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Associated with document Ref. Ares(2017)4842465 - 04/10/2017

EUROPEAN COMMISSION
Research Executive Agency

Director

GRANT AGREEMENT

NUMBER — 778405 — AUTOIGG

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

on the one part,

the **Research Executive Agency (REA)** ('the Agency'), under the powers delegated by the European Commission ('the Commission'), represented for the purposes of signature of this Agreement by Head of Unit, Research Executive Agency , Excellent Science Department, Marie Sklodowska-Curie Research and Innovation Staff Exchanges, Fredrik OLSSON HECTOR,

and

on the other part,

1. 'the coordinator':

FACULTY OF BIOLOGY OF THE UNIVERSITY OF BELGRADE (FBUB), established in STUDENTSKI TRG 3/2, BEOGRAD 11000, Serbia, VAT number: RS100043776, represented for the purposes of signing the Agreement by FBUB representative, Ljubisa STANISAVLJEVIC

and the following other beneficiaries, if they sign their 'Accession Form' (see Annex 3 and Article 56):

2. **YEDITEPE UNIVERSITY VAKIF (YEDITEPE)**, established in KAYISDAGI STREET AGUSTOS CAMPUS 26, Istanbul 81120, Turkey,

3. **ITA-SUOMEN YLIOPISTO (UEF)**, established in YLIOPISTONRANTA 1 E, KUOPIO 70211, Finland, VAT number: FI22857339,

4. **ARGENIT AKILLI BILGI TEKNOLOJILERI SANAYI VE TICARET LIMITED SIRKETI (Argenit)**, established in ITU AYAZAGA KAMPUSU ARI TEKNOKENT ARI 1 BINASI NO 27 MASLAK SARIYER, ISTANBUL 34469, Turkey, VAT number: TR0740487290,

5. **ELVESYS SAS (ELVESYS)**, established in 111 AVENUE VICTOR HUGO, PARIS CEDEX 16 75784, France, VAT number: FR19531301174,

Unless otherwise specified, references to 'beneficiary' or 'beneficiaries' include the coordinator.

The parties referred to above have agreed to enter into the Agreement under the terms and conditions below.

By signing the Agreement or the Accession Form, the beneficiaries accept the grant and agree to

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implement it under their own responsibility and in accordance with the Agreement, with all the obligations and conditions it sets out.

The Agreement is composed of:

Terms and Conditions

Annex 1 Description of the action

Annex 2 Estimated budget for the action

2a Additional information on the estimated budget

Annex 3 Accession Forms

Annex 4 Model for the financial statements

Annex 5 Not applicable

Annex 6 Not applicable

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TERMS AND CONDITIONS

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CHAPTER 1 GENERAL

ARTICLE 1 — SUBJECT OF THE AGREEMENT

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

CHAPTER 2 ACTION

ARTICLE 2 — ACTION TO BE IMPLEMENTED

The grant is awarded for the action entitled '**AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTICS OF NEURODEGENERATIVE DISEASES — AUTOIGG' ('action')**, as described in Annex 1.

ARTICLE 3 — DURATION AND STARTING DATE OF THE ACTION

The duration of the action will be **48 months** as of 1 January 2018 ('**starting date of the action**').

ARTICLE 4 — ESTIMATED BUDGET AND BUDGET TRANSFERS

4.1 Estimated budget

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

It contains the estimated eligible costs and the forms of costs, broken down by beneficiary and budget category (see Articles 5, 6).

4.2 Budget transfers

The estimated budget breakdown indicated in Annex 2 may be adjusted by transfers of amounts between the beneficiaries.

This does not require an amendment according to Article 55, if the action is implemented as described in Annex 1.

CHAPTER 3 GRANT

ARTICLE 5 — GRANT AMOUNT, FORM OF GRANT, REIMBURSEMENT RATES AND FORMS OF COSTS

5.1 Maximum grant amount

The '**maximum grant amount**' is **EUR 954,000.00** (nine hundred and fifty four thousand EURO).

5.2 Form of grant, reimbursement rate and form of costs

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The grant reimburses **100% of the action's eligible costs** (see Article 6) (‘**reimbursement of eligible costs grant**’) (see Annex 2).

The estimated eligible costs of the action are EUR **954,000.00** (nine hundred and fifty four thousand EURO).

Eligible costs (see Article 6) must be declared under the following forms (**'forms of costs'**):

(a) for **costs of seconded staff members**: on the basis of the amount(s) per unit set out in Annex 2 (‘**unit costs**’) and

(b) for **institutional costs** (research, training and networking costs, management and indirect costs): on the basis of the amount per unit set out in Annex 2 (**unit costs**).

5.3 Final grant amount — Calculation

The final grant amount depends on the actual extent to which the action is implemented in accordance with the Agreement’s terms and conditions.

This **amount** is calculated by the Agency — when the payment of the balance is made (see Article 21.4) — in the following steps:

Step 1 – Application of the reimbursement rate

Step 2 – Limit to the maximum grant amount

Step 3 – Reduction due to substantial errors, irregularities or fraud or serious breach of obligations

5.3.1 Step 1 — Application of the reimbursement rate

The reimbursement rate (see Article 5.2) is applied to eligible costs (unit costs; see Article 6) declared by the beneficiaries and approved by the Agency (see Article 21).

5.3.2 Step 2 — Limit to the maximum grant amount

If the amount obtained following Step 1 is higher than the maximum grant amount set out in Article 5.1, it will be limited to the latter.

5.3.3 Step 3 — Reduction due to substantial errors, irregularities or fraud or serious breach of obligations — Reduced grant amount — Calculation

If the grant is reduced (see Article 43), the Agency will calculate the reduced grant amount by deducting the amount of the reduction (calculated in proportion to the seriousness of the errors, irregularities or fraud or breach of obligations, in accordance with Article 43.2) from the maximum grant amount set out in Article 5.1.

The final grant amount will be the lower of the following two:

- the amount obtained following Steps 1 and 2 or
- the reduced grant amount following Step 3.

5.4 Revised final grant amount — Calculation

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If — after the payment of the balance (in particular, after checks, reviews, audits or investigations; see Article 22) — the Agency rejects costs (see Article 42) or reduces the grant (see Article 43), it will calculate the '**revised final grant amount**' for the beneficiary concerned by the findings.

This amount is calculated by the Agency on the basis of the findings, as follows:

- in case of **rejection of costs**: by applying the reimbursement rate to the revised eligible costs approved by the Agency for the beneficiary concerned;

- in case of **reduction of the grant**: by calculating the concerned beneficiary's share in the grant amount reduced in proportion to the seriousness of the errors, irregularities or fraud or breach of obligations (see Article 43.2).

In case of **rejection of costs and reduction of the grant**, the revised final grant amount for the beneficiary concerned will be the lower of the two amounts above.

ARTICLE 6 — ELIGIBLE AND INELIGIBLE COSTS

6.1 General conditions for costs to be eligible

Unit costs are eligible ('eligible costs'), if:

(i) they are calculated as follows:

{amounts per unit set out in Annex 2

multiplied by

the number of actual units}.

(ii) the number of actual units complies with the following:

- the units must be actually used or produced in the period set out in Article 3;

- the units must be necessary for implementing the action or produced by it, and

- the number of units must be identifiable and verifiable, in particular supported by records and documentation (see Article 18).

6.2 Specific conditions for costs to be eligible

Costs are eligible, if they comply with the general conditions (see above) and the specific conditions set out below for each of the following two budget categories:

A. Costs of seconded staff members are eligible, if:

(a) the number of units declared:

(i) corresponds to the actual number of months spent by the seconded staff members on the research and innovation activities and

(ii) does not exceed 12 months (per seconded staff member);

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(b) the seconded staff members comply — at the date of secondment —with the following conditions:

(i) be one of the following:

- an '**early stage researcher**' (i.e. in the first four years of his/her research career and not have a doctoral degree);
- an '**experienced researcher**' (i.e. in possession of a doctoral degree or have at least four years of research experience), or
- **administrative, managerial or technical staff** supporting research and innovation activities under the action, and

(ii) have been actively engaged in or linked to research and innovation activities for at least 6 months at the sending:

- beneficiary (or entity with a capital or legal link[1] to it and located in the same country) or
- partner organisation (or entity with a capital or legal link to it and located in the same country).

(c) the secondments comply with the following conditions:

(i) last at least 1 month and no longer than 12 months (per secondment);

(ii) be between different countries;

(iii) for secondments within the EU (or associated countries)[2]: be between different sectors (academic and non-academic)[3];

(iv) for secondments from EU (or associated countries): be from a beneficiary (or entity with a capital or legal link) established in a EU Member State (or associated country) to a partner organisation (or entity with a capital or legal link) established in a non-EU Member State (or non-associated country), and

(v) for secondments to EU (or associated countries): be from a partner organisation (or entity with a capital or legal link) established in a country listed in General Annex A

[1] '**Entities with a capital or legal link**' are entities that have a link with the beneficiary or partner organisations, in particular, a legal or capital link, which is neither limited to the action nor established for the sole purpose of its implementation.

[2] For the definition, see Article 2.1(3) of Regulation (EU) No 1290/2013 of the European Parliament and of the Council of 11 December 2013 laying down the rules for participation and dissemination in "Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)" ('**Rules for Participation Regulation No 1290/2013**') (OJ L 347, 20.12.2013 p.81): '**associated country**' means a third country which is party to an international agreement with the Union, as identified in Article 7 of the H2020 Framework Programme Regulation No 1291/2013. Article 7 sets out the conditions for association of non-EU countries to Horizon 2020.

[3] For secondments from entities with a capital or legal link to the beneficiaries or partner organisations: only the sector (academic or non-academic) of the beneficiary counts; the entity will be considered to belong to the same sector as their beneficiary.

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of the Main Work Programme to a beneficiary (or entity with a capital or legal link) established in a EU Member State (or associated country).

B. Institutional costs (B.1 Research, training and networking costs and B.2 Management and indirect costs) are eligible if the costs for the seconded staff members (see above) are eligible.

6.3 Ineligible costs

'Ineligible costs' are:

(a) costs that do not comply with the conditions set out above (in Article 6.1), in particular costs incurred during suspension of the action implementation (see Article 49);

(b) costs declared under another EU or Euratom grant (including grants awarded by a Member State and financed by the EU or Euratom budget and grants awarded by bodies other than the Agency for the purpose of implementing the EU budget) in particular, indirect costs if the beneficiary is already receiving an operating grant financed by the EU or Euratom budget in the same period.

6.4 Consequences of declaration of ineligible costs

Declared costs that are ineligible will be rejected (see Article 42).

This may also lead to any of the other measures described in Chapter 6.

CHAPTER 4 RIGHTS AND OBLIGATIONS OF THE PARTIES

SECTION 1 RIGHTS AND OBLIGATIONS RELATED TO IMPLEMENTING THE ACTION

ARTICLE 7 — GENERAL OBLIGATION TO PROPERLY IMPLEMENT THE ACTION

7.1 General 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 and all legal obligations under applicable EU, international and national law.

7.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 8 — RESOURCES TO IMPLEMENT THE ACTION — THIRD PARTIES INVOLVED IN THE ACTION

The beneficiaries must have the appropriate resources to implement the action.

If it is necessary to implement the action, the beneficiaries may:

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- call upon partner organisations to implement certain action tasks described in Annex 1 (i.e. seconding and hosting staff);

- call upon entities with a capital or legal link to the beneficiaries or to partner organisations[4], to implement certain action tasks described in Annex 1 (i.e. seconding staff).

In this case, the beneficiaries retain sole responsibility towards the Agency for implementing the action.

ARTICLE 9 — IMPLEMENTATION OF ACTION TASKS BY BENEFICIARIES NOT RECEIVING EU FUNDING

Not applicable

ARTICLE 10 — PURCHASE OF GOODS, WORKS OR SERVICES

Not applicable

ARTICLE 11 — USE OF IN-KIND CONTRIBUTIONS PROVIDED BY THIRD PARTIES AGAINST PAYMENT

Not applicable

ARTICLE 12 — USE OF IN-KIND CONTRIBUTIONS PROVIDED BY THIRD PARTIES FREE OF CHARGE

Not applicable

ARTICLE 13 — IMPLEMENTATION OF ACTION TASKS BY SUBCONTRACTORS

Not applicable

ARTICLE 14 — IMPLEMENTATION OF ACTION TASKS BY LINKED THIRD PARTIES

Not applicable

ARTICLE 15 — FINANCIAL SUPPORT TO THIRD PARTIES

Not applicable

ARTICLE 16 — PROVISION OF TRANS-NATIONAL OR VIRTUAL ACCESS TO RESEARCH INFRASTRUCTURE

Not applicable

[4] '**Entities with a capital or legal link**' are entities that have a link with the beneficiary or partner organisations, in particular, a legal or capital link, which is neither limited to the action nor established for the sole purpose of its implementation.

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SECTION 2 RIGHTS AND OBLIGATIONS RELATED TO THE GRANT ADMINISTRATION

ARTICLE 17 — GENERAL OBLIGATION TO INFORM

17.1 General obligation to provide information upon request

The beneficiaries must provide — during implementation of the action or afterwards and in accordance with Article 41.2 — any information requested in order to verify eligibility of the costs, proper implementation of the action and compliance with any other obligation under the Agreement.

17.2 Obligation to keep information up to date and to inform about events and circumstances likely to affect the Agreement

Each beneficiary must keep information stored in the Participant Portal Beneficiary Register (via the electronic exchange system; see Article 52) up to date, in particular, its name, address, legal representatives, legal form and organisation type.

Each beneficiary must immediately inform the coordinator — which must immediately inform the Agency and the other beneficiaries — of any of the following:

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

(i) changes in its legal, financial, technical, organisational or ownership situation (or those of an entity with a capital or legal link);

(ii) changes in the name, address, legal form or organisation type of a partner organisation (or those of an entity with a capital or legal link);

(b) **circumstances** affecting:

(i) the decision to award the grant or

(ii) compliance with requirements under the Agreement.

17.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 18 — KEEPING RECORDS — SUPPORTING DOCUMENTATION

18.1 Obligation to keep records and other supporting documentation

The beneficiaries must — for a period of five years after the payment of the balance — keep records and other supporting documentation in order to prove the proper implementation of the action and the costs they declare as eligible.

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They must make them available upon request (see Article 17) or in the context of checks, reviews, audits or investigations (see Article 22).

If there are on-going checks, reviews, audits, investigations, litigation or other pursuits of claims under the Agreement (including the extension of findings; see Articles 22), the beneficiaries must keep the 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 Agency may accept non-original documents if it considers that they offer a comparable level of assurance.

18.1.1 Records and other supporting documentation on the scientific and technical implementation

The beneficiaries must keep records and other supporting documentation on scientific and technical implementation of the action in line with the accepted standards in the respective field.

18.1.2 Records and other documentation to support the costs declared

The beneficiaries must keep adequate records and other supporting documentation to prove the number of units declared.

18.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, costs insufficiently substantiated will be ineligible (see Article 6) and will be rejected (see Article 42), and the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 19 — SUBMISSION OF DELIVERABLES

19.1 Obligation to submit deliverables

The coordinator must:

- submit a '**progress report**' within 30 days after the end of each year, except when the periodic and final reports are due;
- organise a '**mid-term review meeting**' between the beneficiaries, partner organisations, entities with a capital or legal link and the Agency before the deadline for the submission of the report for RP 1 (reporting period 1) and
- submit any **other deliverables** identified in Annex 1, in accordance with the timing and conditions set out in it.

The beneficiaries must:

- submit a '**researcher declaration**' within 20 days after the secondment of each seconded staff member;

19.2 Consequences of non-compliance

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If a beneficiary breaches any of its obligations under this Article, the Agency may apply any of the measures provided for in Chapter 6.

ARTICLE 20 — REPORTING — PAYMENT REQUESTS

20.1 Obligation to submit reports

The coordinator must submit to the Agency (see Article 52) the technical and financial reports set out in this Article. These reports include the requests for payments and must be drawn up using the forms and templates provided in the electronic exchange system (see Article 52).

20.2 Reporting periods

The action is divided into the following '**reporting periods**':

- RP1: from month 1 to month 24
- RP2: from month 25 to month 48

20.3 Periodic reports — Requests for interim payments

The coordinator must submit a periodic report within 60 days following the end of each reporting period.

The **periodic report** must include the following:

(a) a '**periodic technical report**' containing:

(i) an **explanation of the work carried out** by the beneficiaries;

(ii) an **overview of the progress** towards the objectives of the action, including milestones and deliverables identified in Annex 1.

This report must include explanations justifying the differences between work expected to be carried out in accordance with Annex 1 and that actually carried out.

The report must detail the exploitation and dissemination of the results and — if required in Annex 1 — an updated '**plan for the exploitation and dissemination of the results**'.

The report must indicate the communication activities;

(iii) a **summary** for publication by the Agency;

(iv) the answers to the '**questionnaire**', covering issues related to the action implementation and the economic and societal impact, notably in the context of the Horizon 2020 key performance indicators and the Horizon 2020 monitoring requirements;

(b) a '**periodic financial report**' containing:

(i) an '**individual financial statement**' (see Annex 4) from each beneficiary, for the reporting period concerned.

The individual financial statement must detail the eligible costs (see Article 6) for each budget category (see Annex 2).

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The beneficiaries must declare all eligible costs, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Amounts which are not declared in the individual financial statement will not be taken into account by the Agency.

If an individual financial statement is not submitted for a reporting period, it may be included in the periodic financial report for the next reporting period.

Each beneficiary must **certify** that:

- the information provided is full, reliable and true;
- the costs declared are eligible (see Article 6);
- the costs can be substantiated by adequate records and supporting documentation (see Article 18) that will be produced upon request (see Article 17) or in the context of checks, reviews, audits and investigations (see Article 22);

(ii) not applicable;

(iii) not applicable;

(iv) a '**periodic summary financial statement**', created automatically by the electronic exchange system, consolidating the individual financial statements for the reporting period concerned and including — except for the last reporting period — the **request for interim payment**.

20.4 Final report — Request for payment of the balance

In addition to the periodic report for the last reporting period, the coordinator must submit the final report within 60 days following the end of the last reporting period.

The **final report** must include the following:

(a) a '**final technical report**' with a **summary** for publication containing:

(i) an overview of the results and their exploitation and dissemination;

(ii) the conclusions on the action, and

(iii) the socio-economic impact of the action;

(b) a '**final financial report**' containing a '**final summary financial statement**', created automatically by the electronic exchange system, consolidating the individual financial statements for all reporting periods and including the **request for payment of the balance**.

20.5 Information on cumulative expenditure incurred

Not applicable

20.6 Currency for financial statements

Financial statements must be drafted in euro.

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20.7 Language of reports

All reports (technical and financial reports, including financial statements) must be submitted in the language of the Agreement.

20.8 Consequences of non-compliance

If the reports submitted do not comply with this Article, the Agency may suspend the payment deadline (see Article 47) and apply any of the other measures described in Chapter 6.

If the coordinator breaches its obligation to submit the reports and if it fails to comply with this obligation within 30 days following a written reminder, the Agency may terminate the Agreement (see Article 50) or apply any of the other measures described in Chapter 6.

ARTICLE 21 — PAYMENTS AND PAYMENT ARRANGEMENTS

21.1 Payments to be made

The following payments will be made to the coordinator:

- one **pre-financing payment**;
- one or more **interim payments**, on the basis of the request(s) for interim payment (see Article 20), and
- one **payment of the balance**, on the basis of the request for payment of the balance (see Article 20).

21.2 Pre-financing payment — Amount — Amount retained for the Guarantee Fund

The aim of the pre-financing is to provide the beneficiaries with a float.

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

The amount of the pre-financing payment will be EUR **620,100.00** (six hundred and twenty thousand one hundred EURO).

The Agency will — except if Article 48 applies — make the pre-financing payment to the coordinator within 30 days, either from the entry into force of the Agreement (see Article 58) or from 10 days before the starting date of the action (see Article 3), whichever is the latest.

An amount of EUR **47,700.00** (forty seven thousand seven hundred EURO), corresponding to 5% of the maximum grant amount (see Article 5.1), is retained by the Agency from the pre-financing payment and transferred into the '**Guarantee Fund**'.

21.3 Interim payments — Amount — Calculation

Interim payments reimburse the eligible costs incurred for the implementation of the action during the corresponding reporting periods.

The Agency will pay to the coordinator the amount due as interim payment within 90 days from receiving the periodic report (see Article 20.3), except if Articles 47 or 48 apply.

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

The **amount due as interim payment** is calculated by the Agency in the following steps:

Step 1 – Application of the reimbursement rates

Step 2 – Limit to 90% of the maximum grant amount

21.3.1 Step 1 — Application of the reimbursement rates

The reimbursement rate(s) (see Article 5.2) are applied to the eligible costs (actual costs, unit costs and flat-rate costs ; see Article 6) declared by the beneficiaries (see Article 20) and approved by the Agency (see above) for the concerned reporting period.

21.3.2 Step 2 — Limit to 90% of the maximum grant amount

The total amount of pre-financing and interim payments must not exceed 90% of the maximum grant amount set out in Article 5.1. The maximum amount for the interim payment will be calculated as follows:

{90% of the maximum grant amount (see Article 5.1)

minus

{pre-financing and previous interim payments}}.

21.4 Payment of the balance — Amount — Calculation — Release of the amount retained for the Guarantee Fund

The payment of the balance reimburses the remaining part of the eligible costs incurred by the beneficiaries for the implementation of the action.

If the total amount of earlier payments is greater than the final grant amount (see Article 5.3), the payment of the balance takes the form of a recovery (see Article 44).

If the total amount of earlier payments is lower than the final grant amount, the Agency will pay the balance within 90 days from receiving the final report (see Article 20.4), except if Articles 47 or 48 apply.

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

The **amount due as the balance** is calculated by the Agency by deducting the total amount of pre-financing and interim payments (if any) already made, from the final grant amount determined in accordance with Article 5.3:

{final grant amount (see Article 5.3)

minus

{pre-financing and interim payments (if any) made}}.

At the payment of the balance, the amount retained for the Guarantee Fund (see above) will be released and:

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- if the balance is positive: the amount released will be paid in full to the coordinator together with the amount due as the balance;

- if the balance is negative (payment of the balance taking the form of recovery): it will be deducted from the amount released (see Article 44.1.2). If the resulting amount:

    - is positive, it will be paid to the coordinator

    - is negative, it will be recovered.

The amount to be paid may however be offset — without the beneficiaries' consent — against any other amount owed by a beneficiary to the Agency, the Commission or another executive agency (under the EU or Euratom budget), up to the maximum EU contribution indicated, for that beneficiary, in the estimated budget (see Annex 2).

21.5 Notification of amounts due

When making payments, the Agency will formally notify to the coordinator the amount due, specifying whether it concerns an interim payment or the payment of the balance.

For the payment of the balance, the notification will also specify the final grant amount.

In the case of reduction of the grant or recovery of undue amounts, the notification will be preceded by the contradictory procedure set out in Articles 43 and 44.

21.6 Currency for payments

The Agency will make all payments in euro.

21.7 Payments to the coordinator — Distribution to the beneficiaries

Payments will be made to the coordinator.

Payments to the coordinator will discharge the Agency from its payment obligation.

The coordinator must distribute the payments between the beneficiaries without unjustified delay.

Pre-financing may however be distributed only:

(a) if the minimum number of beneficiaries set out in the call for proposals has acceded to the Agreement (see Article 56) and

(b) to beneficiaries that have acceded to the Agreement (see Article 56).

21.8 Bank account for payments

All payments will be made to the following bank account:

Name of bank: DELEGATION UE SERBIA
Full name of the account holder: FACULTY OF BIOLOGY UNIVERSITY OF BELGRADE
Full account number (including bank codes): ()
IBAN code: RS3584000000004979041

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21.9 Costs of payment transfers

The cost of the payment transfers is borne as follows:

- the Agency 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.

21.10 Date of payment

Payments by the Agency are considered to have been carried out on the date when they are debited to its account.

21.11 Consequences of non-compliance

21.11.1 If the Agency 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 three and a half points. 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 upon 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).

Suspension of the payment deadline or payments (see Articles 47 and 48) will not be considered as late payment.

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.

21.11.2 If the coordinator breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or the participation of the coordinator may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 22 — CHECKS, REVIEWS, AUDITS AND INVESTIGATIONS — EXTENSION OF FINDINGS

22.1 Checks, reviews and audits by the Agency and the Commission

22.1.1 Right to carry out checks

The Agency or the Commission will — during the implementation of the action or afterwards — check

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the proper implementation of the action and compliance with the obligations under the Agreement, including assessing deliverables and reports.

For this purpose the Agency or the Commission may be assisted by external persons or bodies.

The Agency or the Commission may also request additional information in accordance with Article 17. The Agency or the Commission may request beneficiaries to provide such information to it directly.

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

22.1.2 Right to carry out reviews

The Agency or the Commission may — during the implementation of the action or afterwards — carry out reviews on the proper implementation of the action (including assessment of deliverables and reports), compliance with the obligations under the Agreement and continued scientific or technological relevance of the action.

Reviews may be started up to two years after the payment of the balance. They will be formally notified to the coordinator or beneficiary concerned and will be considered to have started on the date of the formal notification.

The Agency or the Commission may carry out reviews directly (using its own staff) or indirectly (using external persons or bodies appointed to do so). It will inform the coordinator or beneficiary concerned of the identity of the external persons or bodies. They have the right to object to the appointment on grounds of commercial confidentiality.

The coordinator or beneficiary concerned must 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 Agency or the Commission may request beneficiaries to provide such information to it directly.

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

For **on-the-spot** reviews, the beneficiaries must allow access to their sites and premises, including to external persons or bodies, 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 '**review report**' will be drawn up.

The Agency or the Commission will formally notify the review report to the coordinator or beneficiary concerned, which has 30 days to formally notify observations ('**contradictory review procedure**').

Reviews (including review reports) are in the language of the Agreement.

22.1.3 Right to carry out audits

The Agency or the Commission may — during the implementation of the action or afterwards — carry out audits on the proper implementation of the action and compliance with the obligations under the Agreement.

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Audits may be started up to two years after the payment of the balance. They will be formally notified to the coordinator or beneficiary concerned and will be considered to have started on the date of the formal notification.

The Agency or the Commission may carry out audits directly (using its own staff) or indirectly (using external persons or bodies appointed to do so). It will inform the coordinator or beneficiary concerned of the identity of the external persons or bodies. They have the right to object to the appointment on grounds of commercial confidentiality.

The coordinator or beneficiary concerned must provide — within the deadline requested — any information (including complete accounts, individual salary statements or other personal data) to verify compliance with the Agreement. The Agency or the Commission may request beneficiaries to provide such information to it directly.

For **on-the-spot** audits, the beneficiaries must allow access to their sites and premises, including to external persons or bodies, 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 Agency or the Commission will formally notify the draft audit report to the coordinator or beneficiary concerned, which has 30 days to formally notify observations ('**contradictory audit procedure**'). This period may be extended by the Agency or the Commission in justified cases.

The '**final audit report**' will take into account observations by the coordinator or beneficiary concerned. The report will be formally notified to it.

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

The Agency or the Commission may also access the beneficiaries' statutory records for the periodical assessment of unit costs or flat-rate amounts.

22.2 Investigations by the European Anti-Fraud Office (OLAF)

Under Regulations No 883/2013[5] and No 2185/96[6] (and in accordance with their provisions and procedures) the European Anti-Fraud Office (OLAF) may — at any moment during implementation of the action or afterwards — carry out investigations, including on-the-spot checks and inspections, to establish whether there has been fraud, corruption or any other illegal activity affecting the financial interests of the EU.

22.3 Checks and audits by the European Court of Auditors (ECA)

[5] 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).

[6] 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).

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Under Article 287 of the Treaty on the Functioning of the European Union (TFEU) and Article 161 of the Financial Regulation No 966/2012[8], the European Court of Auditors (ECA) may — at any moment during implementation of the action or afterwards — carry out audits.

The ECA has the right of access for the purpose of checks and audits.

22.4 Checks, reviews, audits and investigations for international organisations

Not applicable

22.5 Consequences of findings in checks, reviews, audits and investigations — Extension of findings

22.5.1 Findings in this grant

Findings in checks, reviews, audits or investigations carried out in the context of this grant may lead to the rejection of ineligible costs (see Article 42), reduction of the grant (see Article 43), recovery of undue amounts (see Article 44) or to any of the other measures described in Chapter 6.

Rejection of costs or reduction of the grant after the payment of the balance will lead to a revised final grant amount (see Article 5.4).

Findings in checks, reviews, audits or investigations may lead to a request for amendment for the modification of Annex 1 (see Article 55).

Checks, reviews, audits or investigations that find systemic or recurrent errors, irregularities, fraud or breach of obligations may also lead to consequences in other EU or Euratom grants awarded under similar conditions ('**extension of findings from this grant to other grants**').

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

22.5.2 Findings in other grants

The Agency or the Commission may extend findings from other grants to this grant ('**extension of findings from other grants to this grant**'), if:

(a) the beneficiary concerned is found, in other EU or Euratom 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 — no later than two years after the payment of the balance of this grant.

The extension of findings may lead to the rejection of costs (see Article 42), reduction of the grant (see Article 43), recovery of undue amounts (see Article 44), suspension of payments (see Article 48), suspension of the action implementation (see Article 49) or termination (see Article 50).

[8] Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council of 25 October 2012 on the financial rules applicable to the general budget of the Union and repealing Council Regulation (EC, Euratom) No 1605/2002 (OJ L 298, 26.10.2012, p. 1).

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22.5.3 Procedure

The Agency or the Commission will formally notify the beneficiary concerned the systemic or recurrent errors and its intention to extend these audit findings, together with the list of grants affected.

22.5.3.1 If the findings concern **eligibility of costs**: the formal 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 by the Agency or the Commission 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.

The beneficiary concerned has 90 days from receiving notification to submit observations, revised financial statements or to propose a duly substantiated **alternative correction method**. This period may be extended by the Agency or the Commission in justified cases.

The Agency or the Commission may then start a rejection procedure in accordance with Article 42, on the basis of:

- the revised financial statements, if approved;
- the proposed alternative correction method, if accepted

or

- the initially notified correction rate for extrapolation, if it does not receive any observations or revised financial statements, does not accept the observations or the proposed alternative correction method or does not approve the revised financial statements.

22.5.3.2 If the findings concern **substantial errors**, **irregularities or fraud** or **serious breach of obligations**: the formal notification will include:

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

(b) the flat-rate the Agency or the Commission intends to apply according to the principle of proportionality.

The beneficiary concerned has 90 days from receiving notification to submit observations or to propose a duly substantiated alternative flat-rate.

The Agency or the Commission may then start a reduction procedure in accordance with Article 43, on the basis of:

- the proposed alternative flat-rate, if accepted

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or

- the initially notified flat-rate, if it does not receive any observations or does not accept the observations or the proposed alternative flat-rate.

22.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, any insufficiently substantiated costs will be ineligible (see Article 6) and will be rejected (see Article 42).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 23 — EVALUATION OF THE IMPACT OF THE ACTION

23.1 Right to evaluate the impact of the action

The Agency or the Commission may carry out interim and final evaluations of the impact of the action measured against the objective of the EU programme.

Evaluations may be started during implementation of the action and up to five years after the payment of the balance. The evaluation is considered to start on the date of the formal notification to the coordinator or beneficiaries.

The Agency or the Commission may make these evaluations directly (using its own staff) or indirectly (using external bodies or persons it has authorised to do so).

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

23.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the Agency may apply the measures described in Chapter 6.

SECTION 3 RIGHTS AND OBLIGATIONS RELATED TO BACKGROUND AND RESULTS

SUBSECTION 1 GENERAL

ARTICLE 23a — MANAGEMENT OF INTELLECTUAL PROPERTY

23a.1 Obligation to take measures to implement the Commission Recommendation on the management of intellectual property in knowledge transfer activities

Beneficiaries that are universities or other public research organisations must take measures to implement the principles set out in Points 1 and 2 of the Code of Practice annexed to the Commission Recommendation on the management of intellectual property in knowledge transfer activities[8].

[8] Commission Recommendation C(2008) 1329 of 10.4.2008 on the management of intellectual property in knowledge

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This does not change the obligations set out in Subsections 2 and 3 of this Section.

The beneficiaries must ensure that the seconded staff members, partner organisations and entities with a capital or legal link are aware of them.

23a.2 Consequences of non-compliance

If a beneficiary breaches its obligations under this Article, the Agency may apply any of the measures described in Chapter 6.

SUBSECTION 2 RIGHTS AND OBLIGATIONS RELATED TO BACKGROUND

ARTICLE 24 — AGREEMENT ON BACKGROUND

24.1 Agreement on background

The beneficiaries must identify and agree (in writing) on the background for the action ('**agreement on background**').

'**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:

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

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

24.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 25 — ACCESS RIGHTS TO BACKGROUND

25.1 Exercise of access rights — Waiving of access rights — No sub-licensing

To exercise access rights, this must first be requested in writing ('**request for access**').

'**Access rights**' means rights to use results or background under the terms and conditions laid down in this Agreement.

Waivers of access rights are not valid unless in writing.

Unless agreed otherwise, access rights do not include the right to sub-license.

25.2 Access rights for other beneficiaries, for implementing their own tasks under the action

The beneficiaries must give each other access — on a royalty-free basis — to background needed to

transfer activities and the Code of Practice for universities and other public research institutions attached to this recommendation.

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implement their own tasks under the action, unless the beneficiary that holds the background has — before acceding to the Agreement —:

(a) informed the other beneficiaries that access to its background is subject to legal restrictions or limits, including those imposed by the rights of third parties (including personnel), or

(b) agreed with the other beneficiaries that access would not be on a royalty-free basis.

25.3 Access rights for other beneficiaries, for exploiting their own results

The beneficiaries must give each other access — under fair and reasonable conditions — to background needed for exploiting their own 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 legal restrictions or limits, including those imposed by the rights of third parties (including personnel).

'**Fair and reasonable conditions**' means 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.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

25.4 Access rights for affiliated entities

Unless otherwise agreed in the consortium agreement, access to background must also be given — under fair and reasonable conditions (see above; Article 25.3) and unless it is subject to legal restrictions or limits, including those imposed by the rights of third parties (including personnel) — to affiliated entities[9] established in an EU Member State or '**associated country**'[10], if this is needed to exploit the results generated by the beneficiaries to which they are affiliated.

Unless agreed otherwise (see above; Article 25.1), the affiliated entity concerned must make the request directly to the beneficiary that holds the background.

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[9] For the definition see Article 2.1(2) Rules for Participation Regulation No 1290/2013: '**affiliated entity**' means any legal entity that is:
- under the direct or indirect control of a participant, or
- under the same direct or indirect control as the participant, or
- directly or indirectly controlling a participant.

'Control' may take any of the following forms:
(a) the direct or indirect holding of more than 50% of the nominal value of the issued share capital in the legal entity concerned, or of a majority of the voting rights of the shareholders or associates of that entity;
(b) the direct or indirect holding, in fact or in law, of decision-making powers in the legal entity concerned.

However the following relationships between legal entities shall not in themselves be deemed to constitute controlling relationships:
(a) the same public investment corporation, institutional investor or venture-capital company has a direct or indirect holding of more than 50% of the nominal value of the issued share capital or a majority of voting rights of the shareholders or associates;
(b) the legal entities concerned are owned or supervised by the same public body.

[10] For the definition, see Article 2.1(3) of the Rules for Participation Regulation No 1290/2013: '**associated country**' means a non EU-country (third country) which is party to an international agreement with the Union, as identified in Article 7 of the H2020 Framework Programme Regulation No 1291/2013. Article 7 sets out the conditions for association of non-EU countries to Horizon 2020.

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Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

25.5 Access rights for seconded staff members

The beneficiaries must — on a royalty-free basis — give access to the seconded staff members to background necessary for their research and innovation activities under the action.

25.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

SUBSECTION 3 RIGHTS AND OBLIGATIONS RELATED TO RESULTS

ARTICLE 26 — OWNERSHIP OF RESULTS

26.1 Ownership by the beneficiary that generates the results

Results are owned by the beneficiary that generates them.

'**Results**' means any (tangible or intangible) output of the action such as data, knowledge or information — whatever its form or nature, whether it can be protected or not — that is generated in the action, as well as any rights attached to it, including intellectual property rights.

26.2 Joint ownership by several beneficiaries

Two or more beneficiaries own results jointly if:

(a) they have jointly generated them and

(b) it is not possible to:

(i) establish the respective contribution of each beneficiary, or

(ii) separate them for the purpose of applying for, obtaining or maintaining their protection (see Article 27).

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, each joint owner may grant non-exclusive licences to third parties to exploit jointly-owned results (without any right to sub-license), if the other joint owners are given:

(a) at least 45 days advance notice and

(b) fair and reasonable compensation.

Once the results have been generated, joint owners may agree (in writing) to apply another regime

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than joint ownership (such as, for instance, transfer to a single owner (see Article 30) with access rights for the others).

26.3 Rights of third parties (including personnel)

If third parties (including personnel) may claim rights to the results, the beneficiary concerned must ensure that it complies with its obligations under the Agreement.

If a third party generates results, the beneficiary concerned must obtain all necessary rights (transfer, licences or other) from the third party, in order to be able to respect its obligations as if those results were generated by the beneficiary itself.

If obtaining the rights is impossible, the beneficiary must refrain from using the third party to generate the results.

26.4 Agency ownership, to protect results

26.4.1 The Agency may — with the consent of the beneficiary concerned — assume ownership of results to protect them, if a beneficiary intends — up to four years after the period set out in Article 3 — to disseminate its results without protecting them, except in any of the following cases:

(a) the lack of protection is because protecting the results is not possible, reasonable or justified (given the circumstances);

(b) the lack of protection is because there is a lack of potential for commercial or industrial exploitation, or

(c) the beneficiary intends to transfer the results to another beneficiary or third party established in an EU Member State or associated country, which will protect them.

Before the results are disseminated and unless any of the cases above under Points (a), (b) or (c) applies, the beneficiary must formally notify the Agency and at the same time inform it of any reasons for refusing consent. The beneficiary may refuse consent only if it can show that its legitimate interests would suffer significant harm.

If the Agency decides to assume ownership, it will formally notify the beneficiary concerned within 45 days of receiving notification.

No dissemination relating to these results may take place before the end of this period or, if the Agency takes a positive decision, until it has taken the necessary steps to protect the results.

26.4.2 The Agency may — with the consent of the beneficiary concerned — assume ownership of results to protect them, if a beneficiary intends — up to four years after the period set out in Article 3 — to stop protecting them or not to seek an extension of protection, except in any of the following cases:

(a) the protection is stopped because of a lack of potential for commercial or industrial exploitation;

(b) an extension would not be justified given the circumstances.

A beneficiary that intends to stop protecting results or not seek an extension must — unless any of the cases above under Points (a) or (b) applies — formally notify the Agency at least 60 days before the protection lapses or its extension is no longer possible and at the same time inform it of any reasons for

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refusing consent. The beneficiary may refuse consent only if it can show that its legitimate interests would suffer significant harm.

If the Agency decides to assume ownership, it will formally notify the beneficiary concerned within 45 days of receiving notification.

26.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to the any of the other measures described in Chapter 6.

ARTICLE 27 — PROTECTION OF RESULTS — VISIBILITY OF EU FUNDING

27.1 Obligation to protect the results

Each beneficiary must examine the possibility of protecting its results and must adequately protect them — for an appropriate period and with appropriate territorial coverage — if:

(a) the results can reasonably be expected to be commercially or industrially exploited and

(b) protecting them is possible, reasonable and justified (given the circumstances).

When deciding on protection, the beneficiary must consider its own legitimate interests and the legitimate interests (especially commercial) of the other beneficiaries.

27.2 Agency ownership, to protect the results

If a beneficiary intends not to protect its results, to stop protecting them or not seek an extension of protection, the Agency may — under certain conditions (see Article 26.4) — assume ownership to ensure their (continued) protection.

27.3 Information on EU funding

Applications for protection of results (including patent applications) filed by or on behalf of a beneficiary must — unless the Agency requests or agrees otherwise or unless it is impossible — include the following:

> *"The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 778405".*

27.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 28 — EXPLOITATION OF RESULTS

28.1 Obligation to exploit the results

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Each beneficiary must — up to four years after the period set out in Article 3 — take measures aiming to ensure '**exploitation**' of its results (either directly or indirectly, in particular through transfer or licensing; see Article 30) by:

(a) using them in further research activities (outside the action);

(b) developing, creating or marketing a product or process;

(c) creating and providing a service, or

(d) using them in standardisation activities.

This does not change the security obligations in Article 37, which still apply.

28.2 Results that could contribute to European or international standards — Information on EU funding

If results are incorporated in a standard, the beneficiary concerned must — unless the Agency requests or agrees otherwise or unless it is impossible — ask the standardisation body to include the following statement in (information related to) the standard:

> *"Results incorporated in this standard received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 778405".*

28.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced in accordance with Article 43.

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 29 — DISSEMINATION OF RESULTS — OPEN ACCESS — VISIBILITY OF EU FUNDING

29.1 Obligation to disseminate results

Unless it goes against their legitimate interests, each beneficiary must — as soon as possible — '**disseminate**' its results by disclosing them to the public by appropriate means (other than those resulting from protecting or exploiting the results), including in scientific publications (in any medium).

This does not change the obligation to protect results in Article 27, the confidentiality obligations in Article 36, the security obligations in Article 37 or the obligations to protect personal data in Article 39, all of which still apply.

A beneficiary that intends to disseminate its results must give advance notice to the other beneficiaries of — unless agreed otherwise — at least 45 days, together with sufficient information on the results it will disseminate.

Any other beneficiary may object within — unless agreed otherwise — 30 days of receiving notification, if it can show that its legitimate interests in relation to the results or background would

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be significantly harmed. In such cases, the dissemination may not take place unless appropriate steps are taken to safeguard these legitimate interests.

If a beneficiary intends not to protect its results, it may — under certain conditions (see Article 26.4.1) — need to formally notify the Agency before dissemination takes place.

29.2 Open access to scientific publications

Each beneficiary must ensure open access (free of charge online access for any user) to all peer-reviewed scientific publications relating to its results.

In particular, it must:

(a) as soon as possible and at the latest on publication, deposit a machine-readable electronic copy of the published version or final peer-reviewed manuscript accepted for publication in a repository for scientific publications;

Moreover, the beneficiary must aim to deposit at the same time the research data needed to validate the results presented in the deposited scientific publications.

(b) ensure open access to the deposited publication — via the repository — at the latest:

(i) on publication, if an electronic version is available for free via the publisher, or

(ii) within six months of publication (twelve months for publications in the social sciences and humanities) in any other case.

(c) ensure open access — via the repository — to the bibliographic metadata that identify the deposited publication.

The bibliographic metadata must be in a standard format and must include all of the following:

- the terms *"Marie Skłodowska-Curie Actions"*;
- the name of the action, acronym and grant number;
- the publication date, and length of embargo period if applicable, and
- a persistent identifier.

29.3 Open access to research data

Not applicable

29.4 Information on EU funding — Obligation and right to use the EU emblem

Unless the Agency requests or agrees otherwise or unless it is impossible, any dissemination of results (in any form, including electronic) must:

(a) display the EU emblem and

(b) include the following text:

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"This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 778405".

When displayed together with another logo, the EU emblem must have appropriate prominence.

For the purposes of their obligations under this Article, the beneficiaries may use the EU emblem without first obtaining approval from the Agency.

This does not however give them the right to exclusive use.

Moreover, they may not appropriate the EU emblem or any similar trademark or logo, either by registration or by any other means.

29.5 Disclaimer excluding Agency responsibility

Any dissemination of results must indicate that it reflects only the author's view and that the Agency is not responsible for any use that may be made of the information it contains.

29.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 30 — TRANSFER AND LICENSING OF RESULTS

30.1 Transfer of ownership

Each beneficiary may transfer ownership of its results.

It must however ensure that its obligations under Articles 26.2, 26.4, 27, 28, 29, 30 and 31 also apply to the new owner and that this owner has the obligation to pass them on in any subsequent transfer.

This does not change the security obligations in Article 37, which still apply.

Unless agreed otherwise (in writing) for specifically-identified third parties or unless impossible under applicable EU and national laws on mergers and acquisitions, a beneficiary that intends to transfer ownership of results must give at least 45 days advance notice (or less if agreed in writing) to the other beneficiaries that still have (or still may request) access rights to the results. This notification must include sufficient information on the new owner to enable any beneficiary concerned to assess the effects on its access rights.

Unless agreed otherwise (in writing) for specifically-identified third parties, any other beneficiary may object within 30 days of receiving notification (or less if agreed in writing), if it can show that the transfer would adversely affect its access rights. In this case, the transfer may not take place until agreement has been reached between the beneficiaries concerned.

30.2 Granting licenses

Each beneficiary may grant licences to its results (or otherwise give the right to exploit them), if:

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(a) this does not impede the access rights under Article 31

(b) not applicable.

In addition to Points (a) and (b), exclusive licences for results may be granted only if all the other beneficiaries concerned have waived their access rights (see Article 31.1).

This does not change the dissemination obligations in Article 29 or security obligations in Article 37, which still apply.

30.3 Agency right to object to transfers or licensing

Not applicable

30.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 31 — ACCESS RIGHTS TO RESULTS

31.1 Exercise of access rights — Waiving of access rights — No sub-licensing

The conditions set out in Article 25.1 apply.

The obligations set out in this Article do not change the security obligations in Article 37, which still apply.

31.2 Access rights for other beneficiaries, for implementing their own tasks under the action

The beneficiaries must give each other access — on a royalty-free basis — to results needed for implementing their own tasks under the action.

31.3 Access rights for other beneficiaries, for exploiting their own results

The beneficiaries must give each other — under fair and reasonable conditions (see Article 25.3) — access to results needed for exploiting their own results.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

31.4 Access rights of affiliated entities

Unless agreed otherwise in the consortium agreement, access to results must also be given — under fair and reasonable conditions (Article 25.3) — to affiliated entities established in an EU Member State or associated country, if this is needed for those entities to exploit the results generated by the beneficiaries to which they are affiliated.

Unless agreed otherwise (see above; Article 31.1), the affiliated entity concerned must make any such request directly to the beneficiary that owns the results.

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Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

31.5 Access rights for the EU institutions, bodies, offices or agencies and EU Member States

The beneficiaries must give access to their results — on a royalty-free basis — to EU institutions, bodies, offices or agencies, for developing, implementing or monitoring EU policies or programmes.

Such access rights are limited to non-commercial and non-competitive use.

This does not change the right to use any material, document or information received from the beneficiaries for communication and publicising activities (see Article 38.2).

31.6 Access rights for seconded staff members

The beneficiaries must — on a royalty-free basis — give access to the seconded staff members to results necessary for their research and innovation activities under the action.

31.7 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

SECTION 4 OTHER RIGHTS AND OBLIGATIONS

ARTICLE 32 — RECRUITMENT AND WORKING CONDITIONS FOR SECONDED STAFF MEMBERS

32.1 Obligations towards seconded staff members

The beneficiaries must respect the following recruitment and working conditions for the seconded staff member under the action:

(a) 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[11] and ensure that the seconded staff members are aware of them;

(b) ensure that the rights and obligations of the seconded staff members remain unchanged during the secondment;

(c) ensure that seconded staff members are reintegrated after the secondment;

(d) ensure that the seconded staff members enjoy at the place of the implementation at least the same standards and working conditions as those applicable to local persons holding a similar position;

[11] Commission Recommendation No 251/2005/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).

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(e) ensure that the seconded staff members are covered by an adequate medical insurance scheme;

(f) ensure that the staff members are seconded full-time;

(g) ensure that the seconded staff members have the relevant expertise for the action;

(h) inform the seconded staff members about:

- the description, conditions, location and the timetable for the implementation of the secondment under the action;
- the rights and obligations of the beneficiary toward the seconded staff members under this Agreement;
- the obligation of the seconded staff members to complete and submit — at the end of the secondment — the evaluation questionnaire and — two years later — the follow-up questionnaire provided by the Agency;
- the arrangements related to the intellectual property rights between the beneficiary and the seconded staff members — during implementation of the secondment and afterwards;
- the obligation of the seconded staff members to maintain confidentiality (see Article 36);
- the obligation of the seconded staff members to ensure the visibility of EU funding in communications or publications and in applications for the protection of results (see Articles 27, 28, 29 and 38);

(i) assist the seconded staff members in the administrative procedures related to their secondment;

(j) use the costs of seconded staff members (see Article 6) to contribute to their subsistence and mobility.

The beneficiaries must ensure that researchers and third parties involved in the action are aware of them.

32.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 33 — GENDER EQUALITY

33.1 Obligation to aim for gender equality

The beneficiaries must take all measures to promote equal opportunities between men and women in the implementation of the action. 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.

33.2 Consequences of non-compliance

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If a beneficiary breaches its obligations under this Article, the Agency may apply any of the measures described in Chapter 6.

ARTICLE 34 — ETHICS AND RESEARCH INTEGRITY

34.1 Obligation to comply with ethical and research integrity principles

The beneficiaries must carry out the action in compliance with:

(a) ethical principles (including the highest standards of research integrity)

and

(b) applicable international, EU and national law.

Funding will not be granted for activities carried out outside the EU if they are prohibited in all Member States or for activities which destroy human embryos (for example, for obtaining stem cells).

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:

(a) aim at human cloning for reproductive purposes;

(b) intend to modify the genetic heritage of human beings which could make such changes heritable (with the exception of research relating to cancer treatment of the gonads, which may be financed), or

(c) 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.

The beneficiaries must respect the highest standards of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity[12].

This implies notably compliance with the following essential principles:

- honesty;
- reliability;
- objectivity;
- impartiality;
- open communication;
- duty of care;

[12] The European Code of Conduct for Research Integrity of ALLEA (All European Academies) and ESF (European Science Foundation) of March 2011.
http://ec.europa.eu/research/participants/data/ref/h2020/other/hi/h2020-ethics_code-of-conduct_en.pdf

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- fairness and
- responsibility for future science generations.

This means that beneficiaries must ensure that persons carrying out research tasks:

- present their research goals and intentions in an honest and transparent manner;
- design their research carefully and conduct it in a reliable fashion, taking its impact on society into account;
- use techniques and methodologies (including for data collection and management) that are appropriate for the field(s) concerned;
- exercise due care for the subjects of research — be they human beings, animals, the environment or cultural objects;
- ensure objectivity, accuracy and impartiality when disseminating the results;
- allow — as much as possible and taking into account the legitimate interest of the beneficiaries — access to research data, in order to enable research to be reproduced;
- make the necessary references to their work and that of other researchers;
- refrain from practicing any form of plagiarism, data falsification or fabrication;
- avoid double funding, conflicts of interest and misrepresentation of credentials or other research misconduct.

34.2 Activities raising ethical issues

Activities raising ethical issues must comply with the '**ethics requirements**' set out as deliverables in Annex 1.

Before the beginning of an activity raising an ethical issue, each beneficiary must have obtained:

(a) any ethics committee opinion required under national law and

(b) any notification or authorisation for activities raising ethical issues required under national and/or European law

needed for implementing the action tasks in question.

The documents must be kept on file and be submitted upon request by the coordinator to the Agency (see Article 52). If they are not in English, they must be submitted together with an English summary, which shows that the action tasks in question are covered and includes the conclusions of the committee or authority concerned (if available).

34.3 Activities involving human embryos or human embryonic stem cells

Activities involving research on human embryos or human embryonic stem cells may be carried out, in addition to Article 34.1, only if:

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- they are set out in Annex 1 or
- the coordinator has obtained explicit approval (in writing) from the Agency (see Article 52).

34.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or participation of the beneficiary may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 35 — CONFLICT OF INTERESTS

35.1 Obligation to avoid a conflict of interests

The beneficiaries must take all measures to prevent any situation where the impartial and objective implementation of the action is compromised for reasons involving economic interest, political or national affinity, family or emotional ties or any other shared interest ('**conflict of interests**').

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

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

35.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or participation of the beneficiary may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 36 — CONFIDENTIALITY

36.1 General obligation to maintain confidentiality

During implementation of the action and for four years after the period set out in Article 3, the parties must keep confidential any data, documents or other material (in any form) that is identified as confidential at the time it is disclosed ('**confidential information**').

If a beneficiary requests, the Agency may agree to keep such information confidential for an additional period beyond the initial four years.

If information has been identified as confidential only orally, it will be considered to be confidential only if this is confirmed in writing within 15 days of the oral disclosure.

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

The beneficiaries may disclose confidential information to their personnel, partner organisations or entities with a capital or legal link only if they:

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(a) need to know to implement the Agreement and

(b) are bound by an obligation of confidentiality.

This does not change the security obligations in Article 37, which still apply.

The Agency may disclose confidential information to its staff, other EU institutions and bodies. It may disclose confidential information to third parties, if:

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

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

Under the conditions set out in Article 4 of the Rules for Participation Regulation No 1290/2013[13], the Commission must moreover make available information on the results to other EU institutions, bodies, offices or agencies as well as Member States or associated countries.

The confidentiality obligations no longer apply if:

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

(b) the information was already known by the recipient or is given to him without obligation of confidentiality by a third party that was not bound by any obligation of confidentiality;

(c) the recipient proves that the information was developed without the use of confidential information;

(d) the information becomes generally and publicly available, without breaching any confidentiality obligation, or

(e) the disclosure of the information is required by EU or national law.

36.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 37 — SECURITY-RELATED OBLIGATIONS

37.1 Results with a security recommendation

Not applicable

37.2 Classified information

Not applicable

[13] Regulation (EU) No 1290/2013 of the European Parliament and of the Council of 11 December 2013 laying down the rules for participation and dissemination in "Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)" (OJ L 347, 20.12.2013 p.81).

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37.3 Activities involving dual-use goods or dangerous materials and substances

Not applicable

37.4 Consequences of non-compliance

Not applicable

ARTICLE 38 — PROMOTING THE ACTION — VISIBILITY OF EU FUNDING

38.1 Communication activities by beneficiaries

38.1.1 Obligation to promote the action and its results

The beneficiaries must promote the action and its results, by providing targeted information to multiple audiences (including the media and the public) in a strategic and effective manner.

This does not change the dissemination obligations in Article 29, the confidentiality obligations in Article 36 or the security obligations in Article 37, all of which still apply.

Before engaging in a communication activity expected to have a mainstream media coverage the beneficiaries must inform the Agency (see Article 52).

38.1.2 Information on EU funding — Obligation and right to use the EU emblem

Unless the Agency requests or agrees otherwise or unless it is impossible, any communication activity related to the action (including in electronic form, via social media, etc.) and any infrastructure, equipment and major results funded by the grant must:

(a) display the EU emblem and

(b) include the following text:

For communication activities: *"This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 778405".*

For infrastructure, equipment and major results: *"This [infrastructure][equipment][insert type of result] is part of a project that has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 778405".*

When displayed together with another logo, the EU emblem must have appropriate prominence.

For the purposes of their obligations under this Article, the beneficiaries may use the EU emblem without first obtaining approval from the Agency.

This does not, however, give them the right to exclusive use.

Moreover, they may not appropriate the EU emblem or any similar trademark or logo, either by registration or by any other means.

38.1.3 Disclaimer excluding Agency and Commission responsibility

Any communication activity related to the action must indicate that it reflects only the author's view

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and that the Agency and the Commission are not responsible for any use that may be made of the information it contains.

38.2 Communication activities by the Agency and the Commission

38.2.1 Right to use beneficiaries' materials, documents or information

The Agency and the Commission may use, for its communication and publicising activities, information relating to the action, documents notably summaries for publication and public deliverables as well as any other material, such as pictures or audio-visual material received from any beneficiary (including in electronic form).

This does not change the confidentiality obligations in Article 36 and the security obligations in Article 37, all of which still apply.

If the Agency's or the Commission's use of these materials, documents or information would risk compromising legitimate interests, the beneficiary concerned may request the Agency or the Commission not to use it (see Article 52).

The right to use a beneficiary's materials, documents and information includes:

(a) **use for its own purposes** (in particular, making them available to persons working for the Agency, the Commission or any other EU institution, body, office or agency or body or institutions in EU Member States; and copying or reproducing them in whole or in part, in unlimited numbers);

(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** for communication and publicising activities (including shortening, summarising, inserting other elements (such as 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) giving **access in response to individual requests** under Regulation No 1049/2001[15], without the right to reproduce or exploit;

(f) **storage** in paper, electronic or other form;

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

(h) the right to authorise **third parties** to act on its behalf or sub-license the modes of use set out in Points (b), (c), (d) and (f) to third parties if needed for the communication and publicising activities of the Agency or the Commission.

[15] Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents, OJ L 145, 31.5.2001, p. 43.

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If the right of use is subject to rights of a third party (including personnel of the beneficiary), the beneficiary must ensure that it complies with its obligations under this Agreement (in particular, by obtaining the necessary approval from the third parties concerned).

Where applicable (and if provided by the beneficiaries), the Agency or the Commission will insert the following information:

> "© – [year] – [name of the copyright owner]. All rights reserved. Licensed to the Research Executive Agency (REA) and the European Union (EU) under conditions."

38.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 39 — PROCESSING OF PERSONAL DATA

39.1 Processing of personal data by the Agency and the Commission

Any personal data under the Agreement will be processed by the Agency or the Commission under Regulation No 45/2001[16] and according to the 'notifications of the processing operations' to the Data Protection Officer (DPO) of the Agency or the Commission (publicly accessible in the DPO register).

Such data will be processed by the '**data controller**' of the Agency or the Commission for the purposes of implementing, managing and monitoring the Agreement or protecting the financial interests of the EU or Euratom (including checks, reviews, audits and investigations; see Article 22).

The persons whose personal data are processed have the right to access and correct their own personal data. For this purpose, they must send any queries about the processing of their personal data to the data controller, via the contact point indicated in the privacy statement(s) that are published on the Agency and the Commission websites.

They also have the right to have recourse at any time to the European Data Protection Supervisor (EDPS).

39.2 Processing of personal data by the beneficiaries

The beneficiaries must process personal data under the Agreement in compliance with applicable EU and national law on data protection (including authorisations or notification requirements).

The beneficiaries may grant their personnel access only to data that is strictly necessary for implementing, managing and monitoring the Agreement.

The beneficiaries must inform the personnel whose personal data are collected and processed by the Agency or the Commission. For this purpose, they must provide them with the privacy statement(s) (see above), before transmitting their data to the Agency or the Commission.

[16] Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data (OJ L 8, 12.01.2001, p. 1).

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39.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under Article 39.2, the Agency may apply any of the measures described in Chapter 6.

ARTICLE 40 — ASSIGNMENTS OF CLAIMS FOR PAYMENT AGAINST THE AGENCY

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

If the Agency has not accepted the assignment or 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 Agency.

CHAPTER 5 DIVISION OF BENEFICIARIES' ROLES AND RESPONSIBILITIES — RELATIONSHIP WITH COMPLEMENTARY BENEFICIARIES — RELATIONSHIP WITH PARTNERS OF A JOINT ACTION

ARTICLE 41 — DIVISION OF BENEFICIARIES' ROLES AND RESPONSIBILITIES — RELATIONSHIP WITH COMPLEMENTARY BENEFICIARIES — RELATIONSHIP WITH PARTNERS OF A JOINT ACTION

41.1 Roles and responsibility towards the Agency

The beneficiaries have full responsibility for implementing the action and complying with the Agreement.

The beneficiaries are jointly and severally liable for the **technical implementation** of the action as described in Annex 1. If a beneficiary fails to implement its part of the action, the other beneficiaries become responsible for implementing this part (without being entitled to any additional EU funding for doing so), unless the Agency expressly relieves them of this obligation.

The **financial responsibility** of each beneficiary is governed by Articles 44, 45 and 46.

41.2 Internal division of roles and responsibilities

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

(a) Each **beneficiary** must:

(i) keep information stored in the Participant Portal Beneficiary Register (via the electronic exchange system) up to date (see Article 17);

(ii) inform the coordinator immediately of any events or circumstances likely to affect significantly or delay the implementation of the action (see Article 17);

(iii) submit to the coordinator in good time:

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- individual financial statements for itself and, if required, certificates on the financial statements (see Article 20);

- the data needed to draw up the technical reports (see Article 20);

- ethics committee opinions and notifications or authorisations for activities raising ethical issues (see Article 34);

- any other documents or information required by the Agency or the Commission under the Agreement, unless the Agreement requires the beneficiary to submit this information directly to the Agency or the Commission.

(b) The **coordinator** must:

(i) monitor that the action is implemented properly (see Article 7);

(ii) act as the intermediary for all communications between the beneficiaries and the Agency (in particular, providing the Agency with the information described in Article 17), unless the Agreement specifies otherwise;

(iii) request and review any documents or information required by the Agency and verify their completeness and correctness before passing them on to the Agency;

(iv) submit the deliverables and reports to the Agency (see Articles 19 and 20);

(v) ensure that all payments are made to the other beneficiaries without unjustified delay (see Article 21);

(vi) inform the Agency of the amounts paid to each beneficiary, when required under the Agreement (see Articles 44 and 50) or requested by the Agency.

The coordinator may not delegate or subcontract the above-mentioned tasks to any other beneficiary or third party (including partner organisations and entities with a capital or legal link).

41.3 Internal arrangements between beneficiaries — Consortium agreement

The beneficiaries must have internal arrangements regarding their operation and co-ordination to ensure that the action is implemented properly. These internal arrangements must be set out in a written '**consortium agreement**' between the beneficiaries, which may cover:

- internal organisation of the consortium;

- management of access to the electronic exchange system;

- distribution of EU funding;

- additional rules on rights and obligations related to background and results (including whether access rights remain or not, if a beneficiary is in breach of its obligations) (see Section 3 of Chapter 4);

- settlement of internal disputes;

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- liability, indemnification and confidentiality arrangements between the beneficiaries.

The consortium agreement must not contain any provision contrary to the Agreement.

41.4 Relationship with complementary beneficiaries — Collaboration agreement

Not applicable

41.5 Relationship with partners of a joint action — Coordination agreement

Not applicable

CHAPTER 6 REJECTION OF COSTS — REDUCTION OF THE GRANT — RECOVERY — SANCTIONS — DAMAGES — SUSPENSION — TERMINATION — FORCE MAJEURE

SECTION 1 REJECTION OF COSTS — REDUCTION OF THE GRANT — RECOVERY — SANCTIONS

ARTICLE 42 — REJECTION OF INELIGIBLE COSTS

42.1 Conditions

The Agency will — after **termination of the participation of a beneficiary**, at the time of an **interim payment**, **at the payment of the balance** or **afterwards** — reject any costs which are ineligible (see Article 6), in particular following checks, reviews, audits or investigations (see Article 22).

The rejection may also be based on the **extension of findings from other grants to this grant** (see Article 22.5.2).

42.2 Ineligible costs to be rejected — Calculation — Procedure

Ineligible costs will be rejected in full.

If the rejection of costs does not lead to a recovery (see Article 44), the Agency will formally notify the coordinator or beneficiary concerned of the rejection of costs, the amounts and the reasons why (if applicable, together with the notification of amounts due; see Article 21.5). The coordinator or beneficiary concerned may — within 30 days of receiving notification — formally notify the Agency of its disagreement and the reasons why.

If the rejection of costs leads to a recovery, the Agency will follow the contradictory procedure with pre-information letter set out in Article 44.

42.3 Effects

If the Agency rejects costs at the time of an **interim payment** or **the payment of the balance**, it will deduct them from the total eligible costs declared, for the action, in the periodic or final summary financial statement (see Articles 20.3 and 20.4). It will then calculate the interim payment or payment of the balance as set out in Articles 21.3 or 21.4.

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If the Agency rejects costs **after termination of the participation of a beneficiary**, it will deduct them from the costs declared by the beneficiary in the termination report and include the rejection in the calculation after termination (see Article 50.2 and 50.3).

If the Agency — **after an interim payment but before the payment of the balance** — rejects costs declared in a periodic summary financial statement, it will deduct them from the total eligible costs declared, for the action, in the next periodic summary financial statement or in the final summary financial statement. It will then calculate the interim payment or payment of the balance as set out in Articles 21.3 or 21.4.

If the Agency rejects costs **after the payment of the balance**, it will deduct the amount rejected from the total eligible costs declared, by the beneficiary, in the final summary financial statement. It will then calculate the revised final grant amount as set out in Article 5.4.

ARTICLE 43 — REDUCTION OF THE GRANT

43.1 Conditions

The Agency may — **after termination of the participation of a beneficiary**, **at the payment of the balance** or **afterwards** — reduce the grant, if :

(a) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under the Agreement or during the award procedure (including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles) or

(b) a beneficiary (or a natural person who has the power to represent or take decision on its behalf) has committed — in other EU or Euratom 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 22.5.2).

43.2 Amount to be reduced — Calculation — Procedure

The amount of the reduction will be proportionate to the seriousness of the errors, irregularities or fraud or breach of obligations.

Before reduction of the grant, the Agency will formally notify a '**pre-information letter**' to the coordinator or beneficiary concerned:

- informing it of its intention to reduce the grant, the amount it intends to reduce and the reasons why and

- inviting it to submit observations within 30 days of receiving notification

If the Agency does not receive any observations or decides to pursue reduction despite the observations it has received, it will formally notify **confirmation** of the reduction (if applicable, together with the notification of amounts due; see Article 21).

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43.3 Effects

If the Agency reduces the grant **after termination of the participation of a beneficiary**, it will calculate the reduced grant amount for that beneficiary and then determine the amount due to that beneficiary (see Article 50.2 and 50.3).

If the Agency reduces the grant at the time of **the payment of the balance**, it will calculate the reduced grant amount for the action and then determine the amount due as payment of the balance (see Articles 5.3.4 and 21.4).

If the Agency reduces the grant **after the payment of the balance**, it will calculate the revised final grant amount for the beneficiary concerned (see Article 5.4). If the revised final grant amount for the beneficiary concerned is lower than its share of the final grant amount, the Agency will recover the difference (see Article 44).

ARTICLE 44 — RECOVERY OF UNDUE AMOUNTS

44.1 Amount to be recovered — Calculation — Procedure

The Agency will — after **termination of the participation of a beneficiary, at the payment of the balance** or **afterwards** — claim back any amount that was paid, but is not due under the Agreement.

Each beneficiary's financial responsibility in case of recovery is limited to its own debt, except for the amount retained for the Guarantee Fund (see Article 21.4).

44.1.1 Recovery after termination of a beneficiary's participation

If recovery takes place after termination of a beneficiary's participation (including the coordinator), the Agency will claim back the undue amount from the beneficiary concerned, by formally notifying it a debit note (see Article 50.2 and 50.3). This note will specify the amount to be recovered, the terms and the date for payment.

If payment is not made by the date specified in the debit note, the Agency or the Commission will **recover** the amount:

(a) by '**offsetting**' it — without the beneficiary's consent — against any amounts owed to the beneficiary concerned by the Agency, the Commission or another executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU's financial interests, the Agency may offset before the payment date specified in the debit note;

(b) not applicable;

(c) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial regulation No 966/2012.

If payment is not made by the date specified in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the payment date in the debit note, up to and including the date the Agency or the Commission receives full payment of the amount.

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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 2007/64/EC[17] applies.

44.1.2 Recovery at payment of the balance

If the payment of the balance takes the form of a recovery (see Article 21.4), the Agency will formally notify a '**pre-information letter**' to the coordinator:

- informing it of its intention to recover, the amount due as the balance and the reasons why;
- specifying that it intends to deduct the amount to be recovered from the amount retained for the Guarantee Fund;
- requesting the coordinator to submit a report on the distribution of payments to the beneficiaries within 30 days of receiving notification, and
- inviting the coordinator to submit observations within 30 days of receiving notification.

If no observations are submitted or the Agency decides to pursue recovery despite the observations it has received, it will **confirm recovery** (together with the notification of amounts due; see Article 21.5) and:

- pay the difference between the amount to be recovered and the amount retained for the Guarantee Fund, **if the difference is positive** or
- formally notify to the coordinator a **debit note** for the difference between the amount to be recovered and the amount retained for the Guarantee Fund, **if the difference is negative**. This note will also specify the terms and the date for payment.

If the coordinator does not repay the Agency by the date in the debit note and has not submitted the report on the distribution of payments: the Agency or the Commission will **recover** the amount set out in the debit note from the coordinator (see below).

If the coordinator does not repay the Agency by the date in the debit note, but has submitted the report on the distribution of payments: the Agency will:

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

{{{{beneficiary's costs declared in the final summary financial statement and approved by the Agency multiplied by the reimbursement rate set out in Article 5.2 for the beneficiary concerned}

divided by

the EU contribution for the action calculated according to Article 5.3.1}

multiplied by

[17] Directive 2007/64/EC of the European Parliament and of the Council of 13 November 2007 on payment services in the internal market amending Directives 97/7/EC, 2002/65/EC, 2005/60/EC and 2006/48/EC and repealing Directive 97/5/EC (OJ L 319, 05.12.2007, p. 1).

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the final grant amount (see Article 5.3)}**,**

minus

{pre-financing and interim payments received by the beneficiary}**}**.

(b) formally notify to each beneficiary identified according to point (a) a **debit note** specifying the terms and date for payment. The amount of the debit note is calculated as follows:

{{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 set out in the debit note formally notified to the coordinator}.

If payment is not made by the date specified in the debit note, the Agency will **recover** the amount:

(a) by '**offsetting**' it — without the beneficiary's consent — against any amounts owed to the beneficiary concerned by the Agency, the Commission or another executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU's financial interests, the Agency may offset before the payment date specified in the debit note;

(b) by **drawing on the Guarantee Fund**. The Agency or the Commission will formally notify the beneficiary concerned the debit note on behalf of the Guarantee Fund and recover the amount:

(i) not applicable;

(ii) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the payment date in the debit note, up to and including the date the Agency or the Commission receives full payment of the amount.

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 2007/64/EC applies.

44.1.3 Recovery of amounts after payment of the balance

If, for a beneficiary, the revised final grant amount (see Article 5.4) is lower than its share of the final grant amount, it must repay the difference to the Agency.

The beneficiary's share of the final grant amount is calculated as follows:

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{{{beneficiary's costs declared in the final summary financial statement and approved by the Agency multiplied by the reimbursement rate set out in Article 5.2 for the beneficiary concerned}

divided by

the EU contribution for the action calculated according to Article 5.3.1}

multiplied by

the final grant amount (see Article 5.3)}.

If the coordinator has not distributed amounts received (see Article 21.7), the Agency will also recover these amounts.

The Agency will formally notify a **pre-information letter** to the beneficiary concerned:

- informing it of its intention to recover, the due amount and the reasons why and
- inviting it to submit observations within 30 days of receiving notification.

If no observations are submitted or the Agency decides to pursue recovery despite the observations it has received, it will **confirm** the amount to be recovered and formally notify to the beneficiary concerned a **debit note**. This note will also specify the terms and the date for payment.

If payment is not made by the date specified in the debit note, the Agency will **recover** the amount:

(a) by '**offsetting**' it — without the beneficiary's consent — against any amounts owed to the beneficiary concerned by the Agency, the Commission or another executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU's financial interests, the Agency may offset before the payment date specified in the debit note;

(b) by **drawing on the Guarantee Fund**. The Agency or the Commission will formally notify the beneficiary concerned the debit note on behalf of the Guarantee Fund and recover the amount:

(i) not applicable;

(ii) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the date for payment in the debit note, up to and including the date the Agency or the Commission receives full payment of the amount.

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 2007/64/EC applies.

ARTICLE 45 — ADMINISTRATIVE SANCTIONS

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In addition to contractual measures, the Agency or the Commission may also adopt administrative sanctions under Articles 106 and 131(4) of the Financial Regulation No 966/2012 (i.e. exclusion from future procurement contracts, grants and expert contracts and/or financial penalties).

SECTION 2 LIABILITY FOR DAMAGES

ARTICLE 46 — LIABILITY FOR DAMAGES

46.1 Liability of the Agency

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

The Agency cannot be held liable for any damage caused by any of the beneficiaries or third parties involved in the action, as a consequence of implementing the Agreement.

46.2 Liability of the beneficiaries

Except in case of force majeure (see Article 51), the beneficiaries must compensate the Agency 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.

SECTION 3 SUSPENSION AND TERMINATION

ARTICLE 47 — SUSPENSION OF PAYMENT DEADLINE

47.1 Conditions

The Agency may — at any moment — suspend the payment deadline (see Article 21.2 to 21.4) if a request for payment (see Article 20) cannot be approved because:

(a) it does not comply with the provisions of the Agreement (see Article 20);

(b) the technical or financial reports have not been submitted or are not complete or additional information is needed, or

(c) there is doubt about the eligibility of the costs declared in the financial statements and additional checks, reviews, audits or investigations are necessary.

47.2 Procedure

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

The suspension will **take effect** the day notification is sent by the Agency (see Article 52).

If the conditions for suspending the payment deadline are no longer met, the suspension will be **lifted** — and the remaining period will resume.

If the suspension exceeds two months, the coordinator may request the Agency if the suspension will continue.

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If the payment deadline has been suspended due to the non-compliance of the technical or financial reports (see Article 20) and the revised report or statement is not submitted or was submitted but is also rejected, the Agency may also terminate the Agreement or the participation of the beneficiary (see Article 50.3.1(l)).

ARTICLE 48 — SUSPENSION OF PAYMENTS

48.1 Conditions

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

(a) a beneficiary (or a natural person who has the power to represent or take decision on its behalf) has committed or is suspected of having committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under the Agreement or during the award procedure (including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles) or

(b) a beneficiary (or a natural person who has the power to represent or take decision on its behalf) has committed — in other EU or Euratom 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 22.5.2).

If payments are suspended for one or more beneficiaries, the Agency will make partial payment(s) for the part(s) not suspended. If suspension concerns the payment of the balance, — once suspension is lifted — the payment or the recovery of the amount(s) concerned will be considered the payment of the balance that closes the action.

48.2 Procedure

Before suspending payments, the Agency will formally notify the coordinator or beneficiary concerned:

- informing it of its intention to suspend payments and the reasons why and
- inviting it to submit observations within 30 days of receiving notification.

If the Agency does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify **confirmation** of the suspension. Otherwise, it will formally notify that the suspension procedure is not continued.

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

If the conditions for resuming payments are met, the suspension will be **lifted**. The Agency will formally notify the coordinator or beneficiary concerned.

During the suspension, the periodic report(s) for all reporting periods except the last one (see Article 20.3), must not contain any individual financial statements from the beneficiary concerned.

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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.

The beneficiaries may suspend implementation of the action (see Article 49.1) or terminate the Agreement or the participation of the beneficiary concerned (see Article 50.1 and 50.2).

ARTICLE 49 — SUSPENSION OF THE ACTION IMPLEMENTATION

49.1 Suspension of the action implementation, by the beneficiaries

49.1.1 Conditions

The beneficiaries may suspend implementation of the action or any part of it, if exceptional circumstances — in particular *force majeure* (see Article 51) — make implementation impossible or excessively difficult.

49.1.2 Procedure

The coordinator must immediately formally notify to the Agency the suspension (see Article 52), stating:

- the reasons why and
- the expected date of resumption.

The suspension will **take effect** the day this notification is received by the Agency.

Once circumstances allow for implementation to resume, the coordinator must immediately formally notify the Agency and request an **amendment** of the Agreement to set the date on which the action will be resumed, extend the duration of the action and make other changes necessary to adapt the action to the new situation (see Article 55) — unless the Agreement or the participation of a beneficiary has been terminated (see Article 50).

The suspension will be **lifted** with effect from the resumption date set out in the amendment. This date may be before the date on which the amendment enters into force.

Costs incurred during suspension of the action implementation are not eligible (see Article 6).

49.2 Suspension of the action implementation, by the Agency

49.2.1 Conditions

The Agency may suspend implementation of the action or any part of it, if:

(a) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed or is suspected of having committed:

(i) substantial errors, irregularities or fraud or

(ii) serious breach of obligations under the Agreement or during the award procedure (including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles);

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(b) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed — in other EU or Euratom 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 22.5.2), or

(c) the action is suspected of having lost its scientific or technological relevance.

49.2.2 Procedure

Before suspending implementation of the action, the Agency will formally notify the coordinator or beneficiary concerned:

- informing it of its intention to suspend the implementation and the reasons why and
- inviting it to submit observations within 30 days of receiving notification.

If the Agency does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify **confirmation** of the suspension. Otherwise, it will formally notify that the procedure is not continued.

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

It will be **lifted** if the conditions for resuming implementation of the action are met.

The coordinator or beneficiary concerned will be formally notified of the lifting and the Agreement will be **amended** to set the date on which the action will be resumed, extend the duration of the action and make other changes necessary to adapt the action to the new situation (see Article 55) — unless the Agreement has already been terminated (see Article 50).

The suspension will be lifted with effect from the resumption date set out in the amendment. This date may be before the date on which the amendment enters into force.

Costs incurred during suspension are not eligible (see Article 6).

The beneficiaries may not claim damages due to suspension by the Agency (see Article 46).

Suspension of the action implementation does not affect the Agency's right to terminate the Agreement or participation of a beneficiary (see Article 50), reduce the grant or recover amounts unduly paid (see Articles 43 and 44).

ARTICLE 50 — TERMINATION OF THE AGREEMENT OR OF THE PARTICIPATION OF ONE OR MORE BENEFICIARIES

50.1 Termination of the Agreement, by the beneficiaries

50.1.1 Conditions and procedure

The beneficiaries may terminate the Agreement.

The coordinator must formally notify termination to the Agency (see Article 52), stating:

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- the reasons why and
- the date the termination will take effect. This date must be after the notification.

If no reasons are given or if the Agency considers the reasons do not justify termination, the Agreement will be considered to have been '**terminated improperly**'.

The termination will **take effect** on the day specified in the notification.

50.1.2 Effects

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

(i) a periodic report (for the open reporting period until termination; see Article 20.3) and

(ii) the final report (see Article 20.4).

If the Agency does not receive the reports within the deadline (see above), only costs which are included in an approved periodic report will be taken into account.

The Agency will **calculate** the final grant amount (see Article 5.3) and the balance (see Article 21.4) on the basis of the reports submitted. Only costs incurred until termination are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

Improper termination may lead to a reduction of the grant (see Article 43).

After termination, the beneficiaries' obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38, 40, 42, 43 and 44) continue to apply.

50.2 Termination of the participation of one or more beneficiaries, by the beneficiaries

50.2.1 Conditions and procedure

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

The coordinator must formally notify termination to the Agency (see Article 52) and inform the beneficiary concerned.

If the coordinator's participation is terminated without its agreement, the formal notification must be done by another beneficiary (acting on behalf of the other beneficiaries).

The notification must include:

- the reasons why;
- the opinion of the beneficiary concerned (or proof that this opinion has been requested in writing);
- the date the termination takes effect. This date must be after the notification, and
- a request for amendment (see Article 55), with a proposal for reallocation of the tasks and the estimated budget of the beneficiary concerned (see Annexes 1 and 2) and, if necessary, the

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addition of one or more new beneficiaries (see Article 56). If termination takes effect after the period set out in Article 3, no request for amendment must be included unless the beneficiary concerned is the coordinator. In this case, the request for amendment must propose a new coordinator.

If this information is not given or if the Agency considers that the reasons do not justify termination, the participation will be considered to have been **terminated improperly**.

The termination will **take effect** on the day specified in the notification.

50.2.2 Effects

The coordinator must — within 30 days from when termination takes effect — submit:

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

(ii) if termination takes effect during the period set out in Article 3, a '**termination report**' from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, an overview of the use of resources, the individual financial statement and, if applicable, the certificate on the financial statement (see Articles 20.3 and 20.4).

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 20.3).

If the request for amendment is rejected by the Agency, (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the Agreement may be terminated according to Article 50.3.1(c).

If the request for amendment is accepted by the Agency, the Agreement is **amended** to introduce the necessary changes (see Article 55).

The Agency will calculate — on the basis of the periodic reports, the termination report and the report on the distribution of payments — **calculate** the amount which is due to the beneficiary and if the (pre-financing and interim) payments received by the beneficiary exceed this amount.

The **amount which is due** is calculated in the following steps:

Step 1 — Application of the reimbursement rate to the eligible costs

The grant amount for the beneficiary is calculated by applying the reimbursement rate(s) to the total eligible costs declared by the beneficiary in the termination report and approved by the Agency.

Only costs incurred by the beneficiary concerned until termination takes effect are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

Step 2 — Reduction due to substantial errors, irregularities or fraud or serious breach of obligations

In case of a reduction (see Article 43), the Agency will calculate the reduced grant

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amount for the beneficiary by deducting the amount of the reduction (calculated in proportion to the seriousness of the errors, irregularities or fraud or breach of obligations, in accordance with Article 43.2) from the grant amount for the beneficiary.

If the payments received **exceed the amounts due**:

- if termination takes effect during the period set out in Article 3 and the request for amendment is accepted, the beneficiary concerned must repay to the coordinator the amount unduly received. The Agency will formally notify the amount unduly received and request the beneficiary concerned to repay it to the coordinator within 30 days of receiving notification. If it does not repay the coordinator, the Agency will draw upon the Guarantee Fund to pay the coordinator and then notify a **debit note** on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

- in all other cases, in particular if termination takes effect after the period set out in Article 3, the Agency will formally notify a **debit note** to the beneficiary concerned. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the Agency the amount due and the Agency will notify a debit note on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

- if the beneficiary concerned is the former coordinator, it must repay the new coordinator according to the procedure above, unless:

  - termination takes effect after an interim payment and

  - the former coordinator has not distributed amounts received as pre-financing or interim payments (see Article 21.7).

  In this case, the Agency will formally notify a **debit note** to the former coordinator. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the Agency the amount due. The Agency will then pay the new coordinator and notify a debit note on behalf of the Guarantee Fund to the former coordinator (see Article 44).

If the payments received **do not exceed the amounts due**: amounts owed to the beneficiary concerned will be included in the next interim or final payment.

If the Agency does not receive the termination report within the deadline (see above), only costs included in an approved periodic report will be taken into account.

If the Agency does not receive the report on the distribution of payments within the deadline (see above), 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.

Improper termination may lead to a reduction of the grant (see Article 43) or termination of the Agreement (see Article 50).

After termination, the concerned beneficiary's obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38, 40, 42, 43 and 44) continue to apply.

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50.3 Termination of the Agreement or the participation of one or more beneficiaries, by the Agency

50.3.1 Conditions

The Agency may terminate the Agreement or the participation of one or more beneficiaries, if:

(a) one or more beneficiaries do not accede to the Agreement (see Article 56);

(b) a change to their legal, financial, technical, organisational or ownership situation (or those of a partner organisation or entity with a capital or legal link) is likely to substantially affect or delay the implementation of the action or calls into question the decision to award the grant;

(c) following termination of participation for one or more beneficiaries (see above), the necessary changes to the Agreement would call into question the decision awarding the grant or breach the principle of equal treatment of applicants (see Article 55);

(d) implementation of the action is prevented by force majeure (see Article 51) or suspended by the coordinator (see Article 49.1) and either:

  (i) resumption is impossible, or

  (ii) the necessary changes to the Agreement would call into question the decision awarding the grant or breach the principle of equal treatment of applicants;

(e) a beneficiary is declared bankrupt, being wound up, having its affairs administered by the courts, has entered into an arrangement with creditors, has suspended business activities, or is subject to any other similar proceedings or procedures under national law;

(f) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has been found guilty of professional misconduct, proven by any means;

(g) a beneficiary does not comply with the applicable national law on taxes and social security;

(h) the action has lost scientific or technological relevance;

(i) not applicable;

(j) not applicable;

(k) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed fraud, corruption, or is involved in a criminal organisation, money laundering or any other illegal activity;

(l) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under the Agreement or during the award procedure (including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles);

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(m) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed — in other EU or Euratom 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 22.5.2).

(n) despite a specific request by the Agency, a beneficiary does not request — through the coordinator — an amendment to the Agreement to end the participation of a partner organisation or entity with a capital or legal link that is in one of the situations under points (e), (f), (g), (k), (l) or (m) and to reallocate its tasks.

50.3.2 Procedure

Before terminating the Agreement or participation of one or more beneficiaries, the Agency will formally notify the coordinator or beneficiary concerned:

- informing it of its intention to terminate and the reasons why and
- inviting it, within 30 days of receiving notification, to submit observations and — in case of Point (l.ii) above — to inform the Agency of the measures to ensure compliance with the obligations under the Agreement.

If the Agency does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify to the coordinator or beneficiary concerned **confirmation** of the termination and the date it will take effect. Otherwise, it will formally notify that the procedure is not continued.

The termination will **take effect**:

- for terminations under Points (b), (c), (e), (g), (h) and (l.ii) above: on the day specified in the notification of the confirmation (see above);
- for terminations under Points (a), (d), (f), (k), (l.i) and (m) above: on the day after the notification of the confirmation is received.

50.3.3 Effects

(a) for **termination of the Agreement**:

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

(i) a periodic report (for the last open reporting period until termination; see Article 20.3) and

(ii) a final report (see Article 20.4).

If the Agreement is terminated for breach of the obligation to submit reports (see Articles 20.8 and 50.3.1(l)), the coordinator may not submit any reports after termination.

If the Agency does not receive the reports within the deadline (see above), only costs which are included in an approved periodic report will be taken into account.

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The Agency will **calculate** the final grant amount (see Article 5.3) and the balance (see Article 21.4) on the basis of the reports submitted. Only costs incurred until termination takes effect are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

This does not affect the Agency's right to reduce the grant (see Article 43) or to impose administrative sanctions (Article 45).

The beneficiaries may not claim damages due to termination by the Agency (see Article 46).

After termination, the beneficiaries' obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38, 40, 42, 43 and 44) continue to apply.

(b) for **termination of the participation of one or more beneficiaries**:

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 request for amendment (see Article 55), with a proposal for reallocation of the tasks and estimated budget of the beneficiary concerned (see Annexes 1 and 2) and, if necessary, the addition of one or more new beneficiaries (see Article 56). If termination is notified after the period set out in Article 3, no request for amendment must be submitted unless the beneficiary concerned is the coordinator. In this case the request for amendment must propose a new coordinator, and

(iii) if termination takes effect during the period set out in Article 3, a **termination report** from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, an overview of the use of resources, the individual financial statement and, if applicable, the certificate on the financial statement (see Article 20).

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 20.3).

If the request for amendment is rejected by the Agency, (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the Agreement may be terminated according to Article 50.3.1(c).

If the request for amendment is accepted by the Agency, the Agreement is **amended** to introduce the necessary changes (see Article 55).

The Agency will calculate — on the basis of the periodic reports, the termination report and the report on the distribution of payments — **calculate** the amount which is due to the beneficiary and if the (pre-financing and interim) payments received by the beneficiary exceed this amount.

The **amount which is due** is calculated in the following steps:

Step 1 — Application of the reimbursement rate to the eligible costs

The grant amount for the beneficiary is calculated by applying the

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reimbursement rate(s) to the total eligible costs declared by the beneficiary in the termination report and approved by the Agency.

Only costs incurred by the beneficiary concerned until termination takes effect are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

Step 2 — Reduction due to substantial errors, irregularities or fraud or serious breach of obligations

In case of a reduction (see Article 43), the Agency will calculate the reduced grant amount for the beneficiary by deducting the amount of the reduction (calculated in proportion to the seriousness of the errors, irregularities or fraud or breach of obligations, in accordance with Article 43.2) from the grant amount for the beneficiary.

If the payments received **exceed the amounts due**:

- if termination takes effect during the period set out in Article 3 and the request for amendment is accepted, the beneficiary concerned must repay to the coordinator the amount unduly received. The Agency will formally notify the amount unduly received and request the beneficiary concerned to repay it to the coordinator within 30 days of receiving notification. If it does not repay the coordinator, the Agency will draw upon the Guarantee Fund to pay the coordinator and then notify a **debit note** on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

- in all other cases, in particular if termination takes effect after the period set out in Article 3, the Agency will formally notify a **debit note** to the beneficiary concerned. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the Agency the amount due and the Agency will notify a debit note on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

- if the beneficiary concerned is the former coordinator, it must repay the new coordinator according to the procedure above, unless:

  - termination takes effect after an interim payment and

  - the former coordinator has not distributed amounts received as pre-financing or interim payments (see Article 21.7).

  In this case, the Agency will formally notify a **debit note** to the former coordinator. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the Agency the amount due. The Agency will then pay the new coordinator and notify a debit note on behalf of the Guarantee Fund to the former coordinator (see Article 44).

If the payments received **do not exceed the amounts due**: amounts owed to the beneficiary concerned will be included in the next interim or final payment.

If the Agency does not receive the termination report within the deadline (see above), only costs included in an approved periodic report will be taken into account.

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If the Agency does not receive the report on the distribution of payments within the deadline (see above), 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.

After termination, the concerned beneficiary's obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38, 40, 42, 43 and 44) continue to apply.

SECTION 4 FORCE MAJEURE

ARTICLE 51 — FORCE MAJEURE

'Force majeure' means any situation or event that:

- prevents either party from fulfilling their obligations under the Agreement,
- was unforeseeable, exceptional situation and beyond the parties' control,
- was not due to error or negligence on their part (or on the part of third parties involved in the action), and
- proves to be inevitable in spite of exercising all due diligence.

The following cannot be invoked as force majeure:

- any default of a service, defect in equipment or material or delays in making them available, unless they stem directly from a relevant case of force majeure,
- labour disputes or strikes, or
- financial difficulties.

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.

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

CHAPTER 7 FINAL PROVISIONS

ARTICLE 52 — COMMUNICATION BETWEEN THE PARTIES

52.1 Form and means of communication

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Communication under the Agreement (information, requests, submissions, 'formal notifications', etc.) must:

- be made in writing and
- bear the number of the Agreement.

Until the payment of the balance: all communication must be made through the electronic exchange system and using the forms and templates provided there.

After the payment of the balance: formal notifications must be made by registered post with proof of delivery ('formal notification on paper').

Communications in the electronic exchange system must be made by persons authorised according to the Participant Portal Terms & 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 his/her appointment letter (see Participant Portal Terms & Conditions).

If the electronic exchange system is temporarily unavailable, instructions will be given on the Agency and Commission websites.

52.2 Date of communication

Communications are considered to have been made when they are sent by the sending party (i.e. on the date and time they are sent through the electronic exchange system).

Formal notifications through the **electronic** exchange system are considered to have been made when they are received by the receiving party (i.e. on the date and time of acceptance by the receiving party, as indicated by the time stamp). A formal notification that has not been accepted within 10 days after sending is considered to have been accepted.

Formal notifications **on paper** sent by **registered post** with proof of delivery (only after the payment of the balance) are considered to have been made on either:

- 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.

52.3 Addresses for communication

The **electronic** exchange system must be accessed via the following URL:

https://ec.europa.eu/research/participants/portal/desktop/en/projects/

The Agency will formally notify the coordinator and beneficiaries in advance any changes to this URL.

Formal notifications on paper (only after the payment of the balance) addressed **to the Agency** must be sent to the following address:

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Research Executive Agency
Marie Sklodowska-Curie Research and Innovation Staff Exchanges
REA A3 secretariat COV2
B-1049 Brussels Belgium

Formal notifications on paper (only after the payment of the balance) addressed **to the beneficiaries** must be sent to their legal address as specified in the Participant Portal Beneficiary Register.

ARTICLE 53 — INTERPRETATION OF THE AGREEMENT

53.1 Precedence of the Terms and Conditions over the Annexes

The provisions in the Terms and Conditions of the Agreement take precedence over its Annexes.

Annex 2 takes precedence over Annex 1.

53.2 Privileges and immunities

Not applicable

ARTICLE 54 — CALCULATION OF PERIODS, DATES AND DEADLINES

In accordance with Regulation No 1182/71[18], 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.

ARTICLE 55 — AMENDMENTS TO THE AGREEMENT

55.1 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.

55.2 Procedure

The party requesting an amendment must submit a request for amendment signed in the electronic exchange system (see Article 52).

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).

[18] 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).

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The request for amendment must include:

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

The Agency may request additional information.

If the party receiving the request agrees, it must sign the amendment in the electronic exchange system within 45 days of receiving notification (or any additional information the Agency 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 agreed by the parties or, in the absence of such an agreement, on the date on which the amendment enters into force.

ARTICLE 56 — ACCESSION TO THE AGREEMENT

56.1 Accession of the beneficiaries mentioned in the Preamble

The other beneficiaries must accede to the Agreement by signing the Accession Form (see Annex 3) in the electronic exchange system (see Article 52) within 30 days after its entry into force (see Article 58).

They will assume the rights and obligations under the Agreement with effect from the date of its entry into force (see Article 58).

If a beneficiary does not accede to the Agreement within the above deadline, the coordinator must — within 30 days — request an amendment to make any changes necessary to ensure proper implementation of the action. This does not affect the Agency's right to terminate the Agreement (see Article 50).

56.2 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 55. It must include an Accession Form (see Annex 3) signed by the new beneficiary in the electronic exchange system (see Article 52).

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

ARTICLE 57 — APPLICABLE LAW AND SETTLEMENT OF DISPUTES

57.1 Applicable law

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

57.2 Dispute settlement

If a dispute concerning the interpretation, application or validity of the Agreement cannot be settled amicably, the General Court — or, on appeal, the Court of Justice of the European Union — has sole jurisdiction. Such actions must be brought under Article 272 of the Treaty on the Functioning of the EU (TFEU).

As an exception, if such a dispute is between the Agency and FACULTY OF BIOLOGY OF THE UNIVERSITY OF BELGRADE, YEDITEPE UNIVERSITY VAKIF, ARGENIT AKILLI BILGI TEKNOLOJILERI SANAYI VE TICARET LIMITED SIRKETI, the competent Belgian courts have sole jurisdiction.

If a dispute concerns administrative sanctions, offsetting or an enforceable decision under Article 299 TFEU (see Articles 44, 45 and 46), the beneficiaries must bring action before the General Court — or, on appeal, the Court of Justice of the European Union — under Article 263 TFEU. Actions against enforceable decisions must be brought against the Commission (not against the Agency).

ARTICLE 58 — ENTRY INTO FORCE OF THE AGREEMENT

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

SIGNATURES

For the coordinator

Ljubisa STANISAVLJEVIC with ECAS id nstaljub signed in the Participant Portal on 04/10/2017 at 23:21:03 (transaction id SigId-66891-2OLYQlfenwZwoOklhNzSfOZQ11xDsgYHpFwlzpHFRpnDXVFGnTloKFNPAnT8jrPPfMD8cbNHHEHuTTuCDC2JAzW-Jj71zxYb8yrGXJFnP0oDp0-vJziclNIIFZELHVMQkH8WdLfwW0meKUZIoNgu7dTzZxm) . Timestamp by third party at Thu Oct 05 00:21:22 CEST 2017

For the Agency

Signed by Fredrik OLSSON HECTOR with ECAS id olssofr as an authorised representative on 05-10-2017 14:47:07 (transaction id SigId-75493-IlzHRSevkztzViSDnaSlTdQ0tfSDkFqZ5LONoSX8M9Rd6U8TlPBVcYSmqc4kFwZTV1JQhjRSzVD6Kn6n1ec9L1G-Jj71zxYb8yrGXJFnP0oDp0-po7Van7DaMS0rME8pYexx6zL1cRAgiXfjaTO6K1n5AA) Thu Oct 05 14:47:11 CEST 2017

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

EUROPEAN COMMISSION
Research Executive Agency

Marie Sklodowska-Curie Research and Innovation Staff Exchanges

ANNEX 1 (part A)

RISE

NUMBER — 778405 — AUTOIGG

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

Table of Contents

1.1. The project summary

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

Project Number [1]	778405	Project Acronym [2]	AUTOIGG

One form per project

General information	
Project title [3]	AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTICS OF NEURODEGENERATIVE DISEASES
Starting date [4]	01/01/2018
Duration in months [5]	48
Call (part) identifier [6]	H2020-MSCA-RISE-2017
Topic	MSCA-RISE-2017 Research and Innovation Staff Exchange
Fixed EC Keywords	Diagnostic tools (e.g. genetic, imaging), Innate immunity and inflammation, Neurological disorders (e.g. Alzheimer's disease, Huntington's disease, Parkinson's disease), Molecular and cellular neuroscience
Free keywords	Amyotrophic lateral sclerosis, astrocytes, immunoglobulins, calcium, ROS, voltage sensitive dyes, MEA

Abstract [7]

The project proposes to organize the exchange of staff of three Academic institutions from Serbia (coordinator), Turkey and Finland, two SMEs from France and Turkey and three TC institutions (two from USA and one from Costa Rica) towards the production of an innovative automated multifunctional device for diagnostics of neurodegenerative diseases.
The objectives addressed will be:
• Development of experimental cellular models and procedures with immunoglobulins (IgGs) from patient sera as diagnostic and prognostic technologies related to neurodegenerative diseases (particularly based on studies of amyotrophic lateral sclerosis - ALS).
• Defining mark-up characteristics of the standardized in vitro approach for personalized diagnostic protocols.
• Design of a small-scale platform based on automated fluorescence microscopy.
These objectives are based on previous studies on ALS of the coordinators group, however the project also proposes to study the applications on other neuroinflammations and neurodegenerative conditions. This addresses a relevant R & I as well as a socioeconomic medical issue. It is the right timing for addresing this research chalange towards application by means of networking that will deal with interesectorial and international exchange of expertise. In addition, three workshops and two training schools will be organized followed by an elaborate dissemination programme. Carrier plans will be designed for the seconded staff in order to maintain the sustainability of the Action.

1.2. List of Beneficiaries

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

Project Number [1]	778405	Project Acronym [2]	AUTOIGG

List of Beneficiaries

No	Name	Short name	Country	Project entry month[8]	Project exit month
1	FACULTY OF BIOLOGY OF THE UNIVERSITY OF BELGRADE	FBUB	Serbia	1	48
2	YEDITEPE UNIVERSITY VAKIF	YEDITEPE	Turkey	1	48
3	ITA-SUOMEN YLIOPISTO	UEF	Finland	1	48
4	ARGENIT AKILLI BILGI TEKNOLOJILERI SANAYI VE TICARET LIMITED SIRKETI	Argenit	Turkey	1	48
5	ELVESYS SAS	ELVESYS	France	1	48

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

1.3. Workplan Tables - Detailed implementation

1.3.1. WT1 List of work packages

WP Number[9]	WP Title	Lead beneficiary[10]	Start month[12]	End month[13]
WP1	Standardization and benchmarking	1 - FBUB	6	46
WP2	Pilot platform design	1 - FBUB	6	47
WP3	Dissemination, communication and networking	1 - FBUB	3	48
WP4	Project management and sustainability	1 - FBUB	1	48
WP5	Ethics requirements	1 - FBUB	1	48

1.3.2. WT2 list of deliverables

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D1.1	Report on ROS imaging standardisation, benchmarking and diagnostic value	WP1	3 - UEF	Report	Confidential, only for members of the consortium (including the Commission Services)	19
D1.2	Report on Ca2+ imaging and vesicle trafficking standardisation and diagnostic value	WP1	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	19
D1.3	Report on benchmarking protocols in Ca2+ imaging and in vesicle trafficking	WP1	4 - Argenit	Report	Confidential, only for members of the consortium (including the Commission Services)	22
D1.4	Report on subcellular microscopy markers	WP1	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	40
D1.5	Report on benchmarking protocols in electrophysiology (voltage-sensitive dyes and MEA)	WP1	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	34
D1.6	Report on testing comparative antibody samples	WP1	2 - YEDITEPE	Report	Confidential, only for members of the consortium (including the Commission Services)	43
D2.1	Report on microscope stage prototype	WP2	4 - Argenit	Report	Confidential, only for members of the consortium (including the Commission Services)	32
D2.2	Report on fluorescence detector prototype and software demo	WP2	5 - ELVESYS	Report	Confidential, only for members of the consortium (including the Commission Services)	32

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D2.3	Validation report on automated measurement device	WP2	2 - YEDITEPE	Report	Confidential, only for members of the consortium (including the Commission Services)	34
D3.1	Training schools	WP3	3 - UEF	Websites, patents filling, etc.	Confidential, only for members of the consortium (including the Commission Services)	31
D3.2	Workshops 1, 2, 3	WP3	2 - YEDITEPE	Websites, patents filling, etc.	Public	35
D3.3	Report on outreach activities with compendium of press clippings and publications	WP3	1 - FBUB	Report	Public	48
D4.1	Kick-off meeting; Ethical guidelines and website up and running	WP4	1 - FBUB	Other	Confidential, only for members of the consortium (including the Commission Services)	3
D4.2	Annual meetings (inc. Final) with Minutes and financial updates	WP4	1 - FBUB	Other	Public	48
D4.3	Progress report 1	WP4	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	12
D4.4	Mid-term meeting	WP4	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	16
D4.5	Final reports on workshops, and training schools	WP4	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	37
D4.6	Progress report 2	WP4	1 - FBUB	Report	Confidential, only for members of the consortium (including the	36

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
					Commission Services)	
D5.1	A - Requirement No. 6	WP5	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	6
D5.2	A - Requirement No. 7	WP5	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	6
D5.3	GEN - Requirement No. 11	WP5	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	1
D5.4	NEC - Requirement No. 12	WP5	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	4
D5.5	H - Requirement No. 13	WP5	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	3

1.3.3. WT3 Work package descriptions

Work package number [9]	WP1	**Lead beneficiary** [10]	1 - FBUB
Work package title	Standardization and benchmarking		
Start month	6	**End month**	46

Objectives

- rigorous standardization in the lab
- selection of best practice for cell cultures
- benchmarking of protocols
- defining patterns of correlation of parameters of cell reactivity and disease stage
- software design and testing
- autoantibody testing with clinical samples
- recruitment of women for secondments as ERs, and ESRs, in order to reach a minimal 40% participation in the network

Description of work and role of partners

WP1 - Standardization and benchmarking [Months: 6-46]
FBUB
T1.1. ROS imaging – UEF, FBUB (standardization of activity parameters and correlation with disease parameters), ArGenit and ELVESYS (benchmarking of measurement protocols).
T1.2. Ca2+ imaging – FBUB, UCONN, UChic (standardization of activity parameters and correlation with disease parameters), ArGenit and ELVESYS (benchmarking of measurement protocols).
T1.3. Vesicle trafficking – FBUB (standardization of activity parameters and correlation with disease parameters), ArGenit (benchmarking of measurement protocols), ELVESYS (benchmarking of measurement protocols and software pilot).
T1.4 Advanced microscopy – LANOTEC, FBUB (subcellular characterization of inflammatory markers).
T1.5. Synaptic activity – following with voltage sensitive dyes (UCONN), FBUB (complementary electrophysiology and in vitro implementation in neuronal cultures), UChic (complementary measurements in MEA systems), ArGenit and ELVESYS (benchmarking of measurement protocols).
T1.6 Autoantibody testing in clinical environment – YEDITEPE (collection of clinical samples of autoimmune diseases vs ALS, complementary analysis and testing), FBUB (testing of samples).

Participation per Partner

Partner number and short name [10]
1 - FBUB
2 - YEDITEPE
3 - UEF
4 - Argenit
5 - ELVESYS
6 - LANOTEC-CENAT-CONARE
7 - UCHC
8 - University of Chicago

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D1.1	Report on ROS imaging standardisation, benchmarking and diagnostic value	3 - UEF	Report	Confidential, only for members of the consortium (including the Commission Services)	19
D1.2	Report on Ca2+ imaging and vesicle trafficking standardisation and diagnostic value	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	19
D1.3	Report on benchmarking protocols in Ca2+ imaging and in vesicle trafficking	4 - Argenit	Report	Confidential, only for members of the consortium (including the Commission Services)	22
D1.4	Report on subcellular microscopy markers	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	40
D1.5	Report on benchmarking protocols in electrophysiology (voltage-sensitive dyes and MEA)	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	34
D1.6	Report on testing comparative antibody samples	2 - YEDITEPE	Report	Confidential, only for members of the consortium (including the Commission Services)	43

Description of deliverables

Reports on standardization and benchmarking of IgG effects.

D1.1 : Report on ROS imaging standardisation, benchmarking and diagnostic value [19]

standardisation of activity parameters and correlation with disease parameters, benchmarking of measurement protocols

D1.2 : Report on Ca2+ imaging and vesicle trafficking standardisation and diagnostic value [19]

standardisation of activity parameters and correlation with disease parameters, benchmarking of measurement protocols

D1.3 : Report on benchmarking protocols in Ca2+ imaging and in vesicle trafficking [22]

standardisation of activity parameters and correlation with disease parameters, benchmarking of measurement protocols and software pilot

D1.4 : Report on subcellular microscopy markers [40]

subcellular characterization of inflammatory markers

D1.5 : Report on benchmarking protocols in electrophysiology (voltage-sensitive dyes and MEA) [34]

following with voltage sensitive dyes, complementary electrophysiology and in vitro implementation in neuronal cultures, complementary measurements in MEA systems, benchmarking of measurement protocols

D1.6 : Report on testing comparative antibody samples [43]

collection of clinical samples of autoimmune diseases vs ALS, complementary analysis and testing of samples

Schedule of relevant Milestones

Milestone number[18]	**Milestone title**	**Lead beneficiary**	**Due Date (in months)**	**Means of verification**
MS1	Standardisation of IgG effects on Ca2+ and relation to disease stage	1 - FBUB	19	Lab protocol established and available
MS2	Standardisation of IgG effects on ROS and relation to disease stage	3 - UEF	19	Lab protocol established and available
MS3	Standardisation of IgG effects on vesicle trafficking and relation to disease stage	1 - FBUB	22	Lab protocol established and available
MS4	Standardisation of electrophysiological IgG effects .(voltage-sensitive dyes and MEA)	1 - FBUB	29	Lab protocol established and available

Work package number [9]	WP2	Lead beneficiary [10]	1 - FBUB
Work package title	Pilot platform design		
Start month	6	End month	47

Objectives

- design and validation of the lab platform
- defining quantitative parameters
- conversion of activity parameters onto pseudo color matrices that are software-readable
- recruitment of women for secondments as ERs, and ESRs, in order to reach a minimal 40% participation in the network

Description of work and role of partners

WP2 - Pilot platform design [Months: 6-47]
FBUB
T2.1. Designing the automated microscopic stage – ArGenit (main design), FBUB & UCONN, LANOTEC (experimental data support)
T2.2. Designing the fluorescence detector for dynamic measurements – ELVESYS (main design), FBUB, UCONN & UCHIC (experimental data support) and software – ELVESYS (main design), FBUB, YEDITEPE, UCONN & UCHIC (experimental data support)
T2.3. Validation of the measurement device with clinical samples – FBUB & YEDITEPE (near to operational environment), ArGenit & ELVESYS (technical support).

Participation per Partner

Partner number and short name [10]
1 - FBUB
2 - YEDITEPE
4 - Argenit
5 - ELVESYS
6 - LANOTEC-CENAT-CONARE
8 - University of Chicago

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D2.1	Report on microscope stage prototype	4 - Argenit	Report	Confidential, only for members of the consortium (including the Commission Services)	32
D2.2	Report on fluorescence detector prototype and software demo	5 - ELVESYS	Report	Confidential, only for members of the consortium (including the Commission Services)	32

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D2.3	Validation report on automated measurement device	2 - YEDITEPE	Report	Confidential, only for members of the consortium (including the Commission Services)	34

Description of deliverables

Reports and validation of the point of care fluorescence detection platform

D2.1 : Report on microscope stage prototype [32]

Designing the automated microscopic stage: main design, experimental data support

D2.2 : Report on fluorescence detector prototype and software demo [32]

Designing the fluorescence detector for dynamic measurements: main design, experimental data support Software design: main design, experimental data support

D2.3 : Validation report on automated measurement device [34]

Validation of the measurement device with clinical samples: near to operational environment, technical support

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS5	Blueprint of automated device	4 - Argenit	31	Design draft completed and validated
MS6	Software demo for dynamic fluorescence acquisition and vesicle trafficking	5 - ELVESYS	31	Software demo released and functional

Work package number [9]	WP3	**Lead beneficiary** [10]	1 - FBUB
Work package title	Dissemination, communication and networking		
Start month	3	**End month**	48

Objectives

- finding the best communication channels
- organization of meetings and workshops
- disseminating project outcomes for the community as a whole
- to communicate to key stakeholders the existence of the project and provide regular updates on new data generated

Description of work and role of partners

WP3 - Dissemination, communication and networking [Months: 3-48]
FBUB
T3.1. Trainings and workshops. (FBUB, YEDITEPE, UEF)
T3.2. Outreach and publications: website. (FBUB, ELVESYS), approaching governments and Ministries of Health and Science (FBUB, YEDIPE, UEF, LANOTEC); patients associations (FBUB, YEDITEPE, UEF, LANOTEC), public engagement (FBUB, YEDITEPE, UEF, ELVESYS, ArGenit), press releases. (FBUB, YEDITEPE, UEF, LANOTEC), publications (FBUB, YEDITEPE, UEF, LANOTEC),
T3.3. Valorization, entrepreneurship & communication (FBUB, ELVESYS)

Participation per Partner

Partner number and short name [10]
1 - FBUB
2 - YEDITEPE
3 - UEF
4 - Argenit
5 - ELVESYS
6 - LANOTEC-CENAT-CONARE

List of deliverables

Deliverable Number[14]	**Deliverable Title**	**Lead beneficiary**	**Type**[15]	**Dissemination level**[16]	**Due Date (in months)**[17]
D3.1	Training schools	3 - UEF	Websites, patents filling, etc.	Confidential, only for members of the consortium (including the Commission Services)	31
D3.2	Workshops 1, 2, 3	2 - YEDITEPE	Websites, patents filling, etc.	Public	35
D3.3	Report on outreach activities with compendium of press clippings and publications	1 - FBUB	Report	Public	48

Description of deliverables

Reports on outreach and proceedings of training and workshop events

D3.1 : Training schools [31]

Two Training Schools will be organized by UEF: one on free radical (ROS) monitoring – essential for one of the tasks in WG1, and one on inducible pluripotent stem cells (iPSCs) and their applications - as an alternative model for the proposed automated recording platform.

D3.2 : Workshops 1, 2, 3 [35]

Three workshops will be hosted by YEDIPE in Istanbul. Two workshops will deal with the fundamentals of the scientific goals of the project - immunology and detection methods for the IgGs and their effects. The third workshop will be organized in the first year of the project and will deal with an important soft skill – Good Laboratory Practice.

D3.3 : Report on outreach activities with compendium of press clippings and publications [48]

The goal and outcomes of the project wil be communicated to a wider laymen public.

Schedule of relevant Milestones

Milestone number[18]	**Milestone title**	**Lead beneficiary**	**Due Date (in months)**	**Means of verification**
MS7	Training and workshops 1st year	1 - FBUB	12	Proceedings and handouts published
MS8	Training and workshops 3rd year	1 - FBUB	36	Proceedings and handouts published

Work package number [9]	WP4	Lead beneficiary [10]	1 - FBUB
Work package title	Project management and sustainability		
Start month	1	End month	48

Objectives

- formation of the Supervisory Board, Secondments Committee and its R & I Council.
- managing all project phases: solution design, prototyping, testing and validation.
- ensure that AUTOIGG achieves its aims
- coordinating secondments involving all beneficiaries and partners towards exchange of experiences
- controlling the money flow
- quality control of all aspects of the work plan
- maintaining regular relations with REA
- design of a sustainability plan (wider application for other neuroinflammatory diseases)

Description of work and role of partners

WP4 - Project management and sustainability [Months: 1-48]
FBUB
T4.1. Control of all phases of the project and fulfilling all the contractors obligations towards the EC including reporting (FBUB)
T4.2. Assessing progress of the secondment program (FBUB & YEDITEPE)
T4.3. Implementing changes in work sharing, budget and participants (FBUB)
T4.4. Reviewing of the reports regarding workshops, training schools (FBUB, UEF, YEDITEPE, ArGenit, ELVESYS)
T4.5. Reviewing reports regarding IPR issues (ArGenit, ELVESYS).
T4.6. Drafting of Ethical guidelines (FBUB, UEF, YEDITEPE)
T4.7. Agreeing on press releases by the contractors with regard to the project (FBUB, ELVESYS)

Participation per Partner

Partner number and short name [10]
1 - FBUB
2 - YEDITEPE
4 - Argenit
5 - ELVESYS

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D4.1	Kick-off meeting; Ethical guidelines and website up and running	1 - FBUB	Other	Confidential, only for members of the consortium (including the Commission Services)	3
D4.2	Annual meetings (inc. Final) with Minutes and financial updates	1 - FBUB	Other	Public	48
D4.3	Progress report 1	1 - FBUB	Report	Confidential, only for members of the	12

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
				consortium (including the Commission Services)	
D4.4	Mid-term meeting	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	16
D4.5	Final reports on workshops, and training schools	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	37
D4.6	Progress report 2	1 - FBUB	Report	Confidential, only for members of the consortium (including the Commission Services)	36

Description of deliverables

Management reports and meeting minutes

D4.1 : Kick-off meeting; Ethical guidelines and website up and running [3]

A kick-off meeting will indicate the official start of the project. Thus starting points will be established among beneficiaries and partners such as ethics guidelines, secondment plan, and website design.

D4.2 : Annual meetings (inc. Final) with Minutes and financial updates [48]

Annual meetings will be minuted and will update project parties and discuss future maters (finances and mobilities).

D4.3 : Progress report 1 [12]

Progress report after the first year.

D4.4 : Mid-term meeting [16]

Mid-term meeting will validate the project activity so far and the fulfilement of the secondments plan.

D4.5 : Final reports on workshops, and training schools [37]

These reports should sum up the achievements of the workshops and training schools, particularly regarding the transfer of know-how among particpants of the project.

D4.6 : Progress report 2 [36]

Update of the project state of the art after the 3rd year.

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS9	Resource engagement mid-term plan	1 - FBUB	17	Plan drafted, validated and published
MS10	Financial mid-term plan	1 - FBUB	17	Plan drafted, validated and published

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS11	Minutes of 2nd annual meeting incl. mid-term reports	1 - FBUB	24	Minutes and reports collected and published

Work package number [9]	WP5	Lead beneficiary [10]	1 - FBUB
Work package title	Ethics requirements		
Start month	1	End month	48

Objectives

The objective is to ensure compliance with the 'ethics requirements' set out in this work package.

Description of work and role of partners

WP5 - Ethics requirements [Months: 1-48]
FBUB
This work package sets out the 'ethics requirements' that the project must comply with.

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D5.1	A - Requirement No. 6	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	6
D5.2	A - Requirement No. 7	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	6
D5.3	GEN - Requirement No. 11	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	1
D5.4	NEC - Requirement No. 12	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	4
D5.5	H - Requirement No. 13	1 - FBUB	Ethics	Confidential, only for members of the consortium (including the Commission Services)	3

Description of deliverables

The 'ethics requirements' that the project must comply with are included as deliverables in this work package.

D5.1 : A - Requirement No. 6 [6]

5.1. Copies of relevant authorisations (for breeders, suppliers, users, and facilities) for animal experiments must be obtained, kept on file and submitted upon request.

D5.2 : A - Requirement No. 7 [6]

5.4. If applicable, copies of training certificates/personal licenses of the staff involved in animal experiments must be obtained, kept on file and provided upon request.

D5.3 : GEN - Requirement No. 11 [1]

12.4. Due to the severity of the ethics issues raised by the proposed research work, it is required that an independent Ethics Advisor is appointed to oversee the implementation the ethical concerns involved in this research. A report by the ethics Advisor must be submitted to the Agency with the periodic reports.

D5.4 : NEC - Requirement No. 12 [4]

6.3. The applicant must obtain the adequate authorisations on the material which will be imported to/exported from EU, keep them on file and submit them if requested.

D5.5 : H - Requirement No. 13 [3]

2.9. Copies of ethics approvals for the research with humans must be obtained, kept on file and be submitted upon request.

Schedule of relevant Milestones

Milestone number[18]	**Milestone title**	**Lead beneficiary**	**Due Date (in months)**	**Means of verification**
MS12	Ethics requirements acomplishment	1 - FBUB	6	The requieremets of the Ethics report acomplished

1.3.4. WT4 List of milestones

Milestone number[18]	Milestone title	WP number[9]	Lead beneficiary	Due Date (in months)[17]	Means of verification
MS1	Standardisation of IgG effects on Ca2+ and relation to disease stage	WP1	1 - FBUB	19	Lab protocol established and available
MS2	Standardisation of IgG effects on ROS and relation to disease stage	WP1	3 - UEF	19	Lab protocol established and available
MS3	Standardisation of IgG effects on vesicle trafficking and relation to disease stage	WP1	1 - FBUB	22	Lab protocol established and available
MS4	Standardisation of electrophysiological IgG effects .(voltage-sensitive dyes and MEA)	WP1	1 - FBUB	29	Lab protocol established and available
MS5	Blueprint of automated device	WP2	4 - Argenit	31	Design draft completed and validated
MS6	Software demo for dynamic fluorescence acquisition and vesicle trafficking	WP2	5 - ELVESYS	31	Software demo released and functional
MS7	Training and workshops 1st year	WP3	1 - FBUB	12	Proceedings and handouts published
MS8	Training and workshops 3rd year	WP3	1 - FBUB	36	Proceedings and handouts published
MS9	Resource engagement mid-term plan	WP4	1 - FBUB	17	Plan drafted, validated and published
MS10	Financial mid-term plan	WP4	1 - FBUB	17	Plan drafted, validated and published
MS11	Minutes of 2nd annual meeting incl. mid-term reports	WP4	1 - FBUB	24	Minutes and reports collected and published
MS12	Ethics requirements acomplishment	WP5	1 - FBUB	6	The requieremets of the Ethics report acomplished

1.3.5. WT5 Critical Implementation risks and mitigation actions

Risk number	Description of risk	WP Number	Proposed risk-mitigation measures
1	Difficulties in coordinating staff secondments with home tasks	WP1	Host alerts the Supervisory Board and Secondments Committee will be consulted for alternative solutions
2	Fellows do not blend well with the hosting environment	WP1	In addition to the EURAXESS site (http:// ec.europa.eu/euraxess) intranet web site will be used to ease the acquaintance with the particular hosting environment.
3	Difficulties in moving R & I outcomes between partners	WP2	The R & I Council is alerted by the Secondment Committee
4	Difficulty in obtaining secondment outcomes	WP1, WP2	The Secondment Committee will be in close mediating contact with host representative and the invited fellow.
5	Difficulties in synchronising secondments with project R & I goals	WP1, WP2	The Supervisory Board will alert the Secondment Committee to revise or reshuffle and expedite the secondments plan.
6	Lack of progress in individual secondment plans	WP1	The Secondment Committee will meet within the following month to discuss the lack of progress and find solutions. Eventually R & I Council will be alerted.
7	Partners do not integrate.	WP4	Non-integrating partners will be kept informed by the management and helped to integrate. Failing to achieve integration by year 1.5 will result in suspension of secondment funding and reallocation to other partners

1.3.6. WT6 Summary of project effort contribution

	WP1	WP2	WP3	WP4	WP5
1 - FBUB	✓	✓	✓	✓	
2 - YEDITEPE	✓	✓	✓	✓	
3 - UEF	✓		✓		
4 - Argenit	✓	✓	✓	✓	
5 - ELVESYS	✓	✓	✓	✓	
7 - UCHC	✓				
8 - University of Chicago	✓	✓			
6 - LANOTEC-CENAT-CONARE	✓	✓	✓		

1.3.7. WT7 Tentative schedule of project reviews

No project reviews indicated

1.4. List of Partner Organisations

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

Participant number	Partner Organisation Full Name	Partner Organisation Short name	Country
6	FUNDACION CENTRO DE ALTA TECNOLOGIA	LANOTEC-CENAT-CONARE	Costa Rica
7	UNIVERSITY OF CONNECTICUT	UCHC	United States
8	THE UNIVERSITY OF CHICAGO	University of Chicago	United States

1.5. Secondments

1.5.1. Summary of secondments per Participant

Partner number	Partner short name	Country	EU/AC or TC	Academic sector	Total Number of secondments	Total Researcher Months Period 1	Total Researcher Months Period 2	Total Researcher Months Overall	Total Researcher Months (%)
1	FBUB	Serbia	EU/AC	Yes	22	60.00	79.00	139.00	65.57%
2	YEDITEPE	Turkey	EU/AC	Yes	3	9.00	18.00	27.00	12.74%
3	UEF	Finland	EU/AC	Yes	2	8.00	0.00	8.00	3.77%
4	Argenit	Turkey	EU/AC	No	3	15.00	6.00	21.00	9.91%
5	ELVESYS	France	EU/AC	No	2	1.00	1.00	2.00	0.94%
6	LANOTEC-CENAT-CONARE	Costa Rica	TC	Yes	2	15.00	0.00	15.00	7.08%
7	UCHC	United States	TC	Yes	0	0.00	0.00	0.00	0.00%
8	University of Chicago	United States	TC	Yes	0	0.00	0.00	0.00	0.00%
TOTAL					**34**	**108.00**	**104.00**	**212.00**	**100.00%**

1.5.2. Summary of secondments funded by EU per Beneficiary

(secondments from the Beneficiary and from funded Partner Organisations to the Beneficiary)

Partner number	Partner short name	Country	Number of secondments funded by EU	Researcher Months funded by EU Period 1	Researcher Months funded by EU Period 2	Researcher Months funded by EU Overall
1	FBUB	Serbia	24	75.00	79.00	154.00
2	YEDITEPE	Turkey	3	9.00	18.00	27.00
3	UEF	Finland	2	8.00	0.00	8.00
4	Argenit	Turkey	3	15.00	6.00	21.00
5	ELVESYS	France	2	1.00	1.00	2.00
TOTAL			**34**	**108.00**	**104.00**	**212.00**

1.5.3. Secondments plan

Overview of secondments

Staff member ID	Staff member profile	Sending Org. (Short Name)	Sending Org. (Country)	Sending Org. (Region)	Sending Org. (Academic Sector)	Seconded to Org. (Short Name)	Seconded to Org. (Country)	Seconded to Org. (Region)	Seconded to Org. (Academic Sector)	Work package number	Secondment Starting month	Duration of secondment (researcher-months)
1	ER	FBUB	RS	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP2	6	6
1	ER	FBUB	RS	EU/AC	yes	UCHC	US	TC	yes	WP1	26	3
1	ER	FBUB	RS	EU/AC	yes	University of Chicago	US	TC	yes	WP1	17	2

Staff member ID	Staff member profile	Sending Org. (Short Name)	Sending Org. (Country)	Sending Org. (Region)	Sending Org. (Academic Sector)	Seconded to Org. (Short Name)	Seconded to Org. (Country)	Seconded to Org. (Region)	Seconded to Org. (Academic Sector)	Work package number	Secondment Starting month	Duration of secondment (researcher-months)
1	ER	FBUB	RS	EU/AC	yes	LANOTEC-CENAT-CONARE	CR	TC	yes	WP1	39	1
2	Technical_staff	FBUB	RS	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP2	12	10
3	ER	FBUB	RS	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP3	28	10
4	ADM	FBUB	RS	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP3	31	6
5	ER	FBUB	RS	EU/AC	yes	Argenit	TR	EU/AC	no	WP2	12	3
5	ER	FBUB	RS	EU/AC	yes	University of Chicago	US	TC	yes	WP1	18	3
5	ER	FBUB	RS	EU/AC	yes	LANOTEC-CENAT-CONARE	CR	TC	yes	WP1	25	3
5	ER	FBUB	RS	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP3	36	3
6	ER	FBUB	RS	EU/AC	yes	Argenit	TR	EU/AC	no	WP2	11	6
7	ESR	FBUB	RS	EU/AC	yes	Argenit	TR	EU/AC	no	WP1	31	12
8	ESR	FBUB	RS	EU/AC	yes	UCHC	US	TC	yes	WP1	23	7
9	ESR	FBUB	RS	EU/AC	yes	University of Chicago	US	TC	yes	WP1	17	12
10	ER	FBUB	RS	EU/AC	yes	LANOTEC-CENAT-CONARE	CR	TC	yes	WP1	25	10
11	ESR	UEF	FI	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP2	9	6
12	ER	UEF	FI	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP2	12	2
13	ER	YEDITEPE	TR	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP1	15	9
14	ER	YEDITEPE	TR	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP2	34	9
16	ER	ELVESYS	FR	EU/AC	no	LANOTEC-CENAT-CONARE	CR	TC	yes	WP2	43	1
17	ER	ELVESYS	FR	EU/AC	no	University of Chicago	US	TC	yes	WP2	22	1
18	ER	Argenit	TR	EU/AC	no	FBUB	RS	EU/AC	yes	WP1	7	6
18	ER	Argenit	TR	EU/AC	no	FBUB	RS	EU/AC	yes	WP2	34	6
19	ESR	Argenit	TR	EU/AC	no	FBUB	RS	EU/AC	yes	WP1	10	9
20	ER	LANOTEC-CENAT-CONARE	CR	TC	yes	FBUB	RS	EU/AC	yes	WP1	17	6
21	ESR	LANOTEC-CENAT-CONARE	CR	TC	yes	FBUB	RS	EU/AC	yes	WP1	10	9
22	ER	FBUB	RS	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP1	28	10
23	Technical_staff	FBUB	RS	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP1	9	10
24	ESR	FBUB	RS	EU/AC	yes	Argenit	TR	EU/AC	no	WP2	19	12
25	ESR	YEDITEPE	TR	EU/AC	yes	ELVESYS	FR	EU/AC	no	WP1	34	9
6	ER	FBUB	RS	EU/AC	yes	UCHC	US	TC	yes	WP1	28	6
10	ER	FBUB	RS	EU/AC	yes	Argenit	TR	EU/AC	no	WP2	19	2
26	ER	FBUB	RS	EU/AC	yes	University of Chicago	US	TC	yes	WP1	17	2

Plan for reporting period 1

Staff member ID	Secondment Starting month	Duration of secondment (researcher-months)	Period 1																							
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
1	6	6						■	■	■	■	■	■													
1	26	3																								
1	17	2																	■	■						
1	39	1																								
2	12	10												■	■	■	■	■	■	■	■	■	■			
3	28	10																								
4	31	6																								
5	12	3												■	■	■										
5	18	3																		■	■	■				
5	25	3																								
5	36	3																								
6	11	6											■	■	■	■	■	■								
7	31	12																								
8	23	7																							■	■
9	17	12																	■	■	■	■	■	■	■	■
10	25	10																								
11	9	6									■	■	■	■	■	■										
12	12	2												■	■											
13	15	9															■	■	■	■	■	■	■	■	■	
14	34	9																								
16	43	1																								
17	22	1																						■		
18	7	6							■	■	■	■	■	■												
18	34	6																								
19	10	9										■	■	■	■	■	■	■	■	■						
20	17	6																	■	■	■	■	■	■		
21	10	9										■	■	■	■	■	■	■	■	■						
22	28	10																								
23	9	10									■	■	■	■	■	■	■	■	■	■						
24	19	12																			■	■	■	■	■	■
25	34	9																								
6	28	6																								
10	19	2																			■	■				
26	17	2																	■	■						

Plan for reporting period 2

Staff member ID	Secondment Starting month	Duration of secondment (researcher-months)	Period 2																							
			25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
1	6	6																								
1	26	3		■	■	■																				
1	17	2																								
1	39	1															■									
2	12	10																								
3	28	10				■	■	■	■	■	■	■	■	■	■											
4	31	6							■	■	■	■	■	■												
5	12	3																								
5	18	3																								
5	25	3	■	■	■																					
5	36	3												■	■	■										
6	11	6																								
7	31	12							■	■	■	■	■	■	■	■	■	■	■	■						
8	23	7	■	■	■	■	■																			
9	17	12	■	■	■	■																				
10	25	10	■	■	■	■	■	■	■	■	■	■														
11	9	6																								
12	12	2																								
13	15	9																								
14	34	9										■	■	■	■	■	■	■	■	■						
16	43	1																			■					
17	22	1																								
18	7	6																								
18	34	6										■	■	■	■	■	■									
19	10	9																								
20	17	6																								
21	10	9																								
22	28	10				■	■	■	■	■	■	■	■	■	■											
23	9	10																								
24	19	12	■	■	■	■	■	■																		
25	34	9										■	■	■	■	■	■	■	■	■						
6	28	6				■	■	■	■	■	■															

Staff member ID	Secondment Starting month	Duration of secondment (researcher-months)	Period 2																							
			25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48
10	19	2																								
26	17	2																								

1. Project number

The project number has been assigned by the Commission as the unique identifier for your project. It cannot be changed. The project number **should appear on each page of the grant agreement preparation documents (part A and part B)** to prevent errors during its handling.

2. Project acronym

Use the project acronym as given in the submitted proposal. It can generally not be changed. The same acronym **should appear on each page of the grant agreement preparation documents (part A and part B)** to prevent errors during its handling.

3. Project title

Use the title (preferably no longer than 200 characters) as indicated in the submitted proposal. Minor corrections are possible if agreed during the preparation of the grant agreement.

4. Starting date

Unless a specific (fixed) starting date is duly justified and agreed upon during the preparation of the Grant Agreement, the project will start on the first day of the month following the entry into force of the Grant Agreement (NB : entry into force = signature by the Commission). Please note that if a fixed starting date is used, you will be required to provide a written justification.

5. Duration

Insert the duration of the project in full months.

6. Call (part) identifier

The Call (part) identifier is the reference number given in the call or part of the call you were addressing, as indicated in the publication of the call in the Official Journal of the European Union. You have to use the identifier given by the Commission in the letter inviting to prepare the grant agreement.

7. Abstract

8. Project Entry Month

The month at which the participant joined the consortium, month 1 marking the start date of the project, and all other start dates being relative to this start date.

9. Work Package number

Work package number: WP1, WP2, WP3, ..., WPn

10. Lead beneficiary

This must be one of the beneficiaries in the grant (not a third party) - Number of the beneficiary leading the work in this work package

11. Person-months per work package

The total number of person-months allocated to each work package.

12. Start month

Relative start date for the work in the specific work packages, month 1 marking the start date of the project, and all other start dates being relative to this start date.

13. End month

Relative end date, month 1 marking the start date of the project, and all end dates being relative to this start date.

14. Deliverable number

Deliverable numbers: D1 - Dn

15. Type

Please indicate the type of the deliverable using one of the following codes:

R	Document, report
DEM	Demonstrator, pilot, prototype
DEC	Websites, patent fillings, videos, etc.
OTHER	
ETHICS	Ethics requirement
ORDP	Open Research Data Pilot

16. Dissemination level

Please indicate the dissemination level using one of the following codes:

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

PU	Public
CO	Confidential, only for members of the consortium (including the Commission Services)
EU-RES	Classified Information: RESTREINT UE (Commission Decision 2005/444/EC)
EU-CON	Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC)
EU-SEC	Classified Information: SECRET UE (Commission Decision 2005/444/EC)

17. Delivery date for Deliverable

Month in which the deliverables will be available, month 1 marking the start date of the project, and all delivery dates being relative to this start date.

18. Milestone number

Milestone number:MS1, MS2, ..., MSn

19. Review number

Review number: RV1, RV2, ..., RVn

20. Installation Number

Number progressively the installations of a same infrastructure. An installation is a part of an infrastructure that could be used independently from the rest.

21. Installation country

Code of the country where the installation is located or IO if the access provider (the beneficiary or linked third party) is an international organization, an ERIC or a similar legal entity.

22. Type of access

VA	if virtual access,
TA-uc	if trans-national access with access costs declared on the basis of unit cost,
TA-ac	if trans-national access with access costs declared as actual costs, and
TA-cb	if trans-national access with access costs declared as a combination of actual costs and costs on the basis of unit cost.

23. Access costs

Cost of the access provided under the project. For virtual access fill only the second column. For trans-national access fill one of the two columns or both according to the way access costs are declared. Trans-national access costs on the basis of unit cost will result from the unit cost by the quantity of access to be provided.

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

Marie Skłodowska-Curie Actions (MSCA)
Research and Innovation Staff Exchange (RISE)
H2020-MSCA-RISE-2017

Project Acronym: AUTOIGG – Project Number: 778405
Annex 1 to the Grant Agreement
(Description of the Action)
Part B

Table of contents

2. Excellence

2.1. *Quality and credibility of the research/innovation project; level of novelty and appropriate consideration of inter/multidisciplinary, intersectoral and gender aspects*

The objectives addressed will be:

- Development of experimental cellular models and procedures with immunoglobulins (IgGs) from patient sera as diagnostic and prognostic technologies related to neurodegenerative diseases, NDs (particularly based on amyotrophic lateral sclerosis - ALS research).
- Defining mark-up characteristics of the standardized in vitro approach for personalized diagnostic protocols for NDs.
- Design of a small-scale platform based on automated fluorescence microscopy.

These objectives are based on previous studies on ALS of the Belgrade group, however the project also proposes to study the applications on other neuroinflammations and neuroinflammatory conditions. This addresses a relevant S&T as well as a socioeconomic medical issue. As can be evidenced by literature search it is the right timing for solving this research challenge towards application by means of networking.

Background studies on ALS

In ALS, production of anti-neuronal IgGs is a significant feature of the immune-inflammatory process. Early studies have shown that human IgGs increase intracellular Ca^{2+} in motor neurons, enhance the glutamate release from synapses residing on lower motor neurons and enhance the release of acetylcholine from the axon terminal at the neuromuscular junction – results being confirmed and further studied also in later years. These crucial events in our own early experiments showed diversity and non-cell autonomous characteristics with effects recorded not only from non-motoneuronal cells (facilitation of synaptic activity and Ca^{2+} transient change) but also on astroglia (Ca^{2+} transients, vesicle trafficking).

Proposed relevance of research and innovation

The idea to use IgGs for *in vitro* diagnostics in NDs is genuinely novel. Based on previous experimental results (see references above) it offers a robust multipurpose processing of a single sample on cell cultures that can give a complex information based on different cellular signalling responses as recorded by electrophysiology/voltage sensitive dyes or fluorescent imaging of Ca^{2+} and ROS generation. This experimental technology will be translated by the SMEs in the project to a clinical platform/devise design based on automated microscopy to be used for point-of-care personalized diagnostics. Standardization of *in vitro* culture media as well as of the multidisciplinary data analysis methodology will improve the performance of diagnosis, prediction, monitoring, intervention or assessment of therapeutic response, with a significant impact on clinical decisions and health outcomes for each ND patient individually. Particular attention will be given to the prediction value of this *in vitro* diagnostics procedure for early diagnostics followed by genetic markers or comorbidities.

Although a vast literature exists on successful preclinical and even on some clinical studies of ALS therapy, this is still a fatal disease without a reliable cure. Often patients being conscious throughout the illness are demanding euthanasia. It is a consensus among researchers and clinicians alike that such a poor prognosis is caused because there is a lack of a robust diagnostic tool that can primarily predict but also follow the therapeutic procedure. **The proposed work is thus highly ambitious and ground breaking in its goal to offer such a tool that can prolong lives and add quality of life and aging to a significant population of patients.** Since ALS is in 90% of cases of sporadic nature the main problem is to recruit patients for screening early enough. This will be achieved first by screening patients for comorbidities (e.g. FTD or muscle cachexia) or recruiting them based on

genetic or proteomic markers (e.g. TDP-43 and FUS/TLS genes) in order to subject them to a **robust point-of-care diagnostics platform** for prediction of disease and/or its stage and later for the follow-up of therapy. Such a multifactorial diagnostic tool is expected to offer a personalized approach to the disease and better patient stratification.

The **diagnostic process of ALS IgG application on stained cell** cultures for an automated recording system is of a **highly innovative potential.** Although experimentally confirmed and used in describing ALS pathogenesis, such phenomena were never used so far in practical terms. Standardizing the procedure for a market pilot will lead to an innovation that could be linked to the *published and patented technology of automated microscopy* (De La Torre-Bueno & McBride, US Patent US 7,272,252, 2007; Gough et al. US Patent US 8,597,899, 2013) for **multidimensional cell profiling for personalized diagnostics**. This approach should lead to the *pilot platform for high-throughput multidimensional cell profile analysis upon ALS IgG challenge*. In such a setup the multivariate single-cell analysis is a starting point for identifying relationships among ALS IgG effects at a systems level and a step toward phenotypic/physiological profiling at the single-cell level.

R & I of this project will outline the relevance of the networking, in terms of increase of interactions among scientists, common utilization of infrastructures, transfer and dissemination of knowledge, and interdisciplinarity. It offers a new approach, based on an innovative combination of state of the art methods, including standardization.

After thorough standardization of in vitro procedures these processes caused by IgGs purified from ALS patient sera will be looked in our animal cell models (cultures of neurons, astrocytes and cell lines) through electrophysiological monitoring (microelectrode array and/or voltage sensitive-dyes), Ca^{2+} and Reactive Oxygen Species (ROS) – imaging (with fluorescent probes). Using this combination of sensitive readouts, ALS IgGs will thus be tested in order to differentiate mark-ups of disease phase and severity for ***personalized*** *in vitro* diagnostics. In order to do this in a *robust point-of-care setup* an ***innovative automate microscopy system*** will be designed.

The project is based on preliminary published results by us and others that have demonstrated easily quantifiable effects of ALS IgGs on cell cultures. This research was of fundamental nature aiming to describe the pathophysiology of the disease. However, in this project we propose to use these findings for establishing **standardized personalized diagnostic technologies**.

The findings obtained with ALS IgGs as milestones for the development of the current project can be divided into the following:

a) **Synaptic activity**.

According to the excitotoxic hypothesis of ALS, overstimulation of glutamate receptors by excessive presynaptic release of glutamate induces a large and sustained increase in intracellular calcium which leads to motoneuronal death. Pathogenic Igs from ALS patients were suggested as the link between the neuroinflammation and the excitotoxic hypothesis. To test if the ALS IgG fraction can indeed affect the presynaptic glutamate release mechanisms we employed an electrophysiological approach based on whole-cell patch clamp recording of spontaneous excitatory postsynaptic currents in rat hippocampal neurons in culture. ALS IgGs (0.1 mg/ml) were focally applied by pressure puffs through a glass pipette placed 100 μm above the patched cell. The main result was **a rise in frequency of post-synaptic currents with ALS IgGs** but not with IgGs from healthy or disease controls. This effect was also proven to be presynaptic. It will be the goal of this project to correlate quantitative parameters of this ALS IgG-induced electrophysiological activity (as the functional biomarker of ALS) with disease specific parameters (ALSFRS, gender, age, duration of the disease and type – spinal/bulbar). The later will be done through long lasting on-going collaboration of neurologists at the Clinical centre of Republic of Serbia in Belgrade recruited through the on-going National project – see below). In addition, more robust technologies of electrophysiological recordings such as the microelectrode array (MEA) or voltage sensitive dyes will be explored.

b) **Ca^{2+} imaging**.

Ca^{2+} imaging with fluorescent dyes gained information on intracellular calcium mobilization in response to ALS IgGs on several cell types (hippocampal neuronal cultures, primary cortical astrocytes, primary microglial cells as well as motoneuronal and microglial BV-2 cell lines). We have previously shown that ALS IgGs induce typical calcium transients in astrocytes where PI3K is activated upstream of PLC. In addition, preliminary (unpublished) experiments on microglial BV-2 cell line (collaboration of Belgrade and Kuopio labs), as well as on primary hippocampal neurons have shown similar effects of ALS IgGs. We intend to explore this ALS IgGs-induced Ca^{2+}-signalling in all *in vitro* models stated above in a systematic manner, with carefully chosen IgGs (from ALS patients with different disease progression, as indicated by ALS functional rating score, ALSFRS, as well as from healthy and disease controls) in order to find the **correlation between the ALS IgGs calcium mobilizing potential (quantified by the amplitude of the Ca^{2+} spike and the integrated calcium elevation over time) and disease specific parameters.** As a corollary this applied research may also give some basic results on the second messengers in this signalling pathway in relevant *in vitro* model system that may facilitate the discovery of cell specific antigens, and consequently significantly simplify the proposed *in vitro* diagnostic technology.

c) **ROS imaging.**

Pilot experiments (collaboration between Belgrade and Kuopio lab in the framework of the recently ended COST Action – see below) on motoneuronal (NSL-34) and microglial (BV-2) cell lines transfected with ROS-sensitive fluorescent constructs HyPer 3 or CyPer have shown that in response to acute exposure to ALS IgGs, ROS signalling is induced in both Vcell lines, with an indicated correlation with disease progression (as measured by ALSFRS). We intend to gather enough data for verification of these results, and test newly available fluorescent constructs designed for site specific ROS signalling, as well as markers of oxidative stress in mitochondria (e.g. Rhodamine 123). Following quantification and estimate of the response in all *in vitro* models results will be correlated with disease parameters which could also lead to **an innovative ROS-based biomarker for the ALS disease that is known to be largely driven by abnormal ROS production.**

d) **Vesicle trafficking.**

We have previously shown that ALS IgGs increase the mobility of acidic vesicles (mostly endosomes and lysosomes) in primary cortical astrocytes, which could suggest long term modulation of endocytosis and/or autophagy. We intend to further **explore this ALS IgGs mobility enhancing effect in all *in vitro* models stated above with the goal to find correlation with disease specific parameters**. In addition, endocytosis and autophagy pathways will be investigated in detail in order to gain close insight into the overall ALS IgGs effect on cellular physiology, with the final goal to simplify the proposed *in vitro* diagnostic technology.

The above approaches evidently need to be considered as *trans-disciplinary* since biologists, physicists, physico-chemists and MDs (neurologists) need to work as a team in order to achieve the proposed methodologies. **Such interdisciplinarity is however already well seeded in the management of the National innovative integrative project** on biomarkers in neurodegeneration (coordinated in Belgrade; see below). The herewith proposed project will also employ software programmers and instrumentation designers.

The project is based on experimental work that is already published as a proof of concept (*Technology Readiness Level* - TRL 3). **The main goal of the project is to bring this concept to a higher level by validating the technology of a small-scale platform in the lab (TRL 4)** by means of standardization and benchmarking (as a necessary phase for the 'lab to market' planning). In order to create sustainability, in the final project phase, with the help of the **SME**, it is planned to propose the technology for an industrially relevant environment (TLR 5).

The work on the project will tightly be linked to the **National Innovative Integrative Research project** "Biomarkers in neurodegenerative and malignant processes" (grant #III41005 to PA) Ministry of Education, Science and Technological Development Republic of Serbia. On the other hand, the collaboration of partners (Belgrade & Kuopio) within the recently ended **COST Action BM1203 EU-ROS** will be continued and strengthened through this project. This proposal is also related and represents a reasonable continuation of a completed (2013) **ROSim Grant No 135179 Photonics Research Program** from the Finnish Academy (with 4 research groups where the Kuopio partner was the coordinator). The ROS imaging techniques optimised through the latter grant will be used within this project.

On the other hand, the participant **YEDITEPE** will bring to the project a clinically relevant immunological research practice.

Two SMEs, **ArGenit** and **ELVESYS**, will bring transectorial knowledge of entrepreneurship and marketing of scientific equipment and software. It is also expected that these participants will share the IPR knowledge with other participants.

In addition, a biophysical approach will be sought through collaboration with the Laboratory of Wim van Drongelen, University of Chicago USA (**UCHIC**) on the application of organotypic brain slices on multielectrode arrays as devices for *in vitro* diagnostics for ALS IgGs as well as with Dr. Antic's lab from University of Connecticut Health, USA (**UCONN**) on voltage-sensitive dyes.

LANOTEC with its state of the art advanced microscopy techniques (AFM, TEM, SEM) adds a complementary biophysical approach to the knowledge sharing of the project.

With one third of female principal investigators, the AUTOIGG consortium compares favourably with most research departments and collaborative networks in the field. Particular attention will be paid to the recruitment of women for secondments as ERs, and ESRs, in order to reach a **minimal 40% participation in the network**. Also, public actions at international level **promoting the participation of women in science and research** will be emphasized and supported during the training events and outreach activities in order to foster scientific vocations among young women and girls. Finally, all research projects on animals and humans delineated within the AUTOIGG program will include equal numbers of male and female subjects and will specifically look for possible sex differences in the biological or medical issues studied by the consortium. In fact, It is shown epidemiologically that there is a gender difference in the infliction of ALS and this was also demonstrated on animal models by the UEF- Kuopio beneficiary on this project. This is going to be included in hope of presenting it as *gender innovation* along with the piloting (WP 2) and sustainability phase.

2.2. *Quality and appropriateness of knowledge sharing among the participating organisations in light of the research and innovation objectives*

The approach for knowledge sharing among participants of AUTOIGG will be presented by the following:

- **A.** Secondments
- **B.** Workshops
- **C.** Training Schools

A. Secondments (see Gantt chart below)

Secondments are the main method for knowledge exchange. The coordinator, FBUB will exchange staff with ELVESYS and ArGenit for intersectorial exchange of expertise on the automated device production. FBUB will also maintain secondments to the TC USA i.e. to UCONN and UCHIC in order to pursue electrophysiology vs fluorescence. FBUB will exchange two staff members with LANOTEC (TC – Costa Rica) in order to synchronize the advanced microscopy protocols with the fluorescence probing in WG1.

Other secondments: UEF – one and YEDITEPE – two staff members will exchange with ELVESYS staff in order to further the expertise in designing the chamber of the automatic system and to validate IgG effects measurement, respectively.

Workshops (Tables 1-3)

Three workshops will be hosted by YEDITEPE in Istanbul. Lecturers will be recruited from Academia and SMEs as well. Two workshops will deal with the fundamentals of the scientific goals of the project - immunology and detection methods for the IgGs and their effects. These workshops will also address the main R & I goal of the project – the automatic system for fluorescent detection of neurodegenerative IgG effects. The third workshop will be organized in the first year of the project and will deal with an important soft skill – Good laboratory practice. In fact, the host, YEDITEPE will be instrumental in preparing the GLP compliant manual for AUTOIGG.

WORKSHOP 1: GOOD LABORATORY PRACTICE (GLP) IN RESEARCH PROJECTS (Month 13)

Organizing Committee: One person from each beneficiary

Venue: Yeditepe University, Rectorate Building, Atasehir, Istanbul, Turkey

PROGRAM		
Time	**Topic**	**Lecturer/Teacher**
Day 1		
09:00-09:20	Welcome and introduction (Pre-workshop questionnaire)	Gulderen Yanikkaya Demirel, Pavle Andjus
09:20-09:50	OECD Principles of GLP	TBA
09:50-10:20	EU regulation on GLP	Authority from EU Commission
10:20-10:40	Coffee break	
10:40-11:10	Resources for GLP (Management/Personnel/Facilities)	TBA (SME representative)
11:10-11:40	Rules for GLP in Research	Gulderen Yanikkaya Demirel
11:40-12:10	How to Handle Results in Research Projects Conforming into GLP	TBA (SME representative)
12:10-13:30	Lunch Break	
13:30-16:15	Small Group Study on Quality Assurance of Research Projects	Pavle Andjus, Gulderen Yanikkaya Demirel
16:15-16:30	Coffee break	
16:30-18:00	Presentations of Small Groups Studies	
18:00-18:15	Concluding Remarks	
Day 2		
09:20-09:50	Notes from the first GLP Workshop	Gulderen Yanikkaya Demirel
09:50-10:20	GLP and Multi-Site Studies	TBA
10.20-10.40	Coffee break	
10.40-11:10	GLP and Computerized Systems	TBA (SME representative)
11:10-11:40	Characterization of Test and Test Systems	TBA (SME representative)

11:40-12:10	GLP and *in vitro* Studies	Gulderen Yanikkaya Demirel
12:10-13:30	Lunch break	
13:30-14:00	How to prepare for an inspection	Pavle Andjus, Gulderen Yanikkaya Demirel
14:00-14:30	Archiving of Research Results	TBA (SME representative)
14:30-15:00	Monitorisation of Research Studies and GLP	TBA
15:00-15.30	Coffee break	
15:30-16:00	Feed-back from the attendees	
16:00-16:30	Post Workshop Questionnaire	
16:30-17:00	Close up and remarks	

WORKSHOP 2: UPDATE on IMMUNOLOGY OF AUTOANTIBODIES (Month 21)

Organizing Committee: One person from each beneficiary

Venue: Yeditepe University, Rectorate Building, Atasehir, Istanbul, Turkey

PROGRAM		
Time	**Topic**	**Lecturer/Teacher**
09:00-09:20	Welcome and introduction	Gulderen Yanikkaya Demirel
09:20-09:50	Autoantibodies and their use in clinical decision making	Sule Yavuz
09:50-10:20	Principles of autoantibody detection	Ishak Tekin
10:20-10:40	Coffee break	
10:40-11:10	Current Biophysical Techniques for Antibody Effects detection	Pavle Andjus
11:10-11:40	Guidelines for Autoantibody Testing	Gulderen Yanikkaya Demirel
11:40-12:10	Future of Autoantibody Detection	TBA
12:10-13:30	Lunch break	
13:30-15:30	Small Group Hands on Training on IFA method*****	Pavle Andjus, Gulderen Yanikkaya Demirel
13:30-15:30	Small Group Hands on Training on Line Blot assays*****	TBA
15:30-16:00	Coffee break	
16:00-17:30	Presentations of Small Group Outcomes	
17:30-18:00	Concluding Remarks	
***** There will be rotations between the groups		

WORKSHOP 3: EVALUATION of AUTOANTIBODY DETECTION and THE NEWLY DEVELOPED AUTOMATIC MEASUREMENT DEVICE (Month 34)

Organizing Committee: One person from each beneficiary

Venue: Yeditepe University, Rectorate Building, Atasehir, Istanbul, Turkey

PROGRAM		
Time	**Topic**	**Lecturer/Teacher**
09:00-09:20	Welcome and introduction	Gulderen Yanikkaya Demirel
09:20-09:50	Recent developments in autoantibody detection	Haner Direskeneli
09:50-10:20	Introduction of the new automated system	Pavle Andjus
10:20-10:40	Coffee break	
10:40-11:10	Advantages of using POC testing for autoantibody detection	TBA
11:10-11:40	TBD	SME representative
11:40-12:10	Future of Autoantibody Detection	TBA
12:10-13:30	Lunch break	
13:30-15:30	Small Group Hands on Training on new system	
15:30-16:00	Coffee break	
16:00-17:30	Feedback from the participants	
17:30-18:00	Concluding Remarks	

C. Training Schools (Tables 4-5)

Two Training Schools will be organized by UEF: one on free radical (ROS) monitoring – essential for one of the tasks in WG1, and one on inducible pluripotent stem cells (iPSCs) and their applications - as an alternative model for the proposed automated recording platform. The Schools host, UEF is in the forefront of stem cell research in Europe as well as in the field of ROS science and detection.

TRAINING SCHOOL 'Mitochondria and ROS signalling' (Month 6)

PROGRAM		
Time	**Topic**	**Lecturer/Teacher**
09:00-09:15	Opening the meeting	
09:15-10:00	Mitochondria as generators of ROS	Andrei Abramov (UCL)
10:00-10:30	ROS induction of ALS IGGs	Pavle Andjus (UB)
10:30-11:00	Redox imaging in neurodegenerative disorders	Pier G Mastroberardino (Rotterdam)
11:00-11:45	Workshop: New applications of the multiphoton microscopy for imaging mitochondria	Leonard Khiroug (U Hki)
11:45-12:15	Mitochondrial production of reactive oxygen species	Gundars Goldsteins (UEF)
12:15-13:00	Lunch break	

13:00-13:30	The role Nrf2 and downstream enzymes in prevention of the oxidative stress primary human retinal pigment epithelium	Anna-Liisa Levonen (UEF)
13:30-14:00	ROS and NOS signalling in modulation of pain stranding ion channels	Rashid Giniatullin (UEF)
14:00-14:30	Diet, antioxidant and ER stress	Mustafa Atalay (UEF)
14:30-15:00	Mechanisms of oxidative stress by microglia	Tarja Malm
15:00-15:30	Sensitivity of mitochondria to neurodegenerative disorders	Eugene Pryagnikov (U Hki)
15:30-15:45	Coffee break	
15:45-17:45	Laboratory demonstrations: Imaging ROS with Flow cytometry	Organized by group of Prof. Jari Koistinaho (UEF)
17:45-19:45	Laboratory demonstrations: Imaging of ROS in neurons and cell lines with pharmacological and genetically encoded ROS sensors	Organized by Prof. Rashid Giniatullin (UEF)
19:45-21:30	Dinner	

TRAINING SCHOOL 'iPSC-based stem cell research' (Month 30)

PROGRAM		
Time	**Topic**	**Lecturer/Teacher**
Day 1 (31.08.)		
09:15-09:30	Opening the meeting	Jari Koistinaho (UEF)
09:30-10:15	Plenary: 3D organoid models from induced pluripotent stem cells	Jürgen Knoblich (U Wien)
10:15-10:45	Derivation of Adult Human Fibroblasts and their Direct Conversion into Expandable Neural Progenitor Cells	Frank Edenhofer (U Innsbruck)
10:45-11:15	Regulation of Human Pluripotent Stem Cell-Derived Hepatic Cell Phenotype by Three-Dimensional Hydrogel Models	Sanna Lehtonen (U Hki)
11:15-12:15	Lunch, at own cost	
12:15-12:45	CRISPR/Cas9-mediate Transcriptional Activation for Maturation of Human Stem Cell derived Beta Cells	Timo Otonkoski (U Hki)
12:45-13:15	Mitochondrial DNA mutations in iPS cells: mtDNA integrity as standard iPSC selection criteria?	Riikka Hämäläinen (UEF)
13:15-13:45	Comparative proteomic analysis of human embryonic stem cell-derived and primary human retinal pigment epithelium	Heli Skottman (U Tre)
13:45-14:00	Coffee break	
14:00-14:30	Modelling Heart: Functional characterization of iPSC/ESC-derived cardiomyocytes	Pasi Tavi (UEF)
14:30-15:00	The Effects of Pharmacological Compounds on Beat Rate Variations in Human Long QT-Syndrome Cardiomyocytes	Katriina Aalto-Setälä (U Tre)

15:00-15:30	Microfluidic 3D cell culture: from tools to tissue models	Paul Vulto (Mimetas, Leiden)
15:30-16:00	Stem cells in as a tool in safety testing	Markku Pasanen (UEF)
18:30-21:00	Posters, Social Networking, Dinner	All
Day 2 (01.09.)		
08:30-09:00	3D modelling of the brain derived from human iPSCs	Katharina Kruszewski (U Innsbruck)
09:00-09:30	iPSC-derived human endothelial cells: Disease mechanisms and biomarkers in Parkinson's Disease and Schizophrenia	Sarka Lehtonen (UEF)
09:30-10:00	iPSC-derived oligodendrocytes in human diseases	Laurent Roybon (U Lund)
10:00-10:15	Coffee break	
10:15-10:45	Role of NeuroD1 in hippocampal neurogenesis	Claire Rampon (U Toulouse)
10:45-11:15	iPSC-derived human astrocytes in neurodegenerative diseases	Jari Koistinaho (UEF)
11:15-11:45	iPSC-derived microglia-like cells in Alzheimer's disease	Tarja Malm (UEF)
11:45-12:45	Lunch, at own cost	
12:45-13:15	Pathology of hiPSC-derived neurons in Alzheimer's disease	Gunnar Gouras (U Lund)
13:15-13:45	Modelling vesicular trafficking by hiPSC-derived brain cell models	Dora Brites (U Lisbon)
13:45-14:15	Neuroinflammation in human neurodegeneration: iPSC-based models	Michael Heneka (U Bonn)
14:15-14:30	Coffee break	
14:30-15:00	Altered differentiation of cells with AMPA receptors from human and mouse fragile X neural progenitors	Maija Castren (U Hki)
15:00-15:30	Development of gonadotropin-releasing hormone-secreting neurons from human pluripotent stem cells	Taneli Raivio (U Hki)
15:30-16:00	Abnormalities in iPSC-derived brain cells of violent substance abusers	Olli Kärkkäinen (UEF)
16:00-16:15	Instructions for Assays based on given articles and lectures: Wrapping up and closing	Tarja Malm (UEF)

2.3. *Quality of the proposed interaction between the participating organisations*

Beneficiaries

1. **Elvflow Microfluidic Innovation Center (**ELVESYS**)** – Paris, France (*SME, MS*) - Device design towards point of care system and diagnostic tool based on microfluidics, will also offer non-scientific soft skills (valorisation & entrepreneurship training) and help in project management and dissemination (website design)

2. **ArGenIt** (linked to the Regenerative and Restorative Medicine Research Center), Technopark of Istanbul Technical University, Turkey (*SME, AC*) – Device design and development of microscopy analysis systems; patient-derived induced pluripotent stem cells, differentiated to motor neurons, oligodendrocytes and astrocytes; stem cell derived cultures for modeling diseases and search for phenotypes.
3. **Yedıtepe University School of Medicine** (YEDITEPE) - Immunology Department, Istanbul, Turkey (*Academic, AC*) – will provide patient samples from different disease groups; patients antibody testing; standardization and method evaluation; Good Laboratory Practice manual for the project; links to SMEs
4. **Dept. Neurobiology, A. I. Virtanen Institute University of Eastern Finland** (UEF) Kuopio (*Academic, AC*) - Fluorescence-probe imaging of ROS signalling and electrophysiology. Expertise in iPSC characterization and applications.
5. **The National Laboratory of Nanotechnology** (LANOTEC) – San Jose, Costa Rica (*TC partner eligible for funding*) – Complementary testing to the fluorescence microscopy analysis and proposing further analysis (AFM, hrTEM, SEM)

Partners

6. **University of Connecticut Health Center** (UCONN), Farmington, USA (*TC*) – Know-how in voltage-sensitive dyes
7. **Dept. Pediatrics, Pritzker School of Medicine, The University of Chicago** (UCHIC), Chicago, USA (*TC*) – Know-how in Microelectrode arrays (MEA) and big data electrophysiology.

All of these participants will interact through the secondments programme (see 2.2A) while participants #3 (YEDITEPE) and #4 (UEF) will be hosting workshops and training schools that rely on their expertise as stated above.

The mobility programme (see 2.2A) involves all participants and is designed around tasks of WG1 and 2. Intersectorial exchange is planned between the academic MS/AC institutions (FBUB, YEDITEPE, UEF) and the two SMEs (ELVESYS and ArGenit). The main goals for these secondments is to exchange experience and know-how on entrepreneurship on one side and translational product development on the other. The staff members of SMEs will also visit Academic participants in order to learn the basic biophysical mechanisms to be exploited in the innovative measuring device. International secondment is also planned with the three TC partners. UCONN will host an ESR followed by an ER from FBUB in order to transfer know-how on its renown expertise in voltage-sensitive dyes as well as the knowledge in optical devise set-ups. Likewise, UCHIC will be the host for know-how on MEA technology. Thus, both of these TC visits are justified for the design of the electrophysiological basis of the proposed measuring device. Regarding LANOTEC since this is a TC legible for funding there will be planned exchanges with FBUB staff in order to exchange expertise in the subcellular markers (also explorable with high resolution advance microscopy techniques at the TC partner) of the observed basic effects of pathological IgGs (to be presented by FBUB as the host).

Two participants #3 (YEDITEPE) and #4 (UEF) will be hosting three workshops and two training schools (see 2.2 B & C, respectively) that are based on their experience as stated above. The staff members of the participant beneficiaries will take part at the workshops and trainings. These workshops as well as trainings will be focused on different aspects of cellular neuroimmunological phenomena to be followed with the proposed device.

The meetings of the Supervisory board organized twice a year will be an opportunity for all beneficiaries to monitor and eventually revise and update the project plan (research, networking and finances). During these meetings, outreach activities will also be planned and evaluated.

Networking with patient organizations through the Supervisory board will bring an added value and a societal dimension to the project.

3. Impact

3.1. *Enhancing the potential and future career perspectives of the staff members*

The project will be open to multidisciplinary staff profiles – biologists, physicists, physical chemists, physicians, technicians, administrators, entrepreneurs. By joining these profiles under the AUTOIGG project we will create conditions for transectorial careers. This will be reinforced through reciprocal secondments between the sectors but also within the Academic sector taking care of different expertise (e.g. neurologist MD vs biologist PhD; biologist PhD vs software designer, academic administrator vs entrepreneur…). It is intended to engage existing staff for secondments but also to recruit new staff in case there will be a lack of some profiles and/or expertise. These new skills will be further strengthened through workshops and training schools. New staff members will thus be offered a career plan (as drafted by the Secondment Committee) for the integration at the host institution after the ending of the grant.

3.2. *Developing new and lasting research collaborations, achieving transfer of knowledge between participating organisations and contribution to improving research and innovation potential at the European and global levels*

This consortium was formed through a NCP-based partner search. A form describing the FBUB Centre in Belgrade and the basics of the project proposal were posted online and the responses collected. A questionnaire was then sent to all relevant organizations. Based on the responses to the questionnaire a selection of organizations was made and these were invited to form the consortium and to start writing their part in the proposal. Thus, except for the previous relationships of FBUB and UEF and TC organizations from USA (UCONN and UCHIC) the partnerships within the consortium are all new. The participants of AUTOIGG are thus carefully selected through a two stage process. The main criteria for the selection of collaborations was based on complementarity of expertise as well as on interdisciplinarity. This selection will be strengthened through the envisaged intersectorial and international secondments reinforced trough a rich programme of workshops and trainings. The main goal of the project – to design a prototype of an automatic diagnostic device for neuroegenerative diseases gathered all participants each demonstrating a particular role and expertise. This engagement of complementary expertise also guarantees a sustained collaboration after the ending of the project period, thus strengthening the European innovation capacity.

The project aims to design a biomedical device for the automatic evaluation of diagnostic potential of ALS IgGs primarily employing primary astrocytes and neurons in culture. There are several lines of this project that will allow for a sustained partnership.

1. This innovative device offers a wider field of applications in respect to possible neurodegenerative / neuroinflammatory phenomena as well as other plated cell populations (stem cells, cell lines etc).
2. The design of the device within the project is planned to reach the prototype level. However, the study of the market and the creation of a business plan for the device production and exploitation needs a sustained collaboration between the academic and SME participants.
3. The project research topics open a new filed of neuroimmunological basic studies to pursue among the academic partners of the AUTOIGG after its completion.

Although the effects of ALS IgGs are well studied and documented in the Belgrade laboratory and elsewhere the process of IgG application for *in vitro* **diagnostics of ALS is completely novel** and **offers a practical multidimensional functional analysis for personalized medicine**. Thus, based on a standard clinical blood sample and upon routine serum separation and IgG purification one can

obtain under an automated microscope actually a pattern of activities in the form of fluorescence intensities in time and space thus establishing a *signature of disease for the individual patient*. The combining of several recording modes raises **the reliability of the obtained diagnostic pattern** still **keeping the cost of the setup effectively low** (main cost is for fluorescent dyes and culture media).

On the other hand, this procedure can give **early diagnosis of ALS** since it has been shown that inflammation markers appear early in the disease model (Beers et al. Proc Natl Acad Sci U S A. 2008 105:15558). The complex multifactorial nature of ALS underlines the need for a personalized treatment and patient stratification. It is strongly believed that the multivariate single-cell analysis offered by the proposed *in vitro* diagnostic technology may present exactly the adequate approach for the **personalized patient care of such a multifocal disease**. At the same time the pattern analysis of the multivariate single-cell response allows for **a robust point-of-care diagnostics necessary for improved and efficient clinical decisions.**

The project will contribute to the *sustainability of the health care* of ALS patients by drafting and planning a large-scale prototype in an operational environment. In addition, the designed personalized diagnostics technology of *in vitro* testing of IgGs from patient sera can be proposed for other motoneuron and neuroinflammatory neurodegenerative processes, thus allowing for **sustainability of the health care system in the particular area of neuroinflammation** as the common mechanism of neurodegenerative diseases.

The proposed project will rise an opportunity not just for the partner **SME** to deliver innovation to the market but also for other **SMEs** that could contribute to the upgrade and strengthening of the designed technology in its many aspects from standardized cell culturing to the hardware and software design for automated microscopy, thus potentially opening new job positions.

3.3. *Quality of the proposed measures to exploit and disseminate the project results*

Publications and scientific meetings. After the IP potential has been evaluated, data and results will be made public through the standard scientific community approaches: scientific and public meetings, posters, high impact publications in peer-reviewed journals. Thesis and dissertation publication of data will be permitted, and specific clause to address this included in the consortium agreement.

Governments and Ministries of Health and Science. These public stakeholders will be addressed by younger researcher with the final goal of reaching the patients. Contacts of developed centres with patient organizations will be particularly emphasized and translated to the emerging centres and their public stakeholders lacking this experience. Thus, a wider transitional societal impact will be attained.

Patients associations. The project participants will take an active part in the dissemination of findings to patients associations. It will be required that they make contact with one patient organizations during the course of the project and that they maintain a regular communication through their representatives. This will be done through the distribution of newsletters and flyers and through the invitation of local patients organizations and patient support groups to the annual meetings of the consortium. The contact with patient groups is of particular interest for emerging countries where this public initiative is just starting.

Press releases. Additionally, publicity to a wider audience will be performed by press release, at the local and national level, interfacing with already contacted publishing desks dedicated to EC programmes (egs. https://danube-inco.net/documents or Projects by British publishers). Existing experience and previous project of partners with TV stations and science programmes will be specifically utilized for this purpose.

Public engagement. Most of the partners belong to institutes that have public engagement plans linked to national (governmental) or international (IBRO, FENS) organizations, such as the

Edu(cational)-Fair, Science fair, NENS Job Fair or Brain Awareness Week. The project will use these links to disseminate its activities to a wider audience. Young researchers funded by AUTOIGG will be required to participate to at least one outreach event during the course of the project. A special initiative named Science and the City will be negotiated with public places of leisure such as town cafes or exhibit halls. It will consist of popular presentations by fellows and experts of science networking for the benefit of society.

***Web site*.** The project will develop a website, based on those the partners have produced for other EU projects and networks. This will be used for internal communication within the network, and will have public area for dissemination of discoveries from the project. The website will be linked to the regional site Danube-inco.net

- A very important dissemination and communication tool will be the web site of AUTOIGG. Besides classical features in line with EC recommendation (i.e., direct links to individual web sites of the partners with information on training activities, recent project developments, and vacancies), the web site shall be central to the dissemination and communication strategy of AUTOIGG. The web site will support an internal interactive communication platform (DokuWiki architecture) as well as an external interactive web tutorial (MediaWiki architecture). In detail this includes:
- Forum for the partners, ER and ESR (membership access only);
- Project-based and scientist-based task pages to facilitate management of closely interlaced multi-host activities (membership access wiki);
- Web tutorial for the underlying experimental protocols, their application and data analysis (this will involve the active participation of many of the partners); AUTOIGG will explore novel collaborative publication techniques via the internet (open access wiki);
- Popular science pages explaining results and problems to the general public and lists of open questions in fields related to the Network.

This area will be the specific responsibility of the Supervisory Board. A critical aspect of the project will be to ensure the protection of IPR without preventing neither creation of new knowledge nor the dissemination of that knowledge to other sectors. IPR activities will comprise: assuring the protection of IPR where appropriate; to promote exploitation via license and patents where appropriate; to maintain an updated list of IPR belonging to each of the partners and generated in the frame of this project; to assist partners in the consortium in any conflict with respect to the IPR with a party outside the consortium.

3.4. *Quality of the proposed measures to communicate the project activities to different target audiences*

Key objectives

- To communicate to key stakeholders the existence of the project and provide regular updates on new data generated
- To ensure that the general population is aware of the impact that the **AUTOIGG** research and innovation has on the community as a whole

Dissemination and promotional activities will include: creating **AUTOIGG** logo, brochure, poster and a web site with web page Forum and a potential Partner list and electronic newsletters, press releases and involving external scientists and SME representatives at project meetings. Considerable efforts will be undertaken regarding interactions with end-users (patients, patient associations, clinicians and other professionals) and the public, addressing new knowledge in neuroscience research and questions arising from its potential application. Senior researchers, in particular, are expected to take a lead in ensuring that research is fruitful and that results are made accessible to the public as well as how they should be exploited commercially. *All this will ensure a*

*continuous process concordant with the European Charter for Researchers, which will enhance visibility and exposure of the **AUTOIGG** initiative, the outcomes and achievements to key end-users at national, regional and international level, and develop general management principles and techniques even beyond the field of neuroscience research.*

Description of work

Every effort will be made to disseminate the existence of the project, creation of an active Academia + SME consortium, its progress and scientific data to as wide an audience as possible.

Publications and scientific meetings. After the IP potential has been evaluated, data and results will be made public through the standard scientific community approaches: scientific and public meetings, posters, high impact publications in peer-reviewed journals. Thesis and dissertation publication of data will be permitted, and specific clause to address this included in the consortium agreement.

Governments and Ministries of Health and Science. The staff and young researchers within the AUTOIGG consortium will take an active part in the dissemination of findings to these public stakeholders with the final goal of reaching the patients. Contacts with patient organizations will be particularly emphasised. Thus a wider transitional societal impact will be attained. This will be done through the distribution of newsletters and flyers and through the invitation of representatives of public stakeholders to the annual meetings of the consortium.

Press releases. Additionally, publicity towards a wider audience will be performed by press release, at the local and national level, interfacing with publishing desks dedicated to EC programmes (egs. see-science.eJournal/wbc-inco.net or Projects by British publishers). Existing experience and previous project of partners with TV stations and science programmes will be specifically utilized for this purpose.

Public engagement. Most of the partners belong to institutes that have public engagement plans linked to national (governmental, National Brain Council) or international (IBRO, FENS, European Brain Council) organizations, such as the *Edu(cational)-Fair*, *Science fair*, *FENS Job Fair* or *Brain Awareness Week*. The project will use these links to disseminate its activities to a wide audience. This effort will be led by senior researchers but young researchers will also be required to participate to the outreach events during the course of the project. A special initiative named *Science and the City* will be negotiated with public places of leisure such as town cafes or exhibit halls. It will consist of popular presentations by fellows and experts of science networking for the benefit of society.

Website. The project will develop a website, based on those that the partners have produced for other EU projects and networks. This will be used for internal communication within the network, and will have public area for dissemination of discoveries from the project.

AUTOIGG dissemination programme – i.e. **Plan for disseminating and exploiting the project's results -** *intends to continuously and systematically expose knowledge, excellence and project results to the widest possible audience for the **benefit of all end-users at national, regional and international level**.*

- The workshops and congresses planned to be organised will present *the main contribution to the dissemination of knowledge, spreading excellence and exploiting results.*
- The project Web site will be the e-base of the project dissemination strategy (newsletter, Forum, Partner list).
- ***Measures of success*** will be clear, relevant and recognizable communication (*transparency*), delivery of the right message to the targeted group (*focus*), effective delivery mechanism for each message (*effectiveness*) and a feedback system to determine effectiveness (*feedback*).

- **AUTOIGG *target groups (end-users)*** will be young scientists, expert neuroscientists, general physiologists, photonics experts, faculties in the region, research centres, SMEs, neurologists, patients & patient associations and general public.

The strengthening and setting up of a multipurpose biomedical imaging capacity of **FBUB,** within the WB region presents a strategic benefit that opens the research area of the region to the ***development of science and education*** and also brings ***jobs and better career opportunities to EU***. Once set-up, the hi-tech biomedical imaging instrumentation will serve as a necessary *interdisciplinary facility* opened to be used *even beyond neuroscience/neurology* e.g. in field of immunology of inflammation.

- ***FBUB** will* **further develop contacts** *with centres of excellence in the region and EU that were already established through different past and ongoing international biomedical programmes (COST, FP-6, FP7, TEMPUS).*
- *Data management* will be organized by a separate *ICT office* hosted by SME **ArGenit** with access to **AUTOIGG** partners and users. *Feedback on data usage* will also be collected and analysed through the **AUTOIGG** R&I council, and finally also stored on the server.
- Approved data by way of internal and external review – feedback will be put on the *Open access server*
- All research published data coming from **AUTOIGG** will be open access by *gold* or *green* standard (as decided by the R&I council).
- *Ownership and access to new knowledge* will be protected by a *Consortium agreement* that will help to pursue market opportunities by way of dissemination and communication towards SMEs and Industry. Marketing advisor(s) will be sought from **AUTOIGG** SMEs **ELVESYS** and **ArGenit** or will be particularly subcontracted for the latter purpose.
- *Management of IPR data* to be sanctioned by the above agreement(s) will first need a programme of training and education of **AUTOIGG** staff that will be organized by SMEs on the project.

Communication activities

By establishing a multidisciplinary consortium the project aims to bridge the gap between science fields but also *between theoretical and applied science* as well, that can serve the *socio-economic needs* by *supporting medical and pharmaceutical research* through planning interactions with *SMEs and Industry*.

- Complementing the knowledge and technologies within the AUTOIGG consortium *research platforms on neurodegenerative diseases* will serve as a basis for the development and dissemination of programmes within Academia and SMEs. The deliverables of such an action will be reached through inviting representatives of Pharma and Biomed Industry to AUTOIGG meetings and workshops, establishing also the consortium's role as an incubator for entrepreneurship, thus ensuring growth and sustainability of the project outcomes, and *spreading excellence towards SMEs and Industry*.
- Molecular diagnostics and therapy follow up will be promoted by the development of the complex innovative practical technique, i.e. *diagnostic protocol at the cellular imaging level*. It is also envisaged that through this dissemination, Academia + SME research units interact with the clinic (medical doctors and patients) in the process of supportive medicine build-up. It would also set grounds for further development of research and health-care system in the Region and ERA.
- Interaction with *patients associations* will be fostered through special publications about AUTOIGG and scientific achievements in dedicated journals and by participating at respective meetings.
- Special attention will be given to the dialogue with the general public. *Popular lectures and public debates* will be directed in order to raise awareness (*"Science and the City"*

programme in main cafes, open spaces, open universities, and life-long learning centres; Brain Awareness Week; National Brain Councils' events).

Through **reinforcement of Academia + SMEs research potential**, **AUTOIGG** network will ensure the **flow of expertise in the WB region and a trans-European equalization of standards** in the field of molecular physiology of neurodegenerative diseases with neuroinflammation. Once the target groups have successfully integrated within the project framework, it should be possible to envisage *further controlled expansion of the network* and ***further dissemination of knowledge and spreading of excellence*** **within ERA**.

4. Implementation

4.1. *Coherence and effectiveness of the work plan, including appropriateness of the allocation of tasks and resources*

The work will be divided in following workpackages.

WP 1. **Standardization and benchmarking (***research and demonstration***).** The experimental protocols used previously to show proof of concept will be submitted to rigorous standardization in the lab. This will start from the **selection of cell type and standardization of best practice for cell cultures and further elaborate benchmarking of protocols** for detecting (based on electrophysiology and fluorescence microscopy) and analysing the obtained parameters of cell activity (software design and testing). Patterns of correlation of the above parameters to disease stage and severity will be investigated and incorporated in the analysis software.

WP 2. Pilot platform design (*piloting***).** Design and validation of the technology of a small-scale platform in the lab. This pilot will be tested for robustness and technical feasibility in a near to operational environment. The main characteristic will be its *modulability*. The main technological basis will be an **automated microscopic stage and fluorescence detector for dynamical measurements**. This can be combined with a simple electrophysiological unit such as MEA or alternatively, voltage sensitive dyes. By means of digital conversion and analysis of these activities quantitative parameters (e.g. area under transients, halftimes of rise, frequency of events) will be extracted and *matrices of patterns* in pseudocolor related to each parameter value will be designed (see Perlman et al. *Science.* 2004 306:1194).

WP 3. Dissemination, communication and networking *(dissemination)*

Every effort will be made to disseminate the existence of the project, to create a vigorous multidisciplinary/intersectorial/transcultural research and innovation network, and to communicate its progress and scientific data to as wide an audience as possible. This will be achieved through publications and scientific meetings, addressing the stakeholders in ministries of health and science, patients associations, press releases, public engagement, website.

WP 4. Project management and sustainability (*management and prototyping*). In close collaboration with the Coordinator the project will be managed by the **SME** partner through all phases (solution design, prototyping, testing and validation) of the **developing of a small-scale prototype in the laboratory or simulated environment**. By the end of the project its sustainability will be designed based on the obtained results and drafting of a plan for a large-scale prototype in an operational environment. A wider application for related motoneuronal diseases as well as for other neuroinflammatory diseases will be investigated.

WP 5. Ethics requirements. Ethical standards and guidelines will be rigorously applied, including: technical framework and security measures for collection, processing and storage of personal and sensitive information, as well as obtaining relevant authorisations for the animal experiments. Patients sera will only be collected from persons who give informed consent, while the material will be anonymous labelled with the number code in order to protect the patient's identity. All project

participants will comply with these requirements, regardless of the country in which the research is carried out.

Each WP will have a WP leader, These will be elected at the AUTOIGG Kick-off meeting.

4.2. *Appropriateness of the management structures and procedures, including quality management and risk management*

Description of work

The main managing body is the ***Supervisory Board*** which is helped by the ***Secondments Committee*** with its ***R & I Council***.

Supervisory Board

Members

Representatives of all *AUTOIGG beneficiaries* plus one representative of *fellow ESRs* and *external members* - representative from the *INFO Office of the Ministry of Sciences* and/or the *H2020 NCP*. Representative of *patient associations* will also be invited to join the Supervisory Board for the annual conference. The Supervisory Board will also name its Ethics Advisor (see B5).

Responsibilities - General

(a) supporting the co-ordinator in fulfilling all the contractors obligations towards the EC including reporting,

(b) ensuring that all work meets functional requirements

(c) assessing progress of the secondments/training programme

(d) implementing changes in work sharing, budget and participants,

(e) reviewing of the reports regarding workshops and training schools.

(f) decides on general ethical issues and drafts with co-ordinator Ethical guidelines

(g) agreeing on press releases by the contractors with regard to the project

(h) quality control of generated data and milestones prior to reporting.

Responsibilities - Specific

a) Planning and implementation of all workshops

b) Ensuring standards and quality of the secondments/training activities

c) Receiving feedbacks from seconded fellows

d) IPR issues

Decisions

All decisions of the Supervisory Board shall be taken by *simple majority* (if at least three-quarters of the members of the contractors are present or duly represented by proxy).

Meetings

The Supervisory Board shall meet six-monthly and in principle at the request of its co-ordinator. Meetings will take place during workshops and annual meetings between the ***kick-off*** and a ***final meeting***. If necessary due to urgent matters tele- or Skype conferencing will be arranged. Extraordinary meetings may be called at any other time at the request of the co-ordinator or at the request of a quarter of the contractors. Meetings of the Supervisory Board shall constitute a quorum if more than two third of the contractors are present or duly represented by proxy.

Financial and administrative management

With the help of NCP for EC finances the project office will lead the administrative management of AUTOIGG by:

a) Providing and managing a financial plan including timely collection and preparation of the documents for EC

b) Managing resource engagement and level of integration

c) Alerts in case of non-delivery and/or default of partners

d) Coordinating management of intellectual property and dissemination

Secondments Committee

Members

A chairman and 4 other members respecting the gender balance will be appointed by the Supervisory Board within the first month of the project. At least one member will be assigned from the SME sector. One fellow member will be added from the R & I Council (see below).

The formation of this committee and its first meeting will take place at the kick off meeting of the Supervisory Board.

Decisions of the Secondments Committee:

All decisions shall be taken by simple majority. Any decision requiring a vote at a Committee meeting will be identified as such in the pre-meeting agenda, unless there is an unanimous agreement to vote on a decision at that meeting and three quarters of the members of the contractors are present or duly represented by proxy.

Meetings

The Committee shall meet every 6 months or at the request of its chairmen. Meetings will take place principally during workshops and annual meetings and if necessary by tele- or Skype - conferencing.

Responsibilities

The Secondments Committee shall coordinate the staff mobility program. They will assume overall responsibility for liaison between the seconded fellows and the Supervisory Board, and for analysing and approving the progress of each secondment project. The Secondments Committee shall be responsible for:

a) Coordinating and advising the different host institutions

b) Ensuring that all seconded project topics meet the common research goal of the consortium

c) Assessing progress of mobility projects towards a *stabile knowledge gain* for the fellows

d) Solving any problems coming up between the staff visitor and the host representative

Researcher and Innovation Council

Members

All staff from the seconded plan and headed by a fellow representative. Being the managing body of the seconded fellows it aims to provide feedback on the training activities to the senior scientists, and co-organize network-wide events. The Council will also be actively involved in the organization of fellow-days, voting for the rotation of the representative in the Supervisory Board, and construction of the web site.

Meetings

After a ‘Welcome meeting’ (on Month 8), this Council gathers yearly or if summoned by the Secondment Committee.

Recruitment strategy will be based on

- Gender balance and equal opportunities

- "Code of Conduct and the European charter" The principles of *The European Charter for Researchers & The Code of Conduct for the Recruitment of Researchers* (as of March 11, 2005) will be taken as guidelines.

Monitoring Activities *(approx. dates)*

1- at *organisational level*:

a) During **the first month**: a standardized assessment procedure will be provided at the *kick-off meeting* that will be held by the Supervisory Board. The standardized procedure will be agreed considering the following aspects: mutual recognition of secondment topics, lab and office hours, reporting, individual staff fellow differences, skills and know-how acquainted, critical evaluation of research output, fostering interaction; quantification of objectives which have been set, level of progress towards objectives.

b) At **month 15** mid-term meeting will be held. During the meeting, all the partners will review the progress of the project, identify possible problems and define contingency measures

c) At **month 47**: the final meeting will be attended by the Supervisory Board in order to present, discuss and organize the final dissemination of results

2- at *scientific level*:

a) Every **two months**: the Secondment Committee will report to the Supervisory Board on the mobility research/innovation/training progress status. Results will be discussed and eventually adjusted or modified

b) At **months 11/23/35/47**: review meetings, organized by the project co-ordinator with the Supervisory Board in order to verify and eventually adjust the hosting activities and/or approaches

c) **Yearly meetings** will be held by the Supervisory Board in order to monitor the quality of secondments and working conditions and a representative of the EC will be invited to attend these meetings.

During the entire duration of the project a call centre will be active at the project coordinating centre. Regular hosting site visits will be conducted by a member of the Supervisory Board, and a monthly conference call will be held by the Secondments Committee for monitoring progress and troubleshooting. Intranet communications will be used for sharing the Supervisory Board meeting minutes and project information as well as documents.

4.3. *Appropriateness of the institutional environment (hosting arrangements, infrastructure)*

FBUB will run the project through its Centre for laser microscopy were all the basic results have been accumulated for the proposed automatic IgG-based diagnostic system. The FBUB team has 2 expert professors, 3 researchers, 3 ESRs and one technician – veterinarian, and an administrative person.

YEDITEPE will bring necessary expertise in immunology, particularly regarding antibody profiling and analysis, as well as connections with the clinics and the availability of patient siPSC-derived in vitro and in vivo models. Here are some papers and a patent related to ALS and biologicals. YEDITEPE will bring 5 researchers and 2 technicians (biologists and molecular biologists in both profiles) to the project. They will host three workshops.

UEF has expertise in ROS signalling studies with specific fluorescent dyes that is essential for one of the functions of the designed innovative device. In addition, UEF are in the European forefront

of iPSC research. They can differentiate these human cells from ALS, AD and PD to various neurons, astrocytes, microglia, endothelial cells and oligodendrocytes. When transplanted into immunodeficient mice these cells get fully integrated. UEF will host two training schools. The team of this beneficiary will consist, in addition to two expert key persons, of 3 ERs and 4 ESRs.

ArGenit is an SME specialized in developing microscopy analysis systems and thus will be instrumental in the design and production of the optical device for the proposed automated diagnostic system. In addition, they will bring a complementary know-how in iPSC research, namely, stem cell derived cultures are used to model diseases and to search for phenotypes. ArGenit will bring 2 experts in addition to technical staff.

ELVESYS is an SME specialized in developing microfluidics systems. It boasts the world widest brand of microfluidic flow control products. ELVESYS will be instrumental in the design of the microfluidic platform for the proposed automated diagnostic system. In addition, this SME will offer soft skills regarding marketing of scientific instrumentation and entrepreneurship in general. The human potential for the project will be 3 engineers (2 PhDs in Biology and 1 PhD in physics and chemistry).

LANOTEC is a listed TC academic institution that will offer expertise in state of the art biophysical methods for subcellular analysis that will offer closer understanding of the IgG effects to be standardized. The human resources employed consist of 3 researchers, 1 ESR and one administrative person.

UCONN - is a TC organization with world renown expertise (Dr Srdjan Anntic) in voltage-sensitive dyes that will be essential for a functionality of the proposed automatic diagnostic device. The laboratory of Dr Antic will also transfer know-how on optical system for *in vivo* recordings of fluorescence. The scientific environment of this lab consist of experienced electrophysiologists, anatomists, chemists (designing voltage-sensitive dyes) and optical technicians.

UCHIC – is a TC organization with particular expertise in the measurements with multielectrode arrays (MEA). The lab of prof. Wim Van Drongelen will be instrumental in helping define electrophysiologic criteria to be complemented with voltage-sensitive dye measurements.

FBUB has the lab facility (within the Centre for laser microscopy) for cell culturing and video microscopy monitoring of calcium, patch-clamp electrophysiology, and confocal laser scanning microscopy.

YEDITEPE has within the Immunology Department two lab facilities: 1) Autoantibodies Lab, and 2) HLA Typing Lab and a Stem Cell Laboratory within the Hematology Department in the Hospital, all with necessary equipment.

UEF is equipped with a live imaging facility for both *in vitro* and *in vivo* (with multiphoton microscope) experiments. Newly fluorescent constructs are available designed for site specific ROS signalling, as well as for markers of oxidative stress in mitochondria. In addition, this centre will transfer know–how on multiphoton imaging of mitochondria *in vivo*. An advanced facility of stem cell culturing also exists.

ArGenit - fluorescent microscopes that are needed during the project, are available in the company head office in Istanbul.

ELVESYS has more than 300 m² of Lab facilities for microfluidic and flow control instrument development also containing soft lithography facilities for microfluidic device fabrication.

UCONN facility is equipped with 3 advanced electrophysiology setups connected with fluorescence measuring time high-resolution video microscopy. This will be used for the purposes of testing and studying of intracellular voltage-sensitive dyes.

UCHIC Centre for epilepsy research is fully equipped for the investigation of neuronal networks properties from theoretical mathematical and computational approaches modelling, single neuron and local network activity with fully established patch clamp and confocal microscopy setups and expertise. Investigation of network architecture and physiological and pathological behaviours in dissociated neuronal cultures are conducted on Microelectrode Array (MEA) setups that will be essential for collecting data for the electrophysiology signalling for the proposed automatic IgG-based device.

4.4. *Competences, experience and complementarity of the participating organisations and their commitment to the project*

The main aim of **UEF** - Kuopio team is to provide live imaging experiments both *in vitro* and *in vivo* (with multiphoton microscope). Collaboration between **FBUB** and **UEF** was seeded within the framework of the recently completed COST Action EU-ROS. Pilot experiments were thus performed that are the basis of innovative ROS-based biomarker recordings with ALS IgGs. These data will further be confirmed at **UEF** by multiphoton imaging of mitochondria *in vivo*. **UEF** will also transfer knowledge to **ELVESYS** and **ArGenit** regarding the ROS measurement modality of the proposed device.

YEDITEPE with its Immunology department will bring complementary knowledge on autoantibodies and their characterization that is essential to the work on ALSIgGs. This participant will also be a necessary link to the clinic as well as a monitor of good laboratory practice.

UCONN will complement the **FBUB** knowledge on synaptic effects of ALS IgGs with the application of voltage sensitive dyes. **UCONN** has ongoing collaboration with **FBUB**, through Dr Antic who is also an alumni of the University of Belgrade. The collaboration is based on research and education. A member of **FBUB** lab is now a postdoc at **UCONN**.

UCHIC will complement the know-how of **UCONN** on voltage-sensitive dyes with MEA measurements. This will offer a necessary complementary knowledge of network responses to ALS IgGs.

ELVESYS and **ArGenit** as the two SMEs on the project will interact with other participants as well as among themselves. Thus, they will work closely together and within the AUTOIGG consortium towards the production of the prototype of the automated IgGs screening diagnostic device. Thus, **ELVESYS** will be designing the microfluidic chamber and the measuring platform while **ArGenit** will take care of the optical system of the measuring device.

5. Ethics Aspects

Ethics self-assessment:

The ethical issues concern the involvement of human sera and the involvement of animals in the research proposed by the AUTOIGG consortium.

1) Describe how the proposal meets the national legal and ethics requirements of the country or countries where the tasks raising ethical issues are to be carried out.

The Supervisory board of AUTOIGG will monitor and control that all participants involved in AUTOIGG will comply with "The EU Charter of Fundamental Rights" and will perform their research to the relevant EU legislation, in particular:

• Council Directive 83/570/EEC of 26 October 1983 amending Directives 65/65/EEC, 75/318/EEC and 75/319/EEC on the approximation laid down by law, regulation or administrative action relating to proprietary medicinal products

• Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnology inventions

• Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council directive 0/220/EEC

• Council Directive 2010/63/EU corrigendum of 24 Jan 2013 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of Animals used for Scientific purposes

• Directive 2003/65/EC of the European Parliament and of the Council of 22 July 2003 amending Council Directive 86/609/EEC on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes (Text with EEA relevance)

• Council Decision 1999/575/EC of 23 March 1998 concerning the conclusion by the Community of the European Convention for the Protection of vertebrate animals used for experimental and other scientific purposes

• Council Decision 2003/584/EC of 22 July 2003 concerning the conclusion of the Protocol of Amendment to the European Convention for the Protection of vertebrate animals used for experimental and other scientific purposes

• Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

Research ethics also concerns research integrity and the AUTOIGG consortium will adopt "the European Code of Conduct for Research integrity" published by the European Science Foundation in 2011.

Ethics issues within the consortium

Objectives:

Dysfunction of the CNS is the main cause of many neurological diseases. A major clinical and societal problem is that there is no cure for the majority of the nervous system diseases, which are often devastating. This affects a huge number of people, as disorders of the nervous system affect 38.2% of the population in Europe, which is a conservative estimate since not all neurological

disorders were taken into account. This underscores that nervous system disorders are currently a core health challenge.

The research proposed by the AUTOIGG consortium will involve human sera and animal experiments.

Methodology:

None of the animal experiments will be initiated before the approval by the appropriate ethical committee has been obtained. The AUTOIGG consortium has ethical approval for most of the proposed experiments and will obtain approvals for the remaining ones.

AUTOIGG participants are fully aware of the ethical issues involved in working with animals.

The Supervisory board of AUTOIGG will monitor and safeguard that all participants involved in AUTOIGG comply with the national and EU legislations.

Every effort will be made to replace, reduce and refine the animal experiments and thus to comply with the 3R's principle.

Replace: whenever possible experiments will be performed on cell culture and human brain tissue;

Reduce: the number of animals in each study will be restricted to the minimum;

Refine: Unnecessary suffering will be prevented at all times. All procedures will be performed by individuals who are adequately trained and competent in the planned procedures. The appropriate anesthesia as approved by the local authorities will be applied and stress will be reduced wherever possible.

Patients sera will be taken from patients based on written informed consent.

Impact:

Insight into nervous system dysfunctions, which is a prerequisite for designing novel therapies that would cure the diseases or improve the neural functioning, requires studies in animal disease models. To reach this goal, basic knowledge about molecular and cellular changes in the nervous system combined with translational and applied research is necessary to connect this knowledge to the patient situation.

Pre –Grant Requirements

HUMANS

2.1 Details on the procedures and criteria that will be used to identify/recruit research participants

Identification and recruitment of human participants will take place through existing co-operation of FBUB and Neurological Clinic, Clinical Center of Serbia. Neurological Clinic is leading neurological center of the region, providing highly specialized diagnostic procedures such as immunological and genetic analyses, neurophysiological and neuroradiological diagnostic procedures.

Patients diagnosed with a neurodgenerative disease with inflammatory symptomatology (e.g. ALS, MS, PD, HD), which have undergone detailed specialist clinical examination and met the entry criteria defined by the research design, will be included in the study.

For the purpose of **AUTOIGG**, during routine blood sampling, additional 10 ml of blood will be collected and only purified IgG fraction from patient sera will further be used in experiments.

Beside neurological patients, samples will be taken from age and sex-matched controls that include healthy individuals and disease-control patients.

Patient specific data that will be collected will include Functional Rating Scales, gender, age, duration of the disease and type. Patients will also be screened for possible genetic mutations linked to inherited form of the disease and potential comorbidities. Additionally, basic demographic and clinical data, relevant to this research, will be gathered. Neurology Clinic has implemented InfoMedis information system for patient data storage.

Patient material will also be provided by the YEDITEPE University (see informed consent form attached).

Sera samples and personal information will only be taken from patients who give informed consent in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

2.2. Detailed information on the informed consent procedures that will be implemented for the participation of humans.

Research involving Patients - Informed Consent

Patients sera will be taken from patients based on written informed consent. Informed Consent is the decision, which is written, dated and signed, taken freely after being duly informed of its nature, significance, implications and risks and appropriately documented, by any person capable of giving consent or, where the person is not capable of giving consent e.g. Alzheimer patients, by his or her legal representative; if the person concerned is unable to write, oral consent in the presence of at least one witness may be given in exceptional cases, as national legislation requires. The European Commission - Research Directorate - General provides guidance on informed consent and this will be respected.

The research planned in this proposal only requires persons able to freely understand and question the consent procedure. Vulnerable persons like children, persons with an IQ below 70, severely-injured patients, etc. will be excluded. Information will be given in lay terms and under no circumstances will pressure of any kind be exercised on the individual participant nor her/his family.

The collection of personal data for human patients in **AUTOIGG** will be performed in Serbia and Turkey.

Methods of obtaining Informed Consent: Informed consent documents (ICDs) will explain in simple terms the objectives, scope, and potential risks and benefits of study participation. If the patient decides after an appropriate time for consideration to participate in the experiments, patients will sign the respective standardized ICD document in duplicate in the presence of the investigator (template attached). One copy of the signed and dated ICD is handed to the patient. The other copy of the ICD is filed at the **AUTOIGG** research center. Patients will be informed that participation in the study is voluntary and that consent can be withdrawn at any time without the need to provide reasons, and without disadvantage or prejudice. Information on data protection will be given before the patient is entered into the study and any study-specific procedures are performed.

2.3. Templates of the informed consent forms and information sheet

INFORMED CONSENT

Original in Serbian

Писана сагласност пацијента за учешће у испитивању

Назив истраживачког пројекта: Аутоматизовани функционални скрининг IgG за дијагностику неуродегенеративних обољења

Руководилац пројекта:

Подаци о пацијенту

АЛС/Контролно обољење/Здрава контрола:

Име и презиме:

Датум рођења:

Број картона: Молимо да обележите поља (X)

1.	У оквиру *Информације за пацијенте* описани су циљеви и план истраживања, као и његови могући ризици и користи. Потврђујем да сам пажљиво ишчитао/-ла *Информацију за пацијенте*, да су ми наведена упутства била разумљива и да располажем са довољно података о истраживању у коме бих учествовао/-ла. Имао/-ла сам прилику да поставим питања у вези са овим истраживањем и добио/-ла сам јасне и разумљиве одговоре.	
2.	Схватам да је моје учешће добровољно, да могу да повучем своју сагласност у било ком тренутку без објашњавања разлога и да то ни на који начин неће утицати на стандард мог садашњег или будућег лечења.	
3.	Добровољно пристајем на све поступке описане у плану истраживања *Информације за пацијенте*.	
4.	Схватам да се подаци сакупљени током мог учешћа у наведеном истраживању шифровано уносе у базу података и анализирају, и да ће се користити искључиво у научне сврхе.	
5.	Дајем дозволу да се моји узорци шаљу у друге земље укључене у пројекат.	
6.	Разумем да ми неће бити саопштени резултати истраживања која ће се спроводити са мојим узорцима, сем уколико је то важно за ток моје болести.	

Не одричем се својих законских права потписом овог информисаног пристанка.
Добићу потписани примерак овог информисаног пристанка.

	Име и презиме	Својеручни потпис	Датум
Испитаник			
Особа које је добила пристанак			

Translation in English

Informed consent form

Title of Research Project: Automated Functional Screening of IgGs for Diagnostics of Neurodegenerative Diseases

Principal Investigator:

Patient Details

ALS/Control disease/Healthy control:

Name and Surname:

DOB:

Hospital No: Please initial box (X)

1.	The document *Patient Information Sheet* gives goals of the research, as well as research plan, potential risks and benefits. I confirm that I have carefully read and understood the information given in *Patient Information Sheet.* Provided information was clear to me and I have enough facts about the proposed research to be able to decide whether I would like to participate. I was given the opportunity to ask everything concerning this research, and I got clear answers.	
2.	I understand that my participation is voluntary, that I can withdraw my consent at any time without giving reasons, and that it will not affect in any way the standards of my current or future health care.	
3.	I agree to all the procedures described in the research plan in the document *Patient Information Sheet.*	
4.	I understand that data collected during my participation will be anonymised and imported in database and it will be used only for scientific purposes.	
5.	I give permission for my samples to be sent to other countries included in the project.	
6.	I understand that I will not be told the results of any test which may be carried out with my samples unless it is relevant for my medical condition.	

I do not give up on my legal rights by signing this informed consent.
I will get a signed copy of this informed consent.

	Name and Surname	Signature	Date
Patient			
Person taking consent			

The original consent form from Yeditepe University, Turkey

YEDİTEPE ÜNİVERSİTESİ HASTANESİ	**Poliklinik Genel Onam Formu**

Değerli Hastamız

Sağlık Bakanlığı yasal Hasta Hakları Yönetmelik gereklilikleri, JCI akreditasyon standart gereklilikleri ve ISO 27001 ve 15189 laboratuvar akreditasyon standartlarını uygulayan bir kurum olarak; hastanemizde bulunduğunuz süre içerisinde ilk başvurduğunuzda ve yıllık olarak güncellenmek üzere uygulanacak muayene, kan alma vb işlemler için yazılı onam alınmaktadır.

Hastanın veya yerine onam verecek kişinin okuma, anlama, konuşma, dil sorunu mevcut mu? Evet ☐ Hayır ☐ Cevabınız EVET ise Hasta Hakları Bölümü ile iletişim kurunuz.	**Tercüman gerektiyse;** Tercümanın adı _____ İmza _____ Tarih _____

Yeditepe Üniversitesi Hastaneleri ve Bağlı kurumlarında sorumlu doktorum ve doktorumun talimatıyla ilgili birimler personelinin bakımı altında olduğumun bilincindeyim.

- Doktora / hemşireye / personele mevcut sağlık problemlerimi, alerjilerimi, aldığım ilaç ve tedavileri belirtmem gerektiğini biliyorum. İnceleme amacı ile kullanılan kan, idrar ve diğer vücut sıvılarımın doku ve ürünlerinin alınmasına ve saklama süresi sonunda testlerin tamamlanmış örneklerin imha edilmesine izin veriyorum. Doktorun, sağlık profesyonelinin, çalışanın veya ilk eylemde bulunan yetkilinin perkütan, mukoza zarı, kan veya başka bir vücut sıvısının açık yaradan çıkışı ile HIV (human immunodeficiency virus) ve / veya HBV (hepatit B virus) veya HCV (hepatit C virus) incelemesinin yeni bir onay alınmadan uygulanabileceğini biliyorum
- Bakım sağlayıcılarımın belirttiği rutin işlemler, muayeneler, incelemeler, bağışıklık sağlayıcıları, teşhis amaçlı işlemlerin uygulanmasına onay veriyorum. Tam anlamamam durumunda, uygun sağlık bakımı personeline soru sorma hakkımın olduğunu ve **bunun benim sorumluluğum olduğunun bilincindeyim.**
- Doktorum tarafından gerekli görülen her tür ilave işlem için, ayrıca işleme özel bilgilendirme onay formu imzalamamın istenebileceğini anlıyorum.
- Hastalığım nedeni ile hastanede uygulanacak tüm tanı ve tedavi yöntemlerinin olası maliyeti konusunda işlem öncesinde bilgilendirileceğim bana söylendi.

- Bağlı olduğum özel ve resmi kurumların talep ettiği bilgileri vermekle yükümlü olduğunuzu biliyor ve kabul ediyorum. Kullandığım, Özel sağlık sigortam nedeniyle, kimlik ve sağlık bilgilerimin, sigorta şirketimle ve onun yetkilendirdiği ağ içinde bulunan diğer şirketlerle paylaşılmasına muvaffakat ediyorum.
- Tesis içerisinde bulunuşum sırasında personele teslim ettiğim kişisel eşyalarımın dışında, kayıp veya zarar görmüş kişisel eşyadan Yeditepe Üniversitesi Hastanesi'ni sorumlu tutamayacağımı anlıyor ve kabul ediyorum.
- Benden alınan kan, idrar vb örneklerimin gerekli tetkiklerim çalışıldıktan sonra kalanlarından (Genetik çalışmalar hariç olmak üzere) ismim kullanılmadan deney / araştırma örneği olarak kullanılabileceğini biliyor ve izin veriyorum.
- Hastanemiz bir üniversite, eğitim ve araştırma hastanesi olup, gerek tıp eğitimi, gerekse hemşirelik, eczacılık, fizyoterapi gibi diğer sağlık alanlarında eğitim verilmektedir. Bu alanlarda eğitim alan stajyer, intörn, tıpta uzmanlık öğrencisi ve diğer öğrenciler, öğretim üyelerinin gözetiminde zaman zaman tedavinizde yer alabilirler.
  Belirtilen ifadelerin çerçevesinde YUKARIDA BAHSEDİLEN İŞLEMİN YAPILMASINI TALEP EDİYORUM.

AŞAĞIDAKİ İMZAM KABUL ETTİĞİMİ GÖSTERİR:

1) Bu form üzerindeki tüm bilgileri okudum veya okuttum ve anladım
2) Soru sorma şansı tanındı ve bu form ile ilgili tüm sorularıma tatmin edici cevaplar verildi.

HASTANIN BİLİNCİ AÇIK ve 15 YAŞ ÜZERİNDE İSE;	**HASTANIN BİLİNCİ KAPALI VEYA 18 YAŞ ALTINDA İSE VE YANINDA YASAL TEMSİLCİSİ VAR İSE;**
Hastanın	**Yasal Temsilci*(Vasi) veya Veli**
Adı Soyadı :	Adı Soyadı :
Adresi :	Adresi :
Telefon Numarası :	Telefon Numarası:
İmza:	**İmza:**
Şahit:**	**Şahit**:**

Adı Soyadı: **İmza:**	**Adı Soyadı:** **İmza:**

Poliklinik Onam Hasta dışındaki Yasal Temsilcisi ve ya Velisi(Vasi) tarafından verildi ise lütfen yakınlık derecesini ve hastanın kendisinin imzalamama gerekçesini belirtiniz.

……

……

Informed consent form from Yeditepe University, Turkey translated into English

YEDİTEPE ÜNİVERSİTESİ HASTANESİ

General Polyclinic Approval Form

Dear Patient,

As required by the Ministry of Health in accordance with Patient Rights Regulations, and as an health organization complying to JCI accreditation, ISO 27001 and ISO 15189 standards; we take your written approval for blood collection, therapeutic applications and such; when you first apply and update this approval on yearly basis.

Do patient or patient's custodian have any problem with reading, comprehension, speaking, language problem? Yes ☐ No ☐ If your answer is YES please contact Patient Rights Office	**If a translator was necessary;** Name and surname of the translator _____ Signature _____ Date _____

I am aware that I am under the care of my doctor and personnel from related departments with the instructions of my doctor in Yeditepe University Hospitals and associated organizations.

I know that I need to declare my present health problems, allergies, medical and other therapies to doctors/nurses/hospital personnel. I give permission to collection and storage of samples of my blood, urine and other body fluids, tissues; and their annihilation after expiry date. I know that in case of percutaneus, through mucosa membrane, blood or other body fluid's leakage to the doctor, health professionals or the initial care persons HIV (Human Immunodeficiency Virus) and/or HBV (Hepatitis B Virus), and/or HCV (Hepatit C virus) will be tested without additional approval.

I give consent to application of routine procedures, examinations, analysis, vaccines, procedures for diagnosis given by the healthcare providers. I realize that, for any issue that I have not understood clearly, I have the right to ask questions to related health care person and that is in my own responsibility.

I comprehend that for any additional procedure that is accepted as necessary by my doctor/s, I may be asked to sign a procedure specific approval.

- I have been informed that I will be given information about the possible cost of all diagnostic and therapeutic applications for my illness before these procedures.
- I know and accept that you are required to provide information to my affliated private or state organizations when requested. I give consent to share of my identity and health information with my insurance company, and their approved companies due to my private health insurance.
- I know that, while I am in the hospital, I cannot hold the Yeditepe University Hospital responsible for lost or damaged belongings except the personal belongings I have declared to personnel at first.

- I have been informed and consent that my left over blood, urine etc. samples can be used for experiments/researches after routine testing except genetic testing without use of my name.
- I have been informed that this hospital is a university's training and research hospital, that gives education to medicine, nursing, pharmacy and physiotherapy. The students in training for these professions, interns, residents and other students may take role in your care from time to time under the supervision of their professors.

  I REQUEST THAT PROCEDURES TO BE COMPLETED in framework of the above mentioned.

MY SIGNATURE BELOW INDICATES THAT I APPROVE:

1) I have read/instructed and understood all of the information provided on this form
2) I was given the chance to ask questions and have received satisfying answers to all my questions

IF THE PATIENT IS CONCIOUS AND OVER 18 YEARS OLD;	**PATIENTS IS UNCONCIOUS AND LESS THAN 18 YEARS OLD AND A LEGAL CUSTODIAN;**
Patient's Name Surname : Address : Phone number : **Signature:**	**Legal Representative*(Custodian) or Parent** Name Surname : Address : Phone Number: **Signature:**
Observant:** **Name/Surname:** **Signature:**	**Observant**:** **Name/Surname:** **Signature:**

If the Polyclinic Approval is given by the legal custodian or parents, please indicate the relation and explain why the patient have signed himself/herself.

……

……

INFORMATION SHEET

Original in Serbian

Информација за пацијенте

Назив истраживачког пројекта: **Аутоматизована функционална анализа IgG за дијагностику неуродегенеративних обољења**

Овај документ садржи податке које је потребно да имате у виду пре него што пристанете да учествујете у овом истраживању. Врло нам је важно да разумете ове информације и да питате све што желите у вези са овим истраживањем. Пројекат „ Аутоматизовани функционални скрининг IgG за дијагностику неуродегенеративних обољења“ је настао са циљем да се омогући што раније успостављање дијагнозе и прецизније предвиђање тока неуродегенеративних обољења као и персонализован приступ лечењу пацијената. На Вама је да одлучите да ли желите да учествујете у истраживању. Објаснићемо Вам студију и детаљно проћи са Вама кроз овај документ. Уколико се одлучите да дате свој пристанак, замолићемо Вас да дате писану сагласност.

У било ком тренутку студије можете да повучете своју сагласност, без објашњавања својих разлога. Такав поступак неће утицати на стандард лечења који добијате.

Поштовани,

Позивамо Вас да учествујете у научном истраживању. Пре него што одлучите да ли ћете дати свој добровољни пристанак, неопходно је да добро разумете разлоге због којих се изводи ово истраживање, циљеве којима тежи и на који начин Ви доприносите њиховом остварењу. Због тога Вас молимо да одвојите довољно времена да пажљиво ишчитате податке о истраживању, да нас питате све што Вас занима и да потом одлучите да ли желите да учествујете.

Уколико одлучите да не желите да учествујете, то неће ни на који начин утицати на стандард лечења и терапије коју добијате. У било ком тренутку студије можете да повучете своју сагласност, без објашњавања својих разлога. Такав поступак неће утицати на стандард лечења који добијате.

Циљ истраживања

Упркос бројим истраживањима међу којима су и врло успешне преклиничке, па чак и клиничке студије о потенцијалним терапијама за амиотрофичну латералну склерозу (АЛС), поуздана и делотворна терапија још увек не постоји. Истраживачи и лекари се слажу да је разлог томе недовољно усавршен процес успостављања дијагнозе што је могуће раније и прецизније, као и система за праћење тока болести на ћелијском и молекуларном нивоу.

Установљено је да се код пацијената оболелих од АЛС стварају анти-неурални имуноглобулини Г (IgG), као важна одлика запаљенског процеса, који доводе до патофизиолошких промена основних параметара ћелија нервног система. Ово истраживање ће омогућити стандардизацију процеса којима се ове промене прате као и повезивање конкретних промена са специфностима развојних фаза болести . На основу прикупљених података, на крају ће се дизајнирати дијагностичка апаратура која ће помоћи предвиђање, праћење болести, процену адекватне терапије и одговора на исту, за сваког пацијента појединачно.

План истраживања

Фокус истраживања је испитивање могућности употребе имуноглобулина Г изолованих из серума пацијената као дијагностичких и прогностичких параметара неуродегенеративних обољења. Пацијенти оболели од амиотрофичне латералне склерозе, који су прошли детаљан клинички преглед и који задовољавају улазни критеријум дефинисан дизајном истраживања, биће укључени у истраживање. Посебно ће се узимати у обзир да ли је код пацијента установљена спорадична форма болести или су идентификоване најчешће узрочне мутације које доводе до развоја наследне форме АЛС, као и да ли постоје и друга пропратна обољења, како би се узели у обзир сви фактори и унапредила дијагностика амиотрофичне латералне склерозе. У истраживање ће бити укључени и пацијенти оболели од других обољења, као и здрави појединци као контролне групе. За потребе овог истраживања, учесницима који дају добровољни пристанак, ће приликом редовног вађења крви бити узет додатни узорак крви (до 10мл), а потом ће се из тог узорка пречистити имуноглобулини Г који ће се користити даље за испитивање патофизиолошких процеса АЛС или као контролини IgG. Од учесника ће се прикупити и основни демографски и клинички подаци од значаја за ово истраживање и унети у базу података ради детаљне анализе. Сакупљени биолошки материјал и резултати овог истраживања биће коришћени само, једино и искључиво у научне сврхе, а у циљу бољег разумевања и прогнозе болести.

Ризик

У стручној литератури нису описани ризици у вези са поступцима који ће бити примењени у овом истраживању.

Тајност података

Узорци Ваше крви, пречишћени имуноглобулини Г и Ваши подаци неће бити означени Вашим личним именом, већ лабораторијском ознаком (бројем) ради заштите Вашег идентитета. Резултати добијени у овом истраживању биће коришћени у оквиру научног пројекта „Аутоматизовани функционални скрининг IgG за дијагностику неуродегенеративних обољења“ , у стручним радовима објављеним у научним часописима и

саопштењима на научним скуповима. Истраживање мора бити одобрено од стране Етичког одбора, што представља потврду о заштити и поштовању права пацијента.

Новчани трошкови испитаника

Испитаници укључени у истраживање неће сносити никакве новчане трошкове за поступке који ће бити примењени у овом истраживању.

Translation in English

Patient Information Sheet

Title of Research Project: Automated Functional Screening of IgGs for Diagnostics of Neurodegenerative Diseases

This document provides information that you need to take into consideration before you agree to take part in this research project. It is very important to us that you completely understand this information and ask us anything concerning this research. Research project “Automated Functional Screening of IgGs for Diagnostics of Neurodegenerative Diseases” includes activities aimed at enabling early diagnostics, precise monitoring of the course of neurodegenerative diseases as well as point-of care personalized diagnostics. You are free to decide whether you want to participate in this research. We will explain the study and go through this information sheet. If you decide to participate, we will then ask you to sign a consent form.

At any point during the study you are free to withdraw, without giving a reason. This will not affect in any way the current or future standard of care and treatment you receive.

Respected Sir/Madame,

We would like to invite you to take part in a research project. Before you decide whether you wish to participate or not, it is necessary for you to understand the reasons for this research, its goals and how you can contribute. Therefore, we kindly ask you to take time and read carefully this Information Sheet, ask us anything you would like to know and then decide whether you would like to participate.

If you decide not to take part, your standard of care will not be affected by your decision. At any point during the study you are free to withdraw, without giving a reason. This will not affect in any way the current or future standard of care and treatment you receive.

The purpose of the study

Although there are many successful preclinical, and even some clinical studies of potential therapy for amyotrophic lateral sclerosis (ALS), there is still no reliable and effective therapy. Researchers and practitioners agree that the reason for this is insufficiently perfected process of establishing diagnosis early enough, and monitoring of the course of the disease on cellular and molecular level. In ALS, production of anti-neuronal immunoglobulin G (IgGs) is a significant feature of the immune-inflammatory process. IgGs further provoke pathophysiological changes of basic parameters in the cells of the central nervous system. This research will enable standardization of processes through which these changes are being monitored as well as linking them with the specificities of the developmental stages of the disease. Based on collected data, fine diagnostic tool will be designed to help prediction and monitoring of the disease, assessment of adequate therapy and responsiveness for each patient.

Research plan

The aim of this research is to examine whether IgGs isolated form sera of patients diagnosed with ALS can be used as diagnostic and prognostic parameters of neurodegenerative disease. ALS patients who have undergone detailed clinical examination and met the entry criteria defined by the experimental design, will be included in the study. In order to include all the potential factors and improve diagnostics, it will be taken into account whether patients are diagnosed with sporadic form of the disease or the presence of some of the mutations related to the inherited form is detected. Patients will be also screened for comorbidities. Patients diagnosed with other disease, as well as healthy individuals will be included in the study as control groups. For the purposes of this research, participants who give informed consent, will be asked to give additional 10 ml of blood during their routine blood sampling. Thereafter, IgG will be purified from sera and used to examine pathophysiological processes in ALS or as control IgGs. Basic demographic and clinical data relevant to the study will also be collected and imported into database for further correlation analysis. Gathered data, biological material and research results will only be used for scientific purposes in order to gain better understanding of disease pathophysiology.

Risks

There are no risks associated with the procedures that will be used in this research.

Confidentiality and Privacy of Personal Data

Your blood samples, purified IgGs and personal data will not be labeled with your name but with laboratory index (number) for protection of your identity. Results obtained throughout this research will be used for the purposes of scientific project “Automated Functional Screening of IgGs for Diagnostics of Neurodegenerative Diseases”, in scientific articles and in announcements on scientific meetings. Research must be approved by Ethic Committee, which represents confirmation of respect and protection of patients` rights.

Patients` expenses

Participants included in this research will not bare any costs for the procedures that will be applied in this research.

PROTECTION OF PERSONAL DATA

4.4. Detailed information must be provided on the procedures that will be implemented for data collection, storage, protection, retention and destruction and confirmation that they comply with national and EU legislation.

AUTOIGG project require the processing and/or storage of personal and sensitive information. Personal and sensitive information that is collected from research will be kept confidential. Such information will be anonymised and kept safe. **AUTOIGG** research complies with relevant legislation and processes/stores all personal information in accordance with it. Personal data will be handled according to the national regulations in vigor regarding research involving humans and personal data protection.

Each patient after signing informed consent will enter the study and study-specific procedures will be performed. Patients blood samples, purified IgGs and personal data will not be labeled with the patients name but with the medical laboratory index (the number code) for protection of the patients identity. Each patient will be assigned a number code. This code is the only fact that will be known about the patient throughout the project. The consortium will exchange the results obtained from the IgG with the code. Only the code will be available, but not patient personal data.

4.5. Detailed information on the informed consent procedures that will be implemented in regard to the collection, storage and protection of personal data must be submitted.

All handling of personal data within this project will be conducted in accordance with legal requirements and only after voluntary consent of the participating patients.

Archiving of Data / Access to Records: Originals of all report forms, administrative documents, patient information, logs, consent forms and documentations will be stored at the **AUTOIGG** research facility for at least 10 years. A list allowing patient identification will be kept for 15 years.

Neurology Clinic, Clinical Center of Serbia has implemented InfoMedis information system for patient data storage. Keeping all information for 10 years is standard procedure. This information will at no time be kept with the participants of the **AUTOIGG** project.

Partner laboratories in the **AUTOIGG** consortium are located in Turkey, Costa Rica, and USA. Patient data will be exchanged between these partners and the rest of the consortium located in the European Union. These will include data of patients IgGs effects on synaptic activity, vesicle trafficking, as well as $Ca^{2+}$and ROS imaging and cellular and subcellular morphology. However, all these data will be rendered anonymous labelled with the number code, before any analysis or exchange is considered. This procedure ensures that no personal data will be exchanged between the EU and the rest of the consortium, and eliminates possible ethical risks related to the exchange of data.

THIRD COUNTRIES

6.1. The applicant must confirm that the ethical standards and guidelines of Horizon2020 will be rigorously applied, regardless of the country in which the research is carried out.

We confirm that the ethical standards and guidelines of Horizon2020 will be rigorously applied, regardless of the country in which the research is carried out.

All experiments performed in the research labs of the **AUTOIGG** partners have received permission by the respective national legal authorities as required by the European Commission guidelines (86/609/CEE), and comply with the national and EU legislations in particular: • Directive

98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnology inventions • Council Directive 2010/63/EU corrigendum of 24 Jan 2013 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of Animals used for Scientific purposes • Directive 2003/65/EC of the European Parliament and of the Council of 22 July 2003 amending Council Directive 86/609/EEC on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes (Text with EEA relevance) • Council Decision 1999/575/EC of 23 March 1998 concerning the conclusion by the Community of the European Convention for the Protection of vertebrate animals used for experimental and other scientific purposes • Council Decision 2003/584/EC of 22 July 2003 concerning the conclusion of the Protocol of Amendment to the European Convention for the Protection of vertebrate animals used for experimental and other scientific purposes • Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

Research ethics also concerns research integrity and the **AUTOIGG** consortium will adopt "the European Code of Conduct for Research integrity" published by the European Science Foundation in 2011.

The **AUTOIGG** projects will fulfill the national criteria for laboratory and safety and the conduction of experimental procedures will be regularly inspected. Disposal of hazardous material will be performed according to the national rules. Protective material and easily readable documents on their use are available as prescribed by the current laws.

6.2. Detailed information that fair benefit-sharing arrangements with stakeholders from low and/or lower-middle income countries are ensured during the project.

Two points have to be taken care off to confirm that fair benefit-sharing arrangements have been assured with stakeholders from low or lower-middle income countries.

A. Sharing the benefits and allocation of the intellectual property rights.

B. Contribution to the capacity building in the developing countries.

AdA:

*We confirm that fair benefit-sharing arrangements with stakeholders from Third Countries are ensured throughout the project. The sharing of the benefits and allocation of the intellectual property rights with the Third countries will follow the Consortium agreement. In general, the benefits will depend on contributions related to design of experiments, software, and the small-scale platform that will be used to accomplish the building of the new diagnostic and prognostic technology.

AdB:

Intellectual capacity: the researchers from the Third country will participate as involved observers in the different stages and development processes of the project. This will allow them to learn the methodologies and protocols related to research and development used by companies and institutes for future developments; respecting the copywriter and agreements.

Infrastructure: The LANOTEC- Costa Rica will be allowed to acquire a prototype of the new technology to be installed in the institute to be payed regarding materials and manufacturing; for future diagnostics in Costa Rica while allowing other scientist from the region to learn about the technique and protocols.

6.3. The applicant must provide details on the material which will be imported to/exported from EU.

The only materials which will be imported to/exported from EU are patients IgGs, and the adequate authorizations will be obtained. This exchange will be kept to minimum between YEDITEPE and/or FBUB on one side and UEF on the other.

6. Letters of Commitment of partner organisations

CeNAT
Centro Nacional de Alta Tecnología

FunCeNAT

CONARE
CONSEJO NACIONAL DE RECTORES
Centro Nacional de Alta Tecnología

2017
Las Universidades Públicas por la Vida, el Diálogo y la Paz

Letter of Commitment

With this letter we would like to express our real and active participation if the project proposal AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTICS OF NEURODEGENERATIVE DISEASES (**AUTOIGG**), (coordinator Prof. Pavle R. Andjus, Faculty of Biology University of Belgrade) will be funded.

The person responsible for this collaboration will be Dr.José Vega Baudrit and Dra. Yendry Corrales Ureña.

Signature of legal representative
MBA. Cynthia Cordero Solis
Administrative Director FUNCENAT

Date: 27/3/2017.

Fundación Centro de Alta Tecnología FUNCENAT 1997

Tel Central (506) 2519-5835, directo (506) 2519-5838
Apartado 1174-1200 Pavas, San José, Costa Rica.
funcenat@cenat.ac.cr
www.cenat.ac.cr

UCONN HEALTH

Center for Molecular Medicine
263 Farmington Avenue
Farmington, CT 06030-3101

31 March 2017

To Whom It May Concern:

This letter confirms that Srdjan D. Antic, M.D., in the Department of Neuroscience at UConn Health is able to host visiting postdoctoral fellows in his laboratory in order to fulfill his obligation to the proposed project entitled:

"AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTIC OF NEURODEGENERATIVE DISEASS (AUTOIGG)"

(Coordinator: Prof. Pavle R. Andjus, Faculty of Biology, University of Belgrade)

Visiting scientists may perform their training at UConn Health for up to one year contingent upon obtaining valid immigration status and availability of funds.

Sincerely yours,

Christopher D. Heinen, Ph.D.
Director of Postdoctoral Affairs
Associate Professor of Medicine
UConn Health
Tel: 1-860-679-8859
cheinen@uchc.edu

The University of Chicago
Pritzker School of Medicine
Department of Pediatrics

5841 S Maryland Avenue
Chicago, Illinois 60637-1470

March 16, 2017

Letter of Commitment

With this letter we would like to express our real and active participation if the project proposal AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTICS OF NEURODEGENERATIVE DISEASES (**AUTOIGG**),
(coordinator Prof. Pavle R. Andjus, Faculty of Biology University of Belrgade)
will be funded.
The person responsible for this collaboration will be ***Dr Wim van Drongelen***.

Sincerely,

Wim van Drongelen, PhD
Professor of Pediatrics, Neurology, Computational Neuroscience
Technical Director of the Pediatric Epilepsy Center
Senior Fellow Computation Institute
KCBD, Room 4124
900 E. 57th Street
Chicago, IL 60637
Phone: 773-834-9049
Fax: 773-702-4786
wvandron@peds.bsd.uchicago.edu

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

Marie Skłodowska-Curie Actions (MSCA)
Research and Innovation Staff Exchange (RISE)
H2020-MSCA-RISE-2017

Project Acronym: AUTOIGG – Project Number: 778405
Annex 1 to the Grant Agreement
(Description of the Action)
Part B

ESTIMATED BUDGET FOR THE ACTION (page 1 of 2)

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

	Number of units ((person-months)
1. FBUB	154.00
2. YEDITEPE	27.00
3. UEF	8.00
4. Argenit	21.00
5. ELVESYS	2.00
Total consortium	212.00

	Estimated eligible[1] costs (per budget category)							EU contribution		
	A. Costs for seconded staff members		B. Institutional costs				Total costs	Reimbursemer rate %	Maximum EU contribution[2]	Maximum grant amount[3]
			B.1. Research, trainingand networking costs		B2. Management andindirect[4] costs					
Form of costs[5]	Unit		Unit		Unit					
	Costs per unit[6]	Total a[7]	Costs per unit[6]	Total b[7]	Costs per unit[6]	Total c[7]	d = a+b+c	e	f	g
1. FBUB	2000.00	308000.00	1800.00	277200.00	700.00	107800.00	693000.00	100.00	693000.00	
2. YEDITEPE	2000.00	54000.00	1800.00	48600.00	700.00	18900.00	121500.00	100.00	121500.00	
3. UEF	2000.00	16000.00	1800.00	14400.00	700.00	5600.00	36000.00	100.00	36000.00	
4. Argenit	2000.00	42000.00	1800.00	37800.00	700.00	14700.00	94500.00	100.00	94500.00	
5. ELVESYS	2000.00	4000.00	1800.00	3600.00	700.00	1400.00	9000.00	100.00	9000.00	
Total consortium		424000.00		381600.00		148400.00	954000.00	100	954000.00	954000.00

1 See Article 6 for conditions for costs to be eligible
2 This is the theoretical amount of EU contribution that the system calculates automatically (by multiplying all the budgeted costs by the reimbursement rate). This theoretical amount is capped by the 'maximum grant amount' (that the Commission/Agency decided to grant for the action) (see Article 5.1).
3 The 'maximum grant amount' is the maximum grant amount decided by the Commission/Agency. It normally corresponds to the requested grant, but may be lower.
4 The indirect costs covered by the operating grant (received under any EU or Euratom funding programme; see Article 6.3(b)) are ineligible under the GA. Therefore, a beneficiary that receives an operating grant during the action's duration cannot declare indirect costs for the year(s)/reporting period(s) covered by the operating grant (i.e. the unit cost for management and indirect costs will be halved for person-months that are incurred during the period covered by the operating grant).
5 See Article 5 for form of costs.
6 See Annex 2a 'Additional information on the estimated budget' for the details on the costs per unit.
7 Total = costs per unit x number of units (person-months).

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

ANNEX 2a

ADDITIONAL INFORMATION ON THE ESTIMATED BUDGET

- **Instructions and footnotes in blue will not appear in the text generated by the IT system (since they are internal instructions only).**
- **For options *[*in square brackets*]*: the applicable option will be chosen by the IT system. Options not chosen will automatically not appear.**
- **For fields in [grey in square brackets] (even if they are part of an option as specified in the previous item): IT system will enter the appropriate data.**

Marie Skłodowska-Curie unit costs

MSC-RISE unit costs

Costs for seconded staff members — Top-up allowance

Units: months spent by the seconded staff member(s) on the research and innovation activities ('person-months')

Amount per unit[1]: see Annex 2

Estimated number of units: see Annex 2

Institutional costs — Research, training and networking costs

Units: months spent by the seconded staff member(s) on the research and innovation activities ('person-months')

Amount per unit[2]: see Annex 2

Estimated number of units: see Annex 2

Institutional costs — Management and indirect costs

Units: months spent by the seconded staff member(s) on the research and innovation activities ('person-months')

Amount per unit[3]: see Annex 2

Estimated number of units: see Annex 2

---

1 Same amount for all beneficiaries.
Average based on the amount for the top-up allowance set out in the Main Work Programme — MSCA in force at the time of the call.

2 Same amount for all beneficiaries.
Average based on the amount for research, training and networking costs set out in the Main Work Programme — MSCA in force at the time of the call.

3 Same amount for all beneficiaries.
Average based on the amount for management and indirect costs set out in the Main Work Programme — MSCA in force at the time of the call.

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

YEDITEPE UNIVERSITY VAKIF (YEDITEPE), established in KAYISDAGI STREET AGUSTOS CAMPUS 26, Istanbul 81120, Turkey, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('2')

in Grant Agreement No 778405 ('the Agreement')

between FACULTY OF BIOLOGY OF THE UNIVERSITY OF BELGRADE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTICS OF NEURODEGENERATIVE DISEASES (AUTOIGG)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

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 conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ITA-SUOMEN YLIOPISTO (UEF), established in YLIOPISTONRANTA 1 E, KUOPIO 70211, Finland, VAT number: FI22857339, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('3')

in Grant Agreement No 778405 ('the Agreement')

between FACULTY OF BIOLOGY OF THE UNIVERSITY OF BELGRADE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTICS OF NEURODEGENERATIVE DISEASES (AUTOIGG)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

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 conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ARGENIT AKILLI BILGI TEKNOLOJILERI SANAYI VE TICARET LIMITED SIRKETI (Argenit), established in ITU AYAZAGA KAMPUSU ARI TEKNOKENT ARI 1 BINASI NO 27 MASLAK SARIYER, ISTANBUL 34469, Turkey, VAT number: TR0740487290, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('4')

in Grant Agreement No 778405 ('the Agreement')

between FACULTY OF BIOLOGY OF THE UNIVERSITY OF BELGRADE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTICS OF NEURODEGENERATIVE DISEASES (AUTOIGG)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

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 conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ELVESYS SAS (ELVESYS), established in 111 AVENUE VICTOR HUGO, PARIS CEDEX 16 75784, France, VAT number: FR19531301174, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('5')

in Grant Agreement No 778405 ('the Agreement')

between FACULTY OF BIOLOGY OF THE UNIVERSITY OF BELGRADE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'AUTOMATED FUNCTIONAL SCREENING OF IgGs FOR DIAGNOSTICS OF NEURODEGENERATIVE DISEASES (AUTOIGG)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

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 conditions it sets out.

SIGNATURE

For the beneficiary

Associated with document Ref. Ares(2017)4842465 - 04/10/2017

ⓘ print format A4

MODEL ANNEX 4 FOR H2020 MGA MSCA-RISE — MULTI

FINANCIAL STATEMENT FOR BENEFICIARY [name] FOR REPORTING PERIOD [reporting period]

Number of units (person-months)	Form of costs [3]	Eligible [1] costs (per budget category)							EU contribution		
		A. Costs for seconded staff members		B. Institutional costs				Total costs	Reimbursement rate %	Maximum EU contribution	Requested EU contribution
				B.1. Research, training and networking costs		B2. Management and indirect [2] costs					
		Unit		Unit		Unit					
		Costs per unit [4]	Total a [5]	Costs per unit [4]	Total b [5]	Costs per unit [4]	Total c [5]	d = a+b+c	e	f	g

Checkbox :	Did you receive any EU/Euratom operating grant during this reporting period?	❍ YES ❍ NO	
	If yes, pls indicate how many of the total person-months (see 'total beneficiary' above) were incurred DURING the period covered by the operating grant?		

The beneficiary hereby confirms that:
The information provided is complete, reliable and true.
The costs declared are eligible (see Article 6).

The costs 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 17, 18 and 22).

ⓘ Please declare all your person-months, even if you exceed the estimated budget (see Annex 2). Only person-month that were declared in your individual financial statements can be taken into account later on, in order to replace other costs that are found to be ineligible.

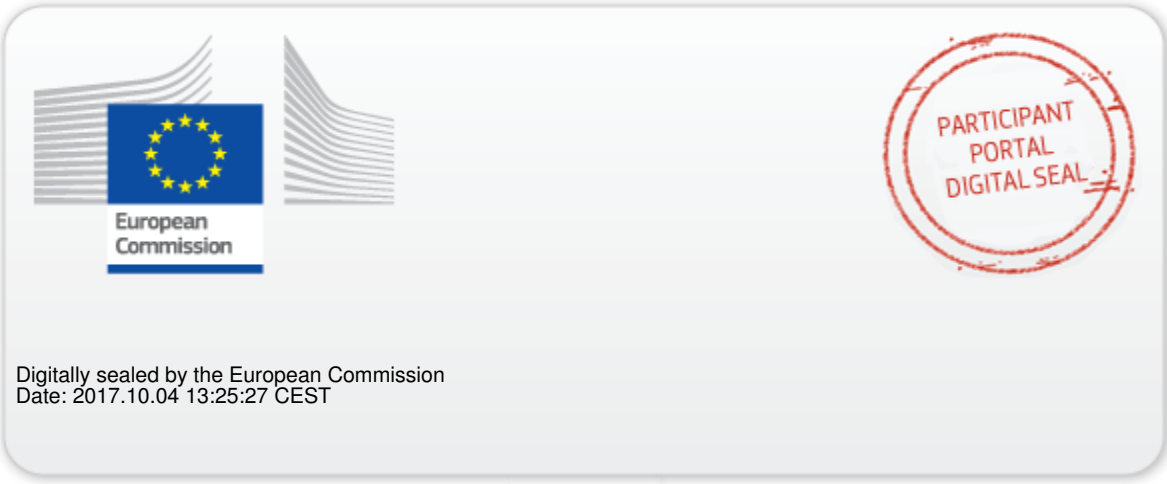
[1] See Article 6 for the eligibility conditions

[2] The indirect costs claimed must be free of any amounts covered by an operating grant (received under any EU or Euratom funding programme; see Article 6.3 (b)). If you have received an operating grant during this reporting period, indirect costs will not be reimbursed for the person-months incurred during the period covered by the operating grant.

[3] See Article 5 for the form of costs

[4] See Annex 2a 'Additional information on the estimated budget' for the details on the costs per unit.

[5] Total = costs per unit x number of units (person-months)



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