forms of Tau inside neurons. CEITEC MU as a member of the Alliance for Life (https://alliance4life.ceitec.cz), which is a bottom-up initiative of twelve leading life science institutions from eleven EU-13 countries closing the divide in European health R&I. Team from faculty of science will combine molecular biology, biochemistry and structural biology techniques (X-ray crystallography and cryo-EM) for better understanding the mechanisms of pathological aggregation of ApoE in neurodegenerative diseases. Team from faculty of medicine will focuses on stem-cell-based models of AD, including neuronal cell cultures or brain organoids derived directly from patients with AD. These models reliably mimic the development of Alzheimer's disease in vitro, they can thus be used to study the mechanisms of the disease initiation and biomarker screening.

BIOVENDOR – Laboratorní medicína a.s. is a part of an internationally operating group of companies with its own R&D and manufacturing capability in clinical diagnostics and biomedical research. The BioVendor group has over 400 employees among its 14 companies or branches operating in 6 countries, 3 R&D facilities and 4 industry sites. BioVendor's R&D efforts are aimed at rapidly growing fields of interest within the international research and diagnostic community, such as diabetes, cardiovascular diseases, infection and inflammation, autoimmunity, oncology, neurological diseases, aging-associated diseases and more. One of the pillars of Biovendor's activity is the introduction of the results of basic research into routine diagnostics. BioVendor cooperates with research institutions and participates in professional consortia, including Alzheimer consortium – helping direct scientific activities to address the needs of immunodiagnostic practice.

GENETON s r.o. The company has long standing expertise in the next generation sequencing technology (NGS) used to identify causal pathogenic variation. The priority of GENETON is an excellent research and development in the field of state-of-the-art molecular genetics and bioinformatics. It has participated on a variety of national and international research project including Horizon programme, such as ALPACA (Algorithms for Pan-genome Computational Analysis) and PANGAIA (Pan-genome Graph Algorithms and Data Integration).

MULTIPLEXDX is one of Slovakia's most innovative biotech companies, created to bring revolutionary technologies to the market of personalized molecular diagnostics. The company has representation in both U.S. and European markets. MDX's IP-based solutions combine visualization and sequencing technologies to quantify 8 or more cancer markers to give each diagnosis a specific "barcode," which will indicate not only the cancer type but also the duration of personalized treatment for that cancer. MDX also uses multiplexing; cross-testing and verifying the same result from at least two independent sources. By embedding numbers into pictures and vice-versa, the diagnostics shed light on the patient's set of cancer markers and profile, enabling oncologists to make evidence-based decisions and prescribe treatment quickly, directly and more accurately. MDX is proud EIC Accelerator holder (Project: Multiplex8+, SME instrument Phase 2, ID: 946693). In 2020, as a response to the global pandemic, MultiplexDX and Slovak researchers (BMC SAS and Science Park of the Comenius University in Bratislava) have joined forces to develop the first Slovak IVD-certified diagnostic PCR test for the detection of SARS-CoV-2.

THE INSTITUTE OF NEUROIMMUNOLOGY of the Slovak Academy of Sciences is a neuroscience research institute focused to investigation of the human neurodegenerative disorders. Since 1997, the NIU SAS is declared by Slovak government „The National scientific center for the cooperation of the Slovak Republic with the International Center for Genetic Engineering and Biotechnology of the Organisation of United nations (ICGEB)". The Institute of Neuroimmunology took part in the international projects: Biomarkers for Alzheimer's disease and Parkinson's disease, Coordination Action in support of the sustainability and globalisation of the Joint Programming Initiative on Neurodegenerative Diseases Pathway complexities of protein misfolding in neurodegenerative diseases: a novel approach to risk evaluation and model development, and Alzheimer's disease data-driven insights on individual outcomes, all funded by Joint Programming Initiative on Neurodegenerative Diseases (JPND). The NII SAS regularly uses synchrotron sources of X-ray radiation for macromolecular crystallography in the frame of INSTRUCT-ERIC, iNext Discovery and calls for beamtime organized by EMBL DESY Hamburg, PSI Villigen, Switzerland etc.

THE BIOMEDICAL RESEARCH CENTER of the Slovak Academy of Sciences is the largest Slovak institution devoted to basic and applied research in biomedical sciences. The principal mission of this novel research center is to foster research excellence, develop interdisciplinary approaches, and stimulate innovative potential for the improvement of our knowledge on human diseases, its better translation to clinic and more effective practical use for benefit of patients and the entire society. The Center of Physical Activity Research (CPA) & Research clinic provide capacity for biomedical research and preventive health care employing exercise as medicine to patients at preclinical/early stages of AD. Exercise intervention studies and long-term programs provide a functional model of implementing effective lifestyle strategy in prevention of dementia. The BMC collaborates with ICRC and MU.

The MEMORY CENTRE (non-profit organisation) was founded in 2002 as a preventive, diagnostic, activation and educational centre. It is a pilot establishment, and the only one of its kind in Slovakia regarding the complexity of offered services. Uniquely, it integrates social and healthcare services across the whole spectrum of activities, from prevention to diagnosis and post-diagnosis care. The centre constitutes a modern diagnostic platform with a strong medical background. The MEMORY CENTRE also implements the Strategic plan of the Alzheimer Europe organisation for the years 2016-2020 at the national level. Via close cooperation with the SLOVAK ALZHEIMER'S SOCIETY it takes part in projects of the international network Alzheimer's Disease International.

The SOUTH MORAVIAN INNOVATION CENTRE (JIC) coordinates the Regional Innovation Strategy (RIS JMK), which helps the academic sector, public sector, companies, and non-profit organisations to communicate with each other. The JIC was established and sponsored by the South Moravian Region, statutory city of Brno, Masaryk University, Brno University of Technology, Mendel University in Brno, and the University of Veterinary Sciences Brno. Since 2003, it facilitates the creation one of the most innovative business ecosystems in Central Europe. Every year JIC supports around one hundred company owners from South Moravia, from new businesses with fresh ideas to well-established companies.

The CZECH BRAIN AGING STUDY (CBAS) is a multicentric longitudinal study which was designed to assess potential early biomarkers and risk/protective factors of cognitive decline and dementia on a prospective longitudinal cohort of subjects. CBAS was established in 2011 using recruitment from two memory clinics at two independent neurology departments based at university hospitals in Prague and Brno, respectively. The program is running on the platform of INTERNATIONAL CLINICAL RESEARCH CENTER AT ST. ANNE´S UNIVERSITY HOSPITAL BRNO. Both

recruiting centers (Brno, Prague) are harmonized in terms of the neuropsychological battery, multimodality magnetic resonance imaging (MRI), PET imaging, genetic testing, blood tests and cerebrospinal fluid (CSF) analysis, the use of questionnaires, and a participant database system. All the data is stored in a synchronized database. The CBAS is complemented by a biological sample bank (serum, plasma, CSF, DNA). CBAS is cooperating with many Czech and international research partners as well as with industrial partners. The CBAS memory Centers have also close collaboration with contact centres of Czech Alzheimer Society.

The CZECH ALZHEIMER SOCIETY, since its establishment in 1997, closely cooperates with service providers on the border between health and community type social services is the crux of their activity, as well as cooperation with contact points – facilities providing quality services for people with dementia throughout the Czech Republic. They gather insight into the current situation of people with dementia, their families and service providers and build on this experience. The goal of the CAS is to help and support people affected by dementia, which includes both the patients and their family members and primary caretakers, as dementia affects both groups equally severely. CAS is the main convenor of Prague Days of Gerontology, dementia focused congress with 200 participants including international ones. It also participates in patient involvement and carers support. It published many practical guides and brochures for caregivers, also a textbook on dementia, short videos providing information etc. It develops tools for cognitive training and carries out a timely diagnosis project (awarded by the Ministry of Health).

SLOVAK ALZHEIMER'S SOCIETY was founded in 1998 and since 2005 it's a member of Alzheimer's Disease International as well as Alzheimer Europe. Its mission is to change perception, policy and practice to improve the lives of people with dementia by providing a voice to them as well to their caregivers. The aim is to combat stigma, raise awareness of brain health and prevention, and support dementia research.

Institute of Research and Development (IRD) at the MINISTRY OF HEALTH OF THE SLOVAK REPUBLIC is, since its creation in November 2016, very active in setting, searching, evaluating and networking of activities in biomedical and health R&D in Slovakia, in line with national and international needs. The Institute has ambitions to support excellent basic and applied R&D, innovations and technology transfer in health, in particular in the biomedical area.

Synergy between institutions of ADDIT-CE consortium

The consortium consists of several experts on cellular and proteomic research, industry researchers having experience with development of diagnostic assays for human neurodegenerative disorders, highly motivated clinicians with an extensive expertise in dementia, and national societies focusing on the social care and having skills in public communications. Core partners bring complementary strengths, diverse expertise and experience. The consortium assembles unique national scientific think tanks with direct connection to society and government.

Biotech companies and academic institutions from Brno and Bratislava regions will create "brain traps" for students who will participate on applied neuroscience research. Shared positions will allow PhD students to apply their theoretical experience and gain practical ones and at the same time contribute to the introduction of new products on the diagnostic market. This is also an opportunity for companies to involve young talents in innovation and new technologies, which ultimately lead to development and profit not only in the industrial sphere. Developments and implementations towards future high-tech applications will encourage the researchers and students at different levels (from Bc to PhD level) to set-up future start-up companies in both countries.

Current state in AD diagnostics as well as the needs for the improvement are motivated by clinicians and their teams within the CBAS and Memory Center that will share their experiences and the good practices in the diagnostics of AD patients and the clinical samples. In close collaboration with Czech and Slovak Alzheimer's societies and Slovak Ministry of Health, they will communicate the need for early diagnostics towards the public and GPs in both countries. Involved academic institutions and the biotech companies in both countries will analyse in deep details different variants of studied proteins and their complexes over course of the AD progress. In addition to the clinical samples, stem-cell-based models of AD will be analysed to get detailed composition of such studied proteins variants (truncation and post-translational modifications) and microRNA molecules. Additionally, we will prepare all relevant protein variants in the form of recombinant analysis and determine their detailed structural properties. This will deepen the knowledge of molecular mechanism of AD initiation and progression and also allow to design much more specific diagnostic assays for AD patients. Involved biotech companies will implement the basic concepts into assays suitable for practical applications. The involved clinicians will not only test the applicability and reliability of the newly designed assays but will also test the impact of non-pharmacological therapies of AD patients in the monitored biomarkers. Close geographical proximity between Brno and Bratislava will allow smooth personnel, students and samples exchanges between the involved institutions within ADDIT-CE consortium whenever needed.

4.1 – Ethical dimension of the objectives, methodology and likely impact

Project objective:

The research project (as one of the activities in the project) will identify new species of tau and amyloid proteins for better early diagnostics of Alzheimer's Disease. To discover these new biomarkers, we will use two existing cohorts of AD patients (in CZ and SK) and these will be also enriched in the project by new recruits. A thorough clinical characteristic of cohorts is needed for validation of the new biomarkers. The usability of identified biomarkers will be tested on samples from patients undergoing non-pharmacological therapy.

We will use samples of blood serum, plasma, and liquor from participants of an already running longitudinal study "Czech Brain Aging Study (CBAS)" and the Slovak AD cohort Memory Center Bratislava.

Methodology:

Mass spectrometry will be used to identify Tau proteins, amyloids, TRAM-2 and ApoE present in blood and CSF samples of AD patients. The identified proteins, which will be subsequently isolated (by chromatography or immunopurification with specific tau antibodies). Similarly, Tau proteins will be identified and isolated from media from cultured cell lines. The two proteomes will be compared. Whole proteome and miRNA analysis of blood, CSF and cell line samples, characterization of post-translational modifications (especially phosphorylation) of selected proteins and targeted analysis of candidate proteins will be performed. For structural (NMR, AFM, cryo-EM) and biophysical (nanoDSF) analyses, selected Tau protein variants potentially relevant in AD pathology will be cloned into a suitable expression vector. Based on the selection of specific tau peptides and results from structural and biophysical analyses, we will design a peptide suitable for immunization. Mice will be immunized for several months to produce specific antibodies recognizing the target. Antibodies will be screened by ELISA, and further confirmation will be performed by Western blots and immunohistochemical staining on AD brain tissues. The affinity of selected antibodies will be analyzed by surface plasmon resonance. The developed assays will be further tested for specificity, sensitivity, positive and negative predictive values and diagnostic accuracy. Samples from AD patients, age-matched controls, patients suffering from other neurodegenerative diseases will be used for this purpose.

The collection of human biological material consist of the collection of approximately 20 ml of blood, which is then sent for laboratory testing to determine blood counts and biochemical substances whose abnormalities may contribute to memory disorders, some of which will be used to determine biomarkers of neurodegeneration.

Lumbar puncture: in some cases it is necessary to perform a lumbar puncture to exclude inflammatory, metabolic or vascular disease of the brain. This examination may also help to confirm an atypical course of Alzheimer's disease or other neurodegenerative diseases. During the research, individual cells or proteins may be isolated from the sample. No interference with genetic information or genetic analysis will be performed on the samples.

Protection of personal data:

The blood and CSF samples will first be anonymised and, without personal data, anonymously coded, will be handed over for further processing to the researchers of the project consortium members. All samples will be available for scientific analysis only under an identification code without any personal data. Identification codes will be maintained in respective databases to which only Kateřina Sheard, MD, (Head of the CBAS study) and Iliana Királyová, MD (Memory Center) will have access.

Potential impact:

There is no danger of environmental damage as a consequence of carrying out this research. This project will not cause any negative effects on the population (i.e. stigmatisation of a particular social group, adverse consequences, etc.). On the contrary, we aim to significantly improve the outlook on quality of life for the population endangered by age-related neurodegenerative diseases.

4.2 Compliance with ethical principles and relevant legislations

The CBAS study from which the biological samples will be obtained has already been approved by the ethics committee of St. Anne's Hospital, the home institution of CBAS study. All participants have signed an informed consent (IS CBAS).

Personal data, demographic data, measurement results, results of clinical examinations are collected in the CBAS study and the participants agree to keep them in an anonymized form by signing the CBAS IS. For the purposes of this project, some anonymised data may be matched with anonymised samples.

Only persons without legal capacity limitations will participate in the project. Vulnerable persons and persons in a dependent position will not participate in the project.

Participation in the study does not pose any significant health risks. The risks associated with the possible performance of special examinations (e.g. cerebrospinal fluid sampling) are described in the separate informed consents for these examinations.

Participation in the research project is completely voluntary. The participant may withdraw his/her consent at any point in the research without giving any reason, even before the start of the research. In case of withdrawal from the study, the samples collected will be destroyed and the data deleted if requested. Refusal to participate in the project will have no effect on standard diagnosis or treatment.

Appropriate regulatory authorities, project sponsors or granting agencies may review project records to ensure that the rights of the biological sample donor are properly safeguarded. However, the identity of the donor will not be available to these reviewing authorities.

All handling of participant data will be in accordance with data protection legislation and the GDPR. The ADDIT-CE project has obtained the approval of the Ethical Commitee for Research of the Masaryk University (coordinator).

5. Correction of Shortcomings Identified in the Evaluation Summary Report

A) Collaborations with other international institutions that could help to achieve the objectives have not been sufficiently considered.

The project partners plan to collaborate with multiple academic institutions across Europe in order to achieve the proposed objectives.

WP4: Development of new diagnostic assays for AD progression

One of the objectives of this work package is to develop novel assays based on ultra-sensitive ELISA that can identify various forms of tau proteins in biofluids such as CSF or blood. We plan to collaborate with professor of clinical chemistry Charlotte Teunissen (h-index 72, 405 publications, >18 000 citations), **Amsterdam UMC, Netherland** who is one of the pioneers in the development of novel diagnostic assays for human neurodegenerative disorders. Charlotte will perform comprehensive validation of the assays in accordance with the validation protocol utilized for a number of diagnostic assays in the field.

We will also collaborate with the 1st and 2nd Neurological Clinics, Faculty of Medicine, **Comenius University, Slovakia** on the collection of CSF and blood samples from patients suffering from Alzheimer's disease. They will partake in the patient recruitment process for clinical studies involving non-pharmacological approaches.

In terms of structural biology studies of Tau protein we plan to collaborate with prof. Isabelle Landrieu (h-index: 42, 102 publications, >5300 citations), **Centre national de la recherche scientifique, CNRS, France** who is well recognized expert in the field of NMR spectroscopy of Tau protein in different forms and complexes with the partner proteins. Tau belongs to the intrinsically disordered proteins for which we currently develop novel efficient computational methods validated by NMR spectroscopy in collaboration with prof. Chris Oostenbrink (h-index: 49, 213 publications, >14500 citations), Institute of Molecular Modeling and Simulation, **University of Natural Resources and Life Sciences, Vienna, Austria**.

WP5: Engagement of end-users

We intend to collaborate with Alzheimer Europe on the communication campaign to incorporate their expertise from other European nations into the strategic communication process, which can enhance societal awareness of dementia and disseminate our findings to the general public. Alzheimer Europe plans to organise their annual conference for 2024 in Slovakia, which constitutes a prime dissemination opportunity to ADDIT-CE project. Alzheimer Europe is also open to discussion about collaboration with ADDIT-CE, mainly in the media communication campaigns.

B) The long clinical progression of the disease poses difficulties in terms of evaluating the value of the biomarkers and preventive non-pharmacological interventions in a 4-years project, which is not adequately addressed in the proposal.

Fluid biomarkers for AD typically do not correspond to the nature of the disease progression. The blood neurofilament light (NfL) is the single exception, which increases over the course of disease. Tau biomarkers are often elevated already at MCI stage of the disease and remain steady throughout the entire course of disease progression.

On the other hand, tau biomarkers reflect the effect of disease modifying therapy – amyloid and tau immunotherapy. Aducanumab, the anti-amyloid antibody, Aducanumab, significantly reduced plasma p-tau181 levels in patients with mild AD patients after 78 weeks of treatment. There was a positive correlation between reduction in plasma levels of p-tau181 and reductions in amyloid PET SUVR (Haeberlein et al., 2022). Similarly, after 104 weeks of treatment, AADvac1 tau vaccine reduced p-tau181 and p-tau217 levels in CSF of mild AD patients (Novak et al., 2021).

Clinical trials on non-pharmacological therapy, which typically last two years (Ngandu et al., 2015; Giuduci et al., 2020) can slow down cognitive deterioration. Data on the effect of this type of therapy on CSF or blood biomarkers are however scarce. Thus, it is reasonable to predict that levels of disease-specific tau species may decrease over the course of two years by effective non-pharmacological therapy, in the event that tau neurodegenerative cascade is affected directly or indirectly.

Citations:

(1) Budd Haeberlein S, Aisen PS, Barkhof F, Chalkias S, Chen T, Cohen S, Dent G, Hansson O, Harrison K, von Hehn C, Iwatsubo T, Mallinckrodt C, Mummery CJ, Muralidharan KK, Nestorov I, Nisenbaum L, Rajagovindan R, Skordos L, Tian Y, van Dyck CH, Vellas B, Wu S, Zhu Y, Sandrock A. Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease. *J Prev Alzheimers Dis*. 2022; 9 (2): 197-210. doi: 10.14283/jpad.2022.30.

(2) Novak, P., Kovacech, B., Katina, S. et al. ADAMANT: a placebo-controlled randomized phase 2 study of

AADvac1, an active immunotherapy against pathological tau in Alzheimer's disease. *Nat Aging* 1, 521–534 (2021). https://doi.org/10.1038/s43587-021-00070-2

(3) Ngandu T, Lehtisalo J, Solomon A, Levälahti E, Ahtiluoto S, Antikainen R, Bäckman L, Hänninen T, Jula A, Laatikainen T, Lindström J, Mangialasche F, Paajanen T, Pajala S, Peltonen M, Rauramaa R, Stigsdotter-Neely A, Strandberg T, Tuomilehto J, Soininen H, Kivipelto M. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *Lancet.* 2015 Jun 6; 385 (9984): 2255-63. doi: 10.1016/S0140-6736(15)60461-5.

(4) Giudici KV, de Souto Barreto P, Beard J, Cantet C, Araujo de Carvalho I, Rolland Y, Vellas B; MAPT DSA group. Effect of long-term omega-3 supplementation and a lifestyle multidomain intervention on intrinsic capacity among community-dwelling older adults: Secondary analysis of a randomized, placebo-controlled trial (MAPT study). *Maturitas.* 2020 Nov; 141: 39-45. doi: 10.1016/j.maturitas.2020.06.012.

C) The quantitative estimation of impacts is based on an indirect general reference from the literature and is not so well defined.

We are aware of this limitation. We had done extensive screening of literature to select the model that best reflected the impact of early diagnosis (based on biomarkers) on cost containment. Collaboration with Prof. Anders Wimo a specialist on geriatric health economy and epidemiology from Karolinska Institutet, Stockholm, Sweden, can further help us to perform a quantitative estimation of the impacts.

Besides, it has been published that the total costs calculated for dementia are estimated to be over £26bn in the UK, with informal care accounting for £11.6bn (44.2%), social care £10.3bn (39.0%) and healthcare £4.3bn (16.4%) (Prince et al., 2014). An early diagnosis and intervention may be offset by subsequent savings, achieved primarily from a reduction in care needs and institutionalization, which may represent 55% of the total costs.

Therefore, in order to do a precise estimation, we need to collect an extensive data which is necessary for modelling (direct, indirect costs per patient in various stages of the diseases). Currently, these data are not available for Slovakia and Czech Republic. Therefore, one of the aims is to set up the epidemiology study and Slovak national program to combat dementia, where we intend to compile large datasets that will allow us to accurately assess the benefit of early diagnosis.

In addition, Institute of Neuroimmunology SAS took part on "Alzheimer's disease data-driven insights on individual outcomes of importance", a JPND project led by Linus Jönsson, Karolinska Institutet, Sweden. The aim of the project is to develop ways of determining the value (to patients, caregivers and society) and cost-effectiveness of new treatment options, as well as ways of organizing the care that take into account the perspective of people living with AD and their caregivers. We expect that the complete data analyses will be available next year.

(1) Prince M, Knapp M, Guerchet M, et al. King's College London and the London School of Economics. Update', second Dementia UK: Alzheimer's Society 2014; Available from www.alzheimers.org.uk/ download/downloads/id/2323/dementia_uk_update.pdf.

D) There is an overall strong academic and single institution bias in the distribution of work package and task leadership roles, which is not sufficiently explained.

The majority of tasks on ADDIT-CE are collaborative across both ecosystem and multiple parts of the quadruple helix. The task leadership reflects the distribution of the responsibility for the task deliverables and meeting the WP's milestones. To better reflect the involvement of business partners in the consortium and to address the evaluators' concerns, the WP2 leadership is assigned to MultiplexDX and the WP3 lead to Biovendor. The single institution bias of MU is caused by two factors:

1) MU is participating in the project with three departments (CEITEC, Faculty of Medicine, Faculty of Sciences) who each take responsibility for different tasks mainly in the WP4.

2) MU as the Coordinating institution has a strong service from administrative departments (project management, grant support, technology transfer department, PR) that will be active in tasks of WP2, WP3, WP6 and WP7.

3) NII SAS is a leading institution in Slovakia focusing on dementia research. The institute coordinates all scientific, medical and project activities in the country. NII SAS is founding institution of JPND program (in collaboration with Ministry of education, science, research and sport of the Slovak Republic) and it has taken part on several prestigious JPND projects. The institute harmonizes diagnostic standards across the clinical centers and is driving force of the transfer of new technologies into the clinical practice. Because of extensive expertise, NII SAS has leadership roles in several tasks.

ANNEX 2

ESTIMATED BUDGET FOR THE ACTION

	Estimated eligible[1] costs (per budget category)										Estimated EU contribution[2]			
	Direct costs								Indirect costs	Total costs	EU contribution to eligible costs			Maximum grant amount[6]
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories	E. Indirect costs[3]		Funding rate %[4]	Maximum EU contribution[5]	Requested EU contribution	
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	D.2 Internally invoiced goods and services	E. Indirect costs					
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Actual costs	Actual costs	Actual costs	Actual costs	Unit costs (usual accounting practices)	Flat-rate costs[8]					
	a1	a2	a3	b	c1	c2	c3	d2	e = 0,25 * (a1 + a2 + a3 + c1 + c2 + c3)	f = a + b + c + d + e	U	g = f * U%	h	m
1 - MU	802 027.00	0.00	0.00	0.00	109 354.00	0.00	418 475.00	22 000.00	332 464.00	1 684 320.00	100	1 684 320.00	1 684 320.00	1 684 320.00
2 - NII SAS	423 180.00	0.00	0.00	0.00	43 316.00	0.00	192 686.00	0.00	164 795.50	823 977.50	100	823 977.50	823 977.50	823 977.50
2.1 - SALS	48 000.00	0.00	0.00	0.00	2 210.00	0.00	6 500.00	0.00	14 177.50	70 887.50	100	70 887.50	70 887.50	70 887.50
3 - ICRC	360 653.00	0.00	0.00	0.00	22 850.00	0.00	63 460.00	22 222.00	111 740.75	580 925.75	100	580 925.75	580 925.75	580 925.75
4 - MC	177 000.00	0.00	0.00	0.00	7 370.00	0.00	6 500.00	0.00	47 717.50	238 587.50	100	238 587.50	238 587.50	238 587.50
5 - BIOVENDOR	125 000.00	0.00	0.00	0.00	5 800.00	0.00	56 400.00	0.00	46 800.00	234 000.00	100	234 000.00	234 000.00	234 000.00
6 - BMC SAS	89 080.00	0.00	0.00	0.00	10 790.00	0.00	47 500.00	32 000.00	36 842.50	216 212.50	100	216 212.50	216 212.50	216 212.50
7 - MH	80 000.00	0.00	0.00	0.00	2 210.00	0.00	1 000.00	0.00	20 802.50	104 012.50	100	104 012.50	104 012.50	104 012.50
8 - MDX	395 017.00	0.00	0.00	0.00	35 245.00	0.00	142 700.00	0.00	143 240.50	716 202.50	100	716 202.50	716 202.50	716 202.50
9 - GENETON	183 639.00	0.00	0.00	0.00	4 000.00	0.00	28 500.00	0.00	54 034.75	270 173.75	100	270 173.75	270 173.75	270 173.75
10 - JIC														
11 - CALS														
Σ consortium	2 683 596.00	0.00	0.00	0.00	243 145.00	0.00	963 721.00	76 222.00	972 615.50	4 939 299.50		4 939 299.50	4 939 299.50	4 939 299.50

[1] See Article 6 for the eligibility conditions. All amounts must be expressed in EUR (see Article 21 for the conversion rules).
[2] The consortium remains free to decide on a different internal distribution of the EU funding (via the consortium agreement; see Article 7).
[3] Indirect costs already covered by an operating grant (received under any EU funding programme) are ineligible (see Article 6.3). Therefore, a beneficiary/affiliated entity that receives an operating grant during the action duration cannot declare indirect costs for the year(s)/reporting period(s) covered by the operating grant, unless they can demonstrate that the operating grant does not cover any costs of the action. This requires specific accounting tools. Please immediately contact us via the EU Funding & Tenders Portal for details.
[4] See Data Sheet for the funding rate(s).
[5] This is the theoretical amount of the EU contribution to costs, if the reimbursement rate is applied to all the budgeted costs. This theoretical amount is then capped by the 'maximum grant amount'.
[6] The 'maximum grant amount' is the maximum grant amount decided by the EU. It normally corresponds to the requested grant, but may be lower.
[7] See Annex 2a 'Additional information on the estimated budget' for the details (units, cost per unit).
[8] See Data Sheet for the flat-rate.

ANNEX 2a

ADDITIONAL INFORMATION ON UNIT COSTS AND CONTRIBUTIONS

SME owners/natural person beneficiaries without salary (Decision C(2020) 7115[1])

Type: unit costs

Units: days spent working on the action (rounded up or down to the nearest half-day)

Amount per unit (daily rate): calculated according to the following formula:

{EUR 5 080 / 18 days = **282,22**}
multiplied by
{country-specific correction coefficient of the country where the beneficiary is established}

The country-specific correction coefficients used are those set out in the Horizon Europe Work Programme (section Marie Skłodowska-Curie actions) in force at the time of the call (see Portal Reference Documents).

HE and Euratom Research Infrastructure actions[2]

Type: unit costs

Units[3]: see (for each access provider and installation) the unit cost table in Annex 2b

Amount per unit*: see (for each access provider and installation) the unit cost table in Annex 2b

* Amount calculated as follows:

For trans-national access:

$$\frac{\text{average annual total trans-national access costs to the installation (over past two years[4])}}{\text{average annual total quantity of trans-national access to the installation (over past two years[5])}}$$

For virtual access:

$$\frac{\text{total virtual access costs to the installation (over the last year[6])}}{\text{total quantity of virtual access to the installation (over the last year[7])}}$$

Euratom staff mobility costs[8]

Monthly living allowance

Type: unit costs

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1 Commission Decision of 20 October 2020 authorising the use of unit costs for the personnel costs of the owners of small and medium-sized enterprises and beneficiaries that are natural persons not receiving a salary for the work carried out by themselves under an action or work programme (C(2020)7715).

2 Decision of 19 April 2021 authorising the use of unit costs for the costs of providing trans-national and virtual access in Research Infrastructure actions under the Horizon Europe Programme (2021-2027) and the Research and Training Programme of the European Atomic Energy Community (2021-2025).

3 Unit of access (e.g. beam hours, weeks of access, sample analysis) fixed by the access provider in proposal.

4 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

5 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

6 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

7 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

8 Decision of 15 March 2021 authorising the use of unit costs for mobility in co-fund actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025).

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit*: see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

* Amount calculated as follows from 1 January 2021:
{**EUR 4 300** multiplied by
country-specific correction coefficient** of the country where the staff member is seconded}[9]

**Country-specific correction coefficients as from 1 January 2021[10]

EU-Member States[11]

Country / Place	Coefficient (%)
Bulgaria	59,1
Czech Rep.	85,2
Denmark	131,3
Germany Bonn Karlsruhe Munich	101,9 95,8 98 113,9
Estonia	82,3
Ireland	129
Greece	81,4
Spain	94,2
France	120,5
Croatia	75,8
Italy Varese	95 90,7
Cyprus	78,2
Latvia	77,5
Lithuania	76,6
Hungary	71,9
Malta	94,7
Netherlands	113,9
Austria	107,9
Poland	70,9
Portugal	91,1
Romania	66,6
Slovenia	86,1

[9] Unit costs for living allowances are calculated by using a method of calculation similar to that applied for the secondment to the European Commission of seconded national experts (SNEs).

[10] For the financial statements, the amount must be adjusted according to the actual place of secondment.
The revised coefficients were adopted in the Decision authorising the use of unit costs for the Fusion Programme co-fund action under the Research and training Programme of the European Atomic Energy Community 2021-2025. They are based on the 2020 Annual update of the remuneration and pensions of the officials and other servants of the European Union and the correction coefficients applied thereto (OJ C 428, 11.12.2020) to ensure purchasing power parity. The revised coefficient are applied as from 1 January 2021 through an amendment to the grant agreement.

[11] No correction coefficient shall be applicable in Belgium and Luxembourg.

Slovakia	80,6
Finland	118,4
Sweden	124,3

Third countries

Country/place	Coefficient (%)
China	82,2
India	72,3
Japan	111,8
Russia	92,7
South Korea	92,3
Switzerland	129.2
Ukraine	82.3
United Kingdom	97.6
United States	101,4 (New-York) 90,5 (Washington)

Mobility allowance

Type: Unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit: **EUR 600** per person-month; see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

Family allowance

Type: unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit: **EUR 660** per person-month; see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

Education allowance

Type: Unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit*: see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

*Amount calculated as follows from 1 January 2021:
{EUR 283.82 x number of dependent children[12]**}**

[12] For the estimated budget (Annex 2): an average should be used. (⚠ For the financial statements, the number of children (and months) must be adjusted according to the actual family status at the moment the secondment starts.)

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

NEUROIMUNOLOGICKY USTAV SLOVENSKEJAKADEMIA VIED (NII SAS), PIC 984972436, established in DUBRAVSKA CESTA 9, BRATISLAVA 84510, Slovakia,

hereby agrees

to become beneficiary

in Agreement No 101087124 — ADDIT-CE ('the Agreement')

between Masarykova univerzita (MU) **and** the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Michal NOVAK with ECAS id nnovakma signed in the Participant Portal on 11/11/2022 at 10:47:03 (transaction id SigId-80658-lV0jUc N7S0ECSbxKZtv04wNhuaC9yoFnk0ZvvbzSiYjK7fIyNxSsbaUFVDrge0r VntGIwx3vyAJf2IEskdWQDa-rS0vSrmBGYCYOonzu9chxJ-2XcNywLzV DhTsHzoCzTMiwGCImTmyxIohHSnsdCBGhbCA2NwfTuVWBfwHzeX KQ2T8mGRGodW4I0Gc5PWIdx7M6m). Timestamp by third party at 2022.11.11 10:47:12 CET

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FAKULTNI NEMOCNICE U SV. ANNY V BRNE (ICRC), PIC 994491822, established in Pekarska 53, Brno 656 91, Czechia,

hereby agrees

to become beneficiary

in Agreement No 101087124 — ADDIT-CE ('the Agreement')

between Masarykova univerzita (MU) **and** the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Vlastimil Vajdák with ECAS id n003jubo signed in the Participant Portal on 09/12/2022 at 15:00:03 (transaction id SigId-151469-qIuWeZptCRVbjfehPCifBWg3Xg4p043lrzjc5C4gq2yU9gQajbYjjkCzJkmlFgh9un6ouy9LN5QGfdzzpGj8jhW-yntOf97TTHqYSWbdLAFzhs-2nP2AbmNUIk0DvLpMUyT8gV7JW8ZJvHQzxttZWw3qctROw8DSy67MUNookxHGZcQpnZ2ZxRIpWzZVq2yqmuDzeG). Timestamp by third party at 2022.12.09 15:00:11 CET

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CENTRUM MEMORY NO (MC), PIC 892489532, established in MLYNAROVICOVA 2571/21, BRATISLAVA 851 03, Slovakia,

hereby agrees

to become beneficiary

in Agreement No 101087124 — ADDIT-CE ('the Agreement')

between Masarykova univerzita (MU) **and** the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Zuzana Habalova with ECAS id n004hv84 signed in the Participant Portal on 10/11/2022 at 17:36:57 (transaction id SigId-75035-EHQV4c5qTTJOfIoeFapDXzkok3txDOtobjfi6i9za4Y4YJ19KcfLqwHG7451AfzejZ03kRNa3YiJqzpzNQSzin1G-rS0vSrmBGYCYOonzu9chxJ-WfzX6lcW0E89jWn2phZIuOIoViBIhhNvUjHvd4NaUeXzIEqVIdQNhrJlBu0FPGWzp0dzrcAQl3SXOwcPYSPFSPC). Timestamp by third party at 2022.11.10 17:37:02 CET

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BIOVENDOR - LABORATORNI MEDICINA AS (BIOVENDOR), PIC 973936455, established in KARASEK 1767/1, BRNO 621 00, Czechia,

hereby agrees

to become beneficiary

in Agreement No 101087124 — ADDIT-CE ('the Agreement')

between Masarykova univerzita (MU) **and** the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Radim Jakubec with ECAS id n00amjq5 signed in the Participant Portal on 11/11/2022 at 09:09:28 (transaction id SigId-78508-cDa5z OH1qMnGpY60pXj5knhI4APBHXjA036zzme9dqBUOMozzzuJdcQzzkl HBipdHVKbrnTCenejkFP5VJoXKPq1-rS0vSrmBGYCYOonzu9chxJ-ru8 n5uDeHXMNGoUwIpZ8sC0uxyhIritkpoRPNd2evbTeLkSadccRCPJHa 3IZKW4v2uszjqf2TkpdmKDYwWVMKK). Timestamp by third party at 2022.11.11 09:09:35 CET

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BIOMEDICINSKE CENTRUM SLOVENSKEJ AKADEMIE VIED, VEREJNA VYSKUMNA INSTITUCIA (BMC SAS), PIC 918583890, established in DUBRAVSKA CESTA 9, BRATISLAVA 845 05, Slovakia,

hereby agrees

to become beneficiary

in Agreement No 101087124 — ADDIT-CE ('the Agreement')

between Masarykova univerzita (MU) **and** the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Silvia PASTOREKOVA with ECAS id npastosa signed in the Participant Portal on 22/11/2022 at 12:00:06 (transaction id SigId-42850-ncEquwGkHmygpzb86MTTrzY2lBzxeOJvvMXYzLbKqqJaEHYczfYiHGzwyvJnnxbTnbh7MBshUtVrMDWIUhrASUwG-jpJZscgsw0KzOcDzY5LHew0-ev0pI6lYJZMhi5SmW3gBKMYoKXhdy74pHuUv2iOkt9vYuO7KklC3bxlnJpKWqGgwE640Y1QJ2Sxzn2PxvzzVBA0). Timestamp by third party at 2022.11.22 12:00:14 CET

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MINISTERSTVO ZDRAVOTNICTVA SLOVENSKEJ REPUBLIKY (MH), PIC 999825173, established in LIMBOVA 2, BRATISLAVA 83752, Slovakia,

hereby agrees

to become beneficiary

in Agreement No 101087124 — ADDIT-CE ('the Agreement')

between Masarykova univerzita (MU) **and** the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Peter Ferjancik with ECAS id n0055f5b signed in the Participant Portal on 24/11/2022 at 13:34:10 (transaction id SigId-79297-61zkUY zznbzmVhmDBb1LtmcmIeohOVZSuBN7Gw8cB1CKO0R87ZzG7TaogR O41IIztzps7h4G5gVZNJcUZeyAgezzG-jpJZscgsw0KzOcDzY5LHew0-bZ i5rQBlIXYkRJIOPrENQmT3ZrEzHDzKH2iajIIgIZvNZLbKMCvYFb8FpYDc 2gfjhEyGg6vsGSunnDCmsdxhcc). Timestamp by third party at 2022.11.24 13:34:16 CET

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

MULTIPLEXDX S.R.O. (MDX), PIC 918777890, established in ILKOVICOVA 8, BRATISLAVA 841 04, Slovakia,

hereby agrees

to become beneficiary

in Agreement No 101087124 — ADDIT-CE ('the Agreement')

between Masarykova univerzita (MU) **and** the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Pavol Cekan with ECAS id nwolfvla signed in the Participant Portal on 10/11/2022 at 16:58:39 (transaction id SigId-74318-eZAyyIeRr694woueUx1XdvqQReuDzLCumHV4b7AinzlxrYFm3AW7CU4fVp1tYDJqk2C43fXpNfSF7s7WCMOBy9-rS0vSrmBGYCYOonzu9chxJ-yatGjFdYE0hfmMQgyV7ZgifONBcxfHQy5zzLoi8Znzzsdf6xTNQ8Yzm0ANHeU8kUvt59UH3qZuKPjA28KuNraEH). Timestamp by third party at 2022.11.10 16:58:46 CET

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

GENETON S.R.O. (GENETON), PIC 951290059, established in ILKOVICOVA 8, BRATISLAVA 841 04, Slovakia,

hereby agrees

to become beneficiary

in Agreement No 101087124 — ADDIT-CE ('the Agreement')

between Masarykova univerzita (MU) **and** the **European Research Executive Agency (REA)** ('EU executive agency' or 'granting authority'), under the powers delegated by the European Commission ('European Commission'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

Radim Bobek with ECAS id n00ap9ln signed in the Participant Portal on 21/11/2022 at 10:45:31 (transaction id SigId-23353-GJESGIoSF8QfYEriXMiPVCmykmjkDvnJCiGHOqQ8QJTlJ8bzomsreXWLpNbrvbzgqQOnDYOY4DA1zGnasX6IvBG-jpJZscgsw0KzOcDzY5LHew0-8eejWLdO0JmQo63V5CkzcrnshSOEezxbhzQIcNm9YlcwHzdfxkiWG25sxkvv64NWPRwrJjRLT4n2FdVsPwA3WWe). Timestamp by third party at 2022.11.21 10:45:40 CET

FINANCIAL STATEMENT FOR [PARTICIPANT NAME] FOR REPORTING PERIOD [NUMBER]

	Eligible[1] costs (per budget category)																EU contribution[2]				Revenues
	Direct costs															Indirect costs	Total costs	EU contribution to eligible costs			Total requested EU contribution	Income generated by the action
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories								E. Indirect costs[2]		Funding rate %[3]	Maximum EU contribution[4]	Requested EU contribution		
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	[D.1 Financial support to third parties]	D.2 Internally invoiced goods and services	[D.3 Transnational access to research infrastructure unit costs]	[D.4 Virtual access to research infrastructure unit costs]	*[OPTION for HE PCP/PPI:* D.5 PCP/PPI procurement costs*]*	*[OPTION for Euratom Programme Cofund Actions:* D.6 Euratom Cofund staff mobility costs*]*	*[OPTION for HE ERC Grants:* D.7 ERC additional funding*]*	*[OPTION for HE ERC Grants:* D.8 ERC additional funding (subcontracting, FSTP and internally invoiced goods and services)*]*	E. Indirect costs						
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[5]	Actual costs	Actual costs	Actual costs	Actual costs	[Actual costs]	Unit costs (usual accounting practices)	[Unit costs[5]]	[Unit costs[5]]	[Actual costs]	[Unit costs[5]]	[Actual costs]	[Actual costs]	Flat-rate costs[6]						
	a1	a2	a3	b	c1	c2	c3	[d1a]	d2	[d3]	[d4]	[d5]	[d6]	[d7]	[d8]	e = 0,25 * (a1 + a2 + a3 ~~+b+~~ c1 +c2 + c3 ~~+d1a + d2 + d3 + d4 [+ d5][+ d6]~~ [+d7] ~~[+ d8]~~)	f = a+b+c+d+e	U	g = f*U%	h	m	n
XX – [short name beneficiary/affiliated entity]																						

The beneficiary/affiliated entity hereby confirms that:

The information provided is complete, reliable and true.

The costs and contributions declared are eligible (see Article 6).

The costs and contributions can be substantiated by adequate records and supporting documentation that will be produced upon request or in the context of checks, reviews, audits and investigations (see Articles 19, 20 and 25).

For the last reporting period: that all the revenues have been declared (see Article 22).

① Please declare all eligible costs and contributions, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Only amounts that were declared in your individual financial statements can be taken into account lateron, in order to replace costs/contributions that are found to be ineligible.

[1] See Article 6 for the eligibility conditions. All amounts must be expressed in EUR (see Article 21 for the conversion rules).

[2] If you have also received an EU operating grant during this reporting period, you cannot claim indirect costs - unless you can demonstrate that the operating grant does not cover any costs of the action. This requires specific accounting tools. Please contact us immediately via the Funding & Tenders Portal for details.

[3] See Data Sheet for the reimbursement rate(s).

[4] This is the *theoretical* amount of EU contribution to costs that the system calculates automatically (by multiplying the reimbursement rates by the costs declared). The amount you request (in the column 'requested EU contribution') may be less.

[5] See Annex 2a 'Additional information on the estimated budget' for the details (units, cost per unit).

[6] See Data Sheet for the flat-rate.

ANNEX 5

SPECIFIC RULES

CONFIDENTIALITY AND SECURITY (— ARTICLE 13)

Sensitive information with security recommendation

Sensitive information with a security recommendation must comply with the additional requirements imposed by the granting authority.

Before starting the action tasks concerned, the beneficiaries must have obtained all approvals or other mandatory documents needed for implementing the task. The documents must be kept on file and be submitted upon request by the coordinator to the granting authority. If they are not in English, they must be submitted together with an English summary.

For requirements restricting disclosure or dissemination, the information must be handled in accordance with the recommendation and may be disclosed or disseminated only after written approval from the granting authority.

EU classified information

If EU classified information is used or generated by the action, it must be treated in accordance with the security classification guide (SCG) and security aspect letter (SAL) set out in Annex 1 and Decision 2015/444[1] and its implementing rules — until it is declassified.

Deliverables which contain EU classified information must be submitted according to special procedures agreed with the granting authority.

Action tasks involving EU classified information may be subcontracted only with prior explicit written approval from the granting authority and only to entities established in an EU Member State or in a non-EU country with a security of information agreement with the EU (or an administrative arrangement with the Commission).

EU classified information may not be disclosed to any third party (including participants involved in the action implementation) without prior explicit written approval from the granting authority.

ETHICS (— ARTICLE 14)

Ethics and research integrity

The beneficiaries must carry out the action in compliance with:

- ethical principles (including the highest standards of research integrity)

[1] Commission Decision 2015/444/EC, Euratom of 13 March 2015 on the security rules for protecting EU classified information (OJ L 72, 17.3.2015, p. 53).

and

- applicable EU, international and national law, including the EU Charter of Fundamental Rights and the European Convention for the Protection of Human Rights and Fundamental Freedoms and its Supplementary Protocols.

No funding can be granted, within or outside the EU, for activities that are prohibited in all Member States. No funding can be granted in a Member State for an activity which is forbidden in that Member State.

The beneficiaries must pay particular attention to the principle of proportionality, the right to privacy, the right to the protection of personal data, the right to the physical and mental integrity of persons, the right to non-discrimination, the need to ensure protection of the environment and high levels of human health protection.

The beneficiaries must ensure that the activities under the action have an exclusive focus on civil applications.

The beneficiaries must ensure that the activities under the action do not:

- aim at human cloning for reproductive purposes
- intend to modify the genetic heritage of human beings which could make such modifications heritable (with the exception of research relating to cancer treatment of the gonads, which may be financed)
- intend to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer, or
- lead to the destruction of human embryos (for example, for obtaining stem cells).

Activities involving research on human embryos or human embryonic stem cells may be carried out only if:

- they are set out in Annex 1 or
- the coordinator has obtained explicit approval (in writing) from the granting authority.

In addition, the beneficiaries must respect the fundamental principle of research integrity — as set out in the European Code of Conduct for Research Integrity[2].

This implies compliance with the following principles:

- reliability in ensuring the quality of research reflected in the design, the methodology, the analysis and the use of resources
- honesty in developing, undertaking, reviewing, reporting and communicating research in a transparent, fair and unbiased way

[2] European Code of Conduct for Research Integrity of ALLEA (All European Academies).

- respect for colleagues, research participants, society, ecosystems, cultural heritage and the environment

- accountability for the research from idea to publication, for its management and organisation, for training, supervision and mentoring, and for its wider impacts

and means that beneficiaries must ensure that persons carrying out research tasks follow the good research practices including ensuring, where possible, openness, reproducibility and traceability and refrain from the research integrity violations described in the Code.

Activities raising ethical issues must comply with the additional requirements formulated by the ethics panels (including after checks, reviews or audits; see Article 25).

Before starting an action task raising ethical issues, the beneficiaries must have obtained all approvals or other mandatory documents needed for implementing the task, notably from any (national or local) ethics committee or other bodies such as data protection authorities.

The documents must be kept on file and be submitted upon request by the coordinator to the granting authority. If they are not in English, they must be submitted together with an English summary, which shows that the documents cover the action tasks in question and includes the conclusions of the committee or authority concerned (if any).

VALUES (— ARTICLE 14)

Gender mainstreaming

The beneficiaries must take all measures to promote equal opportunities between men and women in the implementation of the action and, where applicable, in line with the gender equality plan. They must aim, to the extent possible, for a gender balance at all levels of personnel assigned to the action, including at supervisory and managerial level.

INTELLECTUAL PROPERTY RIGHTS (IPR) — BACKGROUND AND RESULTS — ACCESS RIGHTS AND RIGHTS OF USE (— ARTICLE 16)

Definitions

Access rights — Rights to use results or background.

Dissemination — The public disclosure of the results by appropriate means, other than resulting from protecting or exploiting the results, including by scientific publications in any medium.

Exploit(ation) — The use of results in further research and innovation activities other than those covered by the action concerned, including among other things, commercial exploitation such as developing, creating, manufacturing and marketing a product or process, creating and providing a service, or in standardisation activities.

Fair and reasonable conditions — Appropriate conditions, including possible financial terms or royalty-free conditions, taking into account the specific circumstances of the request for access, for example the actual or potential value of the results or background to which access is requested and/or the scope, duration or other characteristics of the exploitation envisaged.

FAIR principles — 'findability', 'accessibility', 'interoperability' and 'reusability'.

Open access — Online access to research outputs provided free of charge to the end-user.

Open science — An approach to the scientific process based on open cooperative work, tools and diffusing knowledge.

Research data management — The process within the research lifecycle that includes the organisation, storage, preservation, security, quality assurance, allocation of persistent identifiers (PIDs) and rules and procedures for sharing of data including licensing.

Research outputs — Results to which access can be given in the form of scientific publications, data or other engineered results and processes such as software, algorithms, protocols, models, workflows and electronic notebooks.

Scope of the obligations

For this section, references to 'beneficiary' or 'beneficiaries' do not include affiliated entities (if any).

Agreement on background

The beneficiaries must identify in a written agreement the background as needed for implementing the action or for exploiting its results.

Where the call conditions restrict control due to strategic interests reasons, background that is subject to control or other restrictions by a country (or entity from a country) which is not one of the eligible countries or target countries set out in the call conditions and that impact the exploitation of the results (i.e. would make the exploitation of the results subject to control or restrictions) must not be used and must be explicitly excluded from it in the agreement on background — unless otherwise agreed with the granting authority.

Ownership of results

Results are owned by the beneficiaries that generate them.

However, two or more beneficiaries own results jointly if:

- they have jointly generated them and
- it is not possible to:
  - establish the respective contribution of each beneficiary, or
  - separate them for the purpose of applying for, obtaining or maintaining their protection.

The joint owners must agree — in writing — on the allocation and terms of exercise of their joint ownership ('**joint ownership agreement**'), to ensure compliance with their obligations under this Agreement.

Unless otherwise agreed in the joint ownership agreement or consortium agreement, each joint owner may grant non-exclusive licences to third parties to exploit the jointly-owned results (without any right to sub-license), if the other joint owners are given:

- at least 45 days advance notice and
- fair and reasonable compensation.

The joint owners may agree — in writing — to apply another regime than joint ownership.

If third parties (including employees and other personnel) may claim rights to the results, the beneficiary concerned must ensure that those rights can be exercised in a manner compatible with its obligations under the Agreement.

The beneficiaries must indicate the owner(s) of the results (results ownership list) in the final periodic report.

Protection of results

Beneficiaries which have received funding under the grant must adequately protect their results — for an appropriate period and with appropriate territorial coverage — if protection is possible and justified, taking into account all relevant considerations, including the prospects for commercial exploitation, the legitimate interests of the other beneficiaries and any other legitimate interests.

Exploitation of results

Beneficiaries which have received funding under the grant must — up to four years after the end of the action (see Data Sheet, Point 1) — use their best efforts to exploit their results directly or to have them exploited indirectly by another entity, in particular through transfer or licensing.

If, despite a beneficiary's best efforts, the results are not exploited within one year after the end of the action, the beneficiaries must (unless otherwise agreed in writing with the granting authority) use the Horizon Results Platform to find interested parties to exploit the results.

If results are incorporated in a standard, the beneficiaries must (unless otherwise agreed with the granting authority or unless it is impossible) ask the standardisation body to include the funding statement (see Article 17) in (information related to) the standard.

Additional exploitation obligations

Where the call conditions impose additional exploitation obligations (including obligations linked to the restriction of participation or control due to strategic assets, interests, autonomy or security reasons), the beneficiaries must comply with them — up to four years after the end of the action (see Data Sheet, Point 1).

Where the call conditions impose additional exploitation obligations in case of a public emergency, the beneficiaries must (if requested by the granting authority) grant for a limited period of time specified in the request, non-exclusive licences — under fair and reasonable conditions — to their results to legal entities that need the results to address the public emergency and commit to rapidly and broadly exploit the resulting products and services at fair and reasonable conditions. This provision applies up to four years after the end of the action (see Data Sheet, Point 1).

Additional information obligation relating to standards

Where the call conditions impose additional information obligations relating to possible standardisation, the beneficiaries must — up to four years after the end of the action (see Data Sheet, Point 1) — inform the granting authority, if the results could reasonably be expected to contribute to European or international standards.

Transfer and licensing of results

Transfer of ownership

The beneficiaries may transfer ownership of their results, provided this does not affect compliance with their obligations under the Agreement.

The beneficiaries must ensure that their obligations under the Agreement regarding their results are passed on to the new owner and that this new owner has the obligation to pass them on in any subsequent transfer.

Moreover, they must inform the other beneficiaries with access rights of the transfer at least 45 days in advance (or less if agreed in writing), unless agreed otherwise in writing for specifically identified third parties including affiliated entities or unless impossible under the applicable law. This notification must include sufficient information on the new owner to enable the beneficiaries concerned to assess the effects on their access rights. The beneficiaries may object within 30 days of receiving notification (or less if agreed in writing), if they can show that the transfer would adversely affect their access rights. In this case, the transfer may not take place until agreement has been reached between the beneficiaries concerned.

Granting licences

The beneficiaries may grant licences to their results (or otherwise give the right to exploit them), including on an exclusive basis, provided this does not affect compliance with their obligations.

Exclusive licences for results may be granted only if all the other beneficiaries concerned have waived their access rights.

Granting authority right to object to transfers or licensing — Horizon Europe actions

Where the call conditions in Horizon Europe actions provide for the right to object to transfers or licensing, the granting authority may — up to four years after the end of the action (see Data Sheet, Point 1) — object to a transfer of ownership or the exclusive licensing of results, if:

- the beneficiaries which generated the results have received funding under the grant
- it is to a legal entity established in a non-EU country not associated with Horizon Europe, and
- the granting authority considers that the transfer or licence is not in line with EU interests.

Beneficiaries that intend to transfer ownership or grant an exclusive licence must formally notify the granting authority before the intended transfer or licensing takes place and:

- identify the specific results concerned
- describe in detail the new owner or licensee and the planned or potential exploitation of the results, and
- include a reasoned assessment of the likely impact of the transfer or licence on EU interests, in particular regarding competitiveness as well as consistency with ethical principles and security considerations.

The granting authority may request additional information.

If the granting authority decides to object to a transfer or exclusive licence, it must formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information it has requested).

No transfer or licensing may take place in the following cases:

- pending the granting authority decision, within the period set out above
- if the granting authority objects
- until the conditions are complied with, if the granting authority objection comes with conditions.

A beneficiary may formally notify a request to waive the right to object regarding intended transfers or grants to a specifically identified third party, if measures safeguarding EU interests are in place. If the granting authority agrees, it will formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information requested).

Granting authority right to object to transfers or licensing — Euratom actions

Where the call conditions in Euratom actions provide for the right to object to transfers or licensing, the granting authority may — up to four years after the end of the action (see Data Sheet, Point 1) — object to a transfer of ownership or the exclusive or non-exclusive licensing of results, if:

- the beneficiaries which generated the results have received funding under the grant
- it is to a legal entity established in a non-EU country not associated to the Euratom Research and Training Programme 2021-2025 and
- the granting authority considers that the transfer or licence is not in line with the EU interests.

Beneficiaries that intend to transfer ownership or grant a licence must formally notify the granting authority before the intended transfer or licensing takes place and:

- identify the specific results concerned
- describe in detail the results, the new owner or licensee and the planned or potential exploitation of the results, and
- include a reasoned assessment of the likely impact of the transfer or licence on EU interests, in particular regarding competitiveness as well as consistency with

ethical principles and security considerations (including the defence interests of the EU Member States under Article 24 of the Euratom Treaty).

The granting authority may request additional information.

If the granting authority decides to object to a transfer or licence, it will formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information requested).

No transfer or licensing may take place in the following cases:

- pending the granting authority decision, within the period set out above
- if the granting authority objects
- until the conditions are complied with, if the granting authority objection comes with conditions.

A beneficiary may formally notify a request to waive the right to object regarding intended transfers or grants to a specifically identified third party, if measures safeguarding EU interests are in place. If the granting authority agrees, it will formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information requested).

Limitations to transfers and licensing due to strategic assets, interests, autonomy or security reasons of the EU and its Member States

Where the call conditions restrict participation or control due to strategic assets, interests, autonomy or security reasons, the beneficiaries may not transfer ownership of their results or grant licences to third parties which are established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) — unless they have requested and received prior approval by the granting authority.

The request must:

- identify the specific results concerned
- describe in detail the new owner and the planned or potential exploitation of the results, and
- include a reasoned assessment of the likely impact of the transfer or license on the strategic assets, interests, autonomy or security of the EU and its Member States.

The granting authority may request additional information.

Access rights to results and background

Exercise of access rights — Waiving of access rights — No sub-licensing

Requests to exercise access rights and the waiver of access rights must be in writing.

Unless agreed otherwise in writing with the beneficiary granting access, access rights do not include the right to sub-license.

If a beneficiary is no longer involved in the action, this does not affect its obligations to grant access.

If a beneficiary defaults on its obligations, the beneficiaries may agree that that beneficiary no longer has access rights.

Access rights for implementing the action

The beneficiaries must grant each other access — on a royalty-free basis — to background needed to implement their own tasks under the action, unless the beneficiary that holds the background has — before acceding to the Agreement —:

- informed the other beneficiaries that access to its background is subject to restrictions, or

- agreed with the other beneficiaries that access would not be on a royalty-free basis.

The beneficiaries must grant each other access — on a royalty-free basis — to results needed for implementing their own tasks under the action.

Access rights for exploiting the results

The beneficiaries must grant each other access — under fair and reasonable conditions — to results needed for exploiting their results.

The beneficiaries must grant each other access — under fair and reasonable conditions — to background needed for exploiting their results, unless the beneficiary that holds the background has — before acceding to the Agreement — informed the other beneficiaries that access to its background is subject to restrictions.

Requests for access must be made — unless agreed otherwise in writing — up to one year after the end of the action (see Data Sheet, Point 1).

Access rights for entities under the same control

Unless agreed otherwise in writing by the beneficiaries, access to results and, subject to the restrictions referred to above (if any), background must also be granted — under fair and reasonable conditions — to entities that:

- are established in an EU Member State or Horizon Europe associated country

- are under the direct or indirect control of another beneficiary, or under the same direct or indirect control as that beneficiary, or directly or indirectly controlling that beneficiary and

- need the access to exploit the results of that beneficiary.

Unless agreed otherwise in writing, such requests for access must be made by the entity directly to the beneficiary concerned.

Requests for access must be made — unless agreed otherwise in writing — up to one year after the end of the action (see Data Sheet, Point 1).

Access rights for the granting authority, EU institutions, bodies, offices or agencies and national authorities to results for policy purposes — Horizon Europe actions

In Horizon Europe actions, the beneficiaries which have received funding under the grant must grant access to their results — on a royalty-free basis — to the granting authority, EU institutions, bodies, offices or agencies for developing, implementing and monitoring EU policies or programmes. Such access rights do not extend to beneficiaries' background.

Such access rights are limited to non-commercial and non-competitive use.

For actions under the cluster 'Civil Security for Society', such access rights also extend to national authorities of EU Member States for developing, implementing and monitoring their policies or programmes in this area. In this case, access is subject to a bilateral agreement to define specific conditions ensuring that:

- the access rights will be used only for the intended purpose and
- appropriate confidentiality obligations are in place.

Moreover, the requesting national authority or EU institution, body, office or agency (including the granting authority) must inform all other national authorities of such a request.

Access rights for the granting authority, Euratom institutions, funding bodies or the Joint Undertaking Fusion for Energy — Euratom actions

In Euratom actions, the beneficiaries which have received funding under the grant must grant access to their results — on a royalty-free basis — to the granting authority, Euratom institutions, funding bodies or the Joint Undertaking Fusion for Energy for developing, implementing and monitoring Euratom policies and programmes or for compliance with obligations assumed through international cooperation with non-EU countries and international organisations.

Such access rights include the right to authorise third parties to use the results in public procurement and the right to sub-license and are limited to non-commercial and non-competitive use.

Additional access rights

Where the call conditions impose additional access rights, the beneficiaries must comply with them.

COMMUNICATION, DISSEMINATION, OPEN SCIENCE AND VISIBILITY (— ARTICLE 17)

Dissemination

Dissemination of results

The beneficiaries must disseminate their results as soon as feasible, in a publicly available format, subject to any restrictions due to the protection of intellectual property, security rules or legitimate interests.

A beneficiary that intends to disseminate its results must give at least 15 days advance notice to the other beneficiaries (unless agreed otherwise), together with sufficient information on the results it will disseminate.

Any other beneficiary may object within (unless agreed otherwise) 15 days of receiving notification, if it can show that its legitimate interests in relation to the results or background would be significantly harmed. In such cases, the results may not be disseminated unless appropriate steps are taken to safeguard those interests.

Additional dissemination obligations

Where the call conditions impose additional dissemination obligations, the beneficiaries must also comply with those.

Open Science

Open science: open access to scientific publications

The beneficiaries must ensure open access to peer-reviewed scientific publications relating to their results. In particular, they must ensure that:

- at the latest at the time of publication, a machine-readable electronic copy of the published version or the final peer-reviewed manuscript accepted for publication, is deposited in a trusted repository for scientific publications

- immediate open access is provided to the deposited publication via the repository, under the latest available version of the Creative Commons Attribution International Public Licence (CC BY) or a licence with equivalent rights; for monographs and other long-text formats, the licence may exclude commercial uses and derivative works (e.g. CC BY-NC, CC BY-ND) and

- information is given via the repository about any research output or any other tools and instruments needed to validate the conclusions of the scientific publication.

Beneficiaries (or authors) must retain sufficient intellectual property rights to comply with the open access requirements.

Metadata of deposited publications must be open under a Creative Common Public Domain Dedication (CC 0) or equivalent, in line with the FAIR principles (in particular machine-actionable) and provide information at least about the following: publication (author(s), title, date of publication, publication venue); Horizon Europe or Euratom funding; grant project name, acronym and number; licensing terms; persistent identifiers for the publication, the authors involved in the action and, if possible, for their organisations and the grant. Where applicable, the metadata must include persistent identifiers for any research output or any other tools and instruments needed to validate the conclusions of the publication.

Only publication fees in full open access venues for peer-reviewed scientific publications are eligible for reimbursement.

Open science: research data management

The beneficiaries must manage the digital research data generated in the action ('data') responsibly, in line with the FAIR principles and by taking all of the following actions:

- establish a data management plan ('DMP') (and regularly update it)

- as soon as possible and within the deadlines set out in the DMP, deposit the data in a trusted repository; if required in the call conditions, this repository must be federated in the EOSC in compliance with EOSC requirements

- as soon as possible and within the deadlines set out in the DMP, ensure open access — via the repository — to the deposited data, under the latest available version of the Creative Commons Attribution International Public License (CC BY) or Creative Commons Public Domain Dedication (CC 0) or a licence with equivalent rights, following the principle 'as open as possible as closed as necessary', unless providing open access would in particular:

    - be against the beneficiary's legitimate interests, including regarding commercial exploitation, or

    - be contrary to any other constraints, in particular the EU competitive interests or the beneficiary's obligations under this Agreement; if open access is not provided (to some or all data), this must be justified in the DMP

- provide information via the repository about any research output or any other tools and instruments needed to re-use or validate the data.

Metadata of deposited data must be open under a Creative Common Public Domain Dedication (CC 0) or equivalent (to the extent legitimate interests or constraints are safeguarded), in line with the FAIR principles (in particular machine-actionable) and provide information at least about the following: datasets (description, date of deposit, author(s), venue and embargo); Horizon Europe or Euratom funding; grant project name, acronym and number; licensing terms; persistent identifiers for the dataset, the authors involved in the action, and, if possible, for their organisations and the grant. Where applicable, the metadata must include persistent identifiers for related publications and other research outputs.

Open science: additional practices

Where the call conditions impose additional obligations regarding open science practices, the beneficiaries must also comply with those.

Where the call conditions impose additional obligations regarding the validation of scientific publications, the beneficiaries must provide (digital or physical) access to data or other results needed for validation of the conclusions of scientific publications, to the extent that their legitimate interests or constraints are safeguarded (and unless they already provided the (open) access at publication).

Where the call conditions impose additional open science obligations in case of a public emergency, the beneficiaries must (if requested by the granting authority) immediately deposit any research output in a repository and provide open access to it under a CC BY licence, a Public Domain Dedication (CC 0) or equivalent. As an exception, if the access would be against the beneficiaries' legitimate interests, the beneficiaries must grant non-exclusive licenses — under fair and reasonable conditions — to legal entities that need the research output to address the public emergency and commit to rapidly and broadly exploit the resulting products and services at fair and reasonable conditions. This provision applies up to four years after the end of the action (see Data Sheet, Point 1).

Plan for the exploitation and dissemination of results including communication activities

Unless excluded by the call conditions, the beneficiaries must provide and regularly update a plan for the exploitation and dissemination of results including communication activities.

SPECIFIC RULES FOR CARRYING OUT THE ACTION (— ARTICLE 18)

Implementation in case of restrictions due to strategic assets, interests, autonomy or security of the EU and its Member States

Where the call conditions restrict participation or control due to strategic assets, interests, autonomy or security, the beneficiaries must ensure that none of the entities that participate as affiliated entities, associated partners, subcontractors or recipients of financial support to third parties are established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) — unless otherwise agreed with the granting authority.

The beneficiaries must moreover ensure that any cooperation with entities established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) does not affect the strategic assets, interests, autonomy or security of the EU and its Member States.

Recruitment and working conditions for researchers

The beneficiaries must take all measures to implement the principles set out in the Commission Recommendation on the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers[3], in particular regarding:

- working conditions
- transparent recruitment processes based on merit, and
- career development.

The beneficiaries must ensure that researchers and all participants involved in the action are aware of them.

Specific rules for access to research infrastructure activities

Definitions

Research Infrastructures — Facilities that provide resources and services for the research communities to conduct research and foster innovation in their fields. This definition includes the associated human resources, and it covers major equipment or sets of instruments; knowledge-related facilities such as collections, archives or scientific data infrastructures; computing systems, communication networks, and any other infrastructure, of a unique nature and open to external users, essential to achieve excellence in research and innovation. Where relevant, they may be used beyond research, for example

[3] Commission Recommendation 2005/251/EC of 11 March 2005 on the European Charter for Researchers and on a Code of Conduct for the Recruitment of Researchers (OJ L 75, 22.3.2005, p. 67).

for education or public services, and they may be 'single-sited', 'virtual' or 'distributed'[4]:

When implementing access to research infrastructure activities, the beneficiaries must respect the following conditions:

- for transnational access:
  - access which must be provided:

    The access must be free of charge, transnational access to research infrastructure or installations for selected user-groups.

    The access must include the logistical, technological and scientific support and the specific training that is usually provided to external researchers using the infrastructure. Transnational access can be either in person (hands-on), provided to selected users that visit the installation to make use of it, or remote, through the provision to selected user-groups of remote scientific services (e.g. provision of reference materials or samples, remote access to a high-performance computing facility).

  - categories of users that may have access:

    Transnational access must be provided to selected user-groups, i.e. teams of one or more researchers (users).

    The majority of the users must work in a country other than the country(ies) where the installation is located (unless access is provided by an international organisation, the Joint Research Centre (JRC), an ERIC or similar legal entity).

    Only user groups that are allowed to disseminate the results they have generated under the action may benefit from the access (unless the users are working for SMEs).

    Access for user groups with a majority of users not working in a EU Member State or Horizon Europe associated country is limited to 20% of the total amount of units of access provided under the grant (unless a higher percentage is foreseen in Annex 1).

  - procedure and criteria for selecting user groups:

    The user groups must request access by submitting (in writing) a description of the work that they wish to carry out and the names, nationalities and home institutions of the users.

    The user groups must be selected by (one or more) selection panels set up by the consortium.

[4] See Article 2(1) of the Horizon Europe Framework Programme Regulation 2021/695.

The selection panels must be composed of international experts in the field, at least half of them independent from the consortium (unless otherwise specified in Annex 1).

The selection panels must assess all proposals received and recommend a short-list of the user groups that should benefit from access.

The selection panels must base their selection on scientific merit, taking into account that priority should be given to user groups composed of users who:

- have not previously used the installation and
- are working in countries where no equivalent research infrastructure exist.

It will apply the principles of transparency, fairness and impartiality.

Where the call conditions impose additional rules for the selection of user groups, the beneficiaries must also comply with those.

- other conditions:

The beneficiaries must request written approval from the granting authority for the selection of user groups requiring visits to the installations exceeding 3 months (unless such visits are foreseen in Annex 1).

In addition, the beneficiaries must:

- advertise widely, including on a their websites, the access offered under the Agreement
- promote equal opportunities in advertising the access and take into account the gender dimension when defining the support provided to users
- ensure that users comply with the terms and conditions of the Agreement
- ensure that its obligations under Articles 12, 13, 17 and 33 also apply to the users
- keep records of the names, nationalities, and home institutions of users, as well as the nature and quantity of access provided to them

- for virtual access:
  - access which must be provided:

The access must be free of charge, virtual access to research infrastructure or installations.

'Virtual access' means open and free access through communication networks to digital resources and services needed for research, without selecting the users to whom access is provided.

The access must include the support that is usually provided to external users.

Where allowed by the call conditions, beneficiaries may in justified cases define objective eligibility criteria (e.g. affiliation to a research or academic institution) for specific users.

- other conditions:

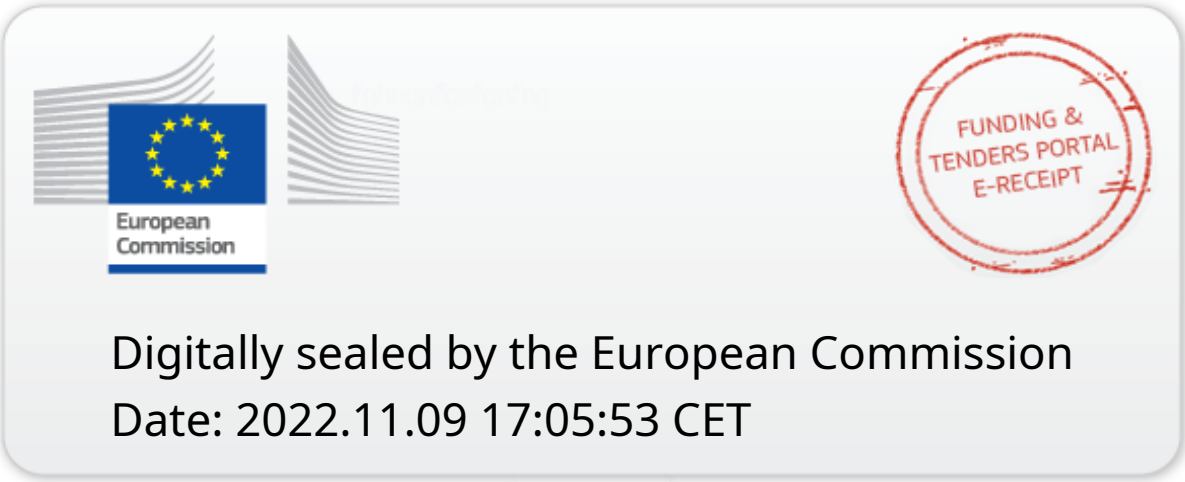
  The beneficiaries must have the virtual access services assessed periodically by a board composed of international experts in the field, at least half of whom must be independent from the consortium (unless otherwise specified in Annex 1). For this purpose, information and statistics on the users and the nature and quantity of the access provided, must be made available to the board.

  The beneficiaries must advertise widely, including on a dedicated website, the access offered under the grant and the eligibility criteria, if any.

  Where the call conditions impose additional traceability[5] obligations, information on the traceability of the users and the nature and quantity of access must be provided by the beneficiaries.

These obligations apply regardless of the form of funding or budget categories used to declare the costs (unit costs or actual costs or a combination of the two).

[5] According to the definition given in ISO 9000, i.e.: "Traceability is the ability to trace the history, application, use and location of an item or its characteristics through recorded identification data." The users can be traced, for example, by authentication and/or by authorization or by other means that allows for analysis of the type of users and the nature and quantity of access provided.



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