VERBALE N. 09 DEL CONSIGLIO DEL DIPARTIMENTO DI BIOSCIENZE, BIOTECNOLOGIE E BIOFARMACEUTICA DEL GIORNO 10.09.2020

Il giorno **10 settembre 2020** il Consiglio del Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica, convocato con nota prot. n. 935-II/9 del 03.09.2020 ed integrato con nota email del 08.09.2020, si è riunito alle ore 09,30, in via telematica mediante l'ausilio della piattaforma Microsoft Teams, per discutere e deliberare il seguente Ordine del Giorno:

Approvazione Verbale del 30.07.2020;
Comunicazioni del Direttore;

1. **Procedure per il reclutamento di n. 9 Ricercatori a tempo determinato ai sensi dell'Art. 24 comma 3 lett. a) Legge 240/2010 a valere sui Fondi "Research for Innovation (REFIN) per l'individuazione dei progetti di ricerca" - POR PUGLIA FESR-FSE 2014/2020. Codice CUP H94I20000410008: individuazione dei componenti le commissioni valutatrici;**
2. **Predisposizione Offerta Formativa 2021-2022;**
3. **Nulla osta per assunzione di incarichi di insegnamento per corsi post-laurea;**
4. **Graduatoria definitiva Bando di mobilità studentesca Erasmus+ 2020/2021: ratifica del Decreto del Direttore n. 16 del 5 Agosto 2020;**
5. **Ripresa degli esami di profitto in presenza: ratifica del Decreto del Direttore n. 17 del 31 Agosto 2020;**
6. **Approvazione grant agreement progetto Marie Curie Nicchia;**
7. **Ripartizione assegni di tutorato AA19/20 per il nostro Dipartimento;**
8. **Richiesta di riproposizione di bando per assegno di ricerca andato deserto (programma 05.129, richiedente Prof. Luigi Palmieri);**
9. **Nomina tutor per assegnisti di ricerca;**
10. **Proposta di contributo straordinario da avanzare al Consiglio di Amministrazione dell'Ateneo;**
11. **Varie ed eventuali.**

Il Consiglio risulta così composto:

Presente (P), Giustificato (G), Assente (A)

	Docenti I Fascia		(P)	(G)	(A)
1	BARILE	Maria	X		
2	CALAMITA	Giuseppe	X		
3	COTECCHIA	Susanna		X	
4	DELL'AQUILA	Maria Elena	X		
5	FIERMONTE	Giuseppe	X		
6	NICCHIA	Grazia Paola	X		
7	PALMIERI	Luigi	X		
8	PESOLE	Graziano	X		
9	VALENTI	Giovanna	X		

	Docenti II Fascia		(P)	(G)	(A)
10	AGRIMI	Gennaro	X		
11	BRUNI	Francesco	X		
12	CASSANO	Giuseppe	X		

13	CASTEGNA	Alessandra	X		
14	CIANI	Elena	X		
15	COLELLA	Matilde	X		
16	DEBELLIS	Lucantonio	X		
17	D'ERCHIA	Anna Maria	X		
18	GISSI	Carmela	X		
19	LASORSA	Massimo	X		
20	LIUZZI	Grazia Maria	X		
21	LOGUERCIO POLOSA	Paola	X		
22	MAROBBIO	Carlo	X		
23	PANARO	Maria Antonietta	X		
24	PESCE	Vito	X		
25	PICARDI	Ernesto	X		
26	PROCINO	Giuseppe	X		
27	RESHKIN	Joel Stephan			X
28	ROBERTI	Marina	X		
29	SCALERA	Vito	X		
30	STORELLI	Maria Maddalena	X		
31	TAMMA	Grazia	X		

	Ricercatori		(P)	(G)	(A)
32	CALVELLO	Rosa	X		
33	CARDONE	Rosa Angela	X		
34	CAROPPO	Rosa	X		
35	CHIMIENTI	Guglielmina	X		
36	CIANCIULLI	Antonia	X		
37	CORMIO	Antonella	X		
38	DE GRASSI	Anna		X	
39	DE PALMA	Annalisa	X		
40	DE VIRGILIO	Caterina	X		
41	DI MISE	Annarita	X		
42	DI NOIA	Maria Antonietta	X		
43	FRATANTONIO	Deborah	X		
44	GUARAGNELLA	Nicoletta	X		
45	GUERRA	Lorenzo	X		
46	LA PIANA	Gianluigi	X		
47	LATRONICO	Tiziana	X		
48	LEZZA	Angela Maria Serena	X		
49	LO GIUDICE	Claudio	X		
50	MAGNIFICO	Maria Chiara	X		
51	MALLAMACI	Rosanna	X		
52	MELELEO	Daniela Addolorata	X		
53	MILANO	Serena	X		
54	PIERRI	Ciro	X		
55	PISANI (*)	Francesco		X	

56	PISANO	Isabella	X		
57	POETA	Luana	X		
58	PORCELLI	Vito	X		
59	RAINALDI	Guglielmo	X		
60	RANIERI	Marianna	X		
61	SCARCIA	Pasquale	X		
62	VOLPICELLA	Mariateresa	X		
63	VOZZA	Angelo	X		

	Personale Tecnico/Amm.vo		(P)	(G)	(A)
64	DE LEONARDIS	Francesco		X	
65	EVANGELISTA	Angela	X		
66	GRAVINA	Roberta	X		
67	LONGO	Rosanna	X		
68	MOLA	Maria Grazia	X		
69	STORELLI	Arianna	X		

	Rappresentanti degli Studenti		(P)	(G)	(A)
70	ABBATANGELO	Elena			X
71	ACQUAVIVA	Francesca			X
72	BRUNO	Francesco			X
73	CANNARELLA	Marco Santo			X
74	DIGREGORIO	Alessandro	X		
75	GALLUZZI	Giovanni	X		
76	LADISA	Francesco		X	
77	MANDORINO	Camilla			X
78	OSELLA	Chiara			X
79	PICCIRILLO	Giulia			X
80	SURIANO	Clelia	X		
81	TRIPIEDI	Vincenzo			X

	Rappresentanti dei Dottorandi		(P)	(G)	(A)
82	LAERA	Luna			X
83	TARANTINO	Nancy	X		

(*) in congedo

TOTALE COMPONENTI: N. 83; PRESENTI N. 68 GIUSTIFICATI N. 5 ASSENTI N. 10.

Segretario verbalizzante: Dott.ssa Margherita Ardito, Coordinatore del Dipartimento.

Alla Seduta partecipa la Dott.ssa Silvana De Leo, Responsabile dell'U.O. Servizi Generali, Logistica e Supporto informatico, con funzioni di supporto alla verbalizzazione.

Il Direttore, verificata la presenza del numero legale, alle 09,40, dichiara aperta la seduta.

In apertura di seduta il Direttore propone di integrare l'odg con il seguente punto:

11. **Richieste di autorizzazione a frequentare il Dipartimento;**

Il Consiglio, unanime, approva.

L'odg viene, quindi, così riformulato:

Approvazione Verbale del 30.07.2020;
Comunicazioni del Direttore;

1. **Procedure per il reclutamento di n. 9 Ricercatori a tempo determinato ai sensi dell'Art. 24 comma 3 lett. a) Legge 240/2010 a valere sui Fondi "Research for Innovation (REFIN) per l'individuazione dei progetti di ricerca" - POR PUGLIA FESR-FSE 2014/2020. Codice CUP H94I20000410008: individuazione dei componenti le commissioni valutatrici;**
2. **Predisposizione Offerta Formativa 2021-2022;**
3. **Nulla osta per assunzione di incarichi di insegnamento per corsi post-laurea;**
4. **Graduatoria definitiva Bando di mobilità studentesca Erasmus+ 2020/2021: ratifica del Decreto del Direttore n. 16 del 5 Agosto 2020;**
5. **Ripresa degli esami di profitto in presenza: ratifica del Decreto del Direttore n. 17 del 31 Agosto 2020;**
6. **Approvazione grant agreement progetto Marie Curie Nicchia;**
7. **Ripartizione assegni di tutorato AA19/20 per il nostro Dipartimento;**
8. **Richiesta di riproposizione di bando per assegno di ricerca andato deserto (programma 05.129, richiedente Prof. Luigi Palmieri);**
9. **Nomina tutor per assegnisti di ricerca;**
10. **Proposta di contributo straordinario da avanzare al Consiglio di Amministrazione dell'Ateneo;**
11. **Richieste di autorizzazione a frequentare il Dipartimento;**
12. **Varie ed eventuali.**

Si dà inizio ai lavori.

Approvazione Verbale del 30.07.2020;

Il Direttore sottopone all'approvazione del Consiglio del Dipartimento il verbale relativo alla seduta del 30.07.2020.

Il Consiglio, con l'astensione degli assenti alla suddetta riunione, approva il verbale relativo alla seduta del 30.07.2020.

Comunicazioni del Direttore;

A) con nota prot. n. 43657-VII/5, del 30.07.2020 (ns. Prot.A. n. 894-VII/5, del 31.07.2020), da parte della Direzione Risorse Umane, è stata trasmessa copia del D.R. n. 1959 del 29.07.2020, con il quale, a decorrere dal 01.10.2020, è stata disposta la mobilità della Dott.ssa Giacomina Brunetti, ricercatore confermato, dal Dipartimento di Scienze mediche di base, Neuroscienze ed Organi di senso al Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica;

B) con nota prot. n. 44927-VII/4, del 05.08.2020 (ns. Prot.A. n. 905-VII/4, del 05.08.2020), da parte della Direzione Risorse Umane, è stata trasmessa copia del D.R. n. 2045 del 04.08.2020, con il quale, a decorrere dal 04.08.2020, al Dott. Pietro Consiglio, funzionario di questa Università, cat. C, pos. ec. 3, è attribuito l'incarico di Responsabile "Focal Point MEPA lato IMPRESA". Al Dott. Pietro Consiglio compete, in virtù dell'incarico conferito, il Coordinamento delle attività amministrative e

gestionali delle vendite da effettuare sul mercato elettronico della pubblica amministrazione lato impresa, nonché la stipula dei contratti quale soggetto delegato del Rettore;

C) con nota prot. n. 45281-I/9, del 06.08.2020 (ns. Prot.A. n. 909-I/9 del 07.08.2020), da parte della Direzione Generale, è stata data comunicazione che con D.D.G. n. 206 del 31.07.2020 è stato adottato un primo aggiornamento dell'elenco dei processi e subprocessi, assegnati alle strutture amministrative di Ateneo, nelle more di una complessiva revisione dei processi da produrre in risposta anche ai contenuti del Documento di Programmazione integrata 2020-2022, analizzate le istanze di revisione/adeguamento di alcuni subprocessi pervenute dalle strutture organizzative e in considerazione dei risultati dell' analisi/revisione effettuata dal Gruppo di lavoro nominato con D .R. n. 632 del 26.02.2020;

D) con nota prot. n. 49276-X/10, del 04.09.2020 (ns. Prot.A. n. 941, del 04.09.2020), da parte della U.O. Sicurezza e Sorveglianza sanitaria - Staff sicurezza, prevenzione e protezione della Direzione generale, è stata trasmessa copia dell'autorizzazione n. 9/2020-UT, in data 12.08.2020, rilasciata al legale rappresentante *pro-tempore*, Prof. Stefano Bronzini, dal Ministero della Salute, per la gestione dello stabilimento utilizzatore di questo Dipartimento presso il Nuovo palazzo sede dei Dipartimenti biologici per le specie animali: topi, ratti, conigli e anfibi. L'autorizzazione ha durata di 6 anni e può essere sospesa o revocata secondo quanto previsto dall'art. 21 del D.Lgs. n. 26/2014. La nota, evidenzia il Direttore, pone il 12 Novembre come termine ultimo per la dismissione del vecchio stabulario.

Il Direttore apre, quindi, la discussione sul primo punto all'O.d.G.:

1. Procedure per il reclutamento di n. 9 Ricercatori a tempo determinato ai sensi dell'Art. 24 comma 3 lett. a) Legge 240/2010 a valere sui Fondi "Research for Innovation (REFIN) per l'individuazione dei progetti di ricerca" - POR PUGLIA FESR-FSE 2014/2020. Codice CUP H94I20000410008: individuazione dei componenti le commissioni valutatrici;

Il Direttore riferisce che, con nota email del 29.07.2020, da parte della Dott.ssa Maria Zerbinotti, Responsabile dell'U.O. Procedure concorsuali della Direzione Risorse Umane, è stata data comunicazione che nella Gazzetta Ufficiale della Repubblica - IV Serie Speciale - Concorsi ed Esami - n. 58 del 28.07.2020 sono stati pubblicati gli avvisi relativi all'indizione delle selezioni per n. 110 Ricercatori universitari a tempo determinato, mediante stipula di contratto di lavoro subordinato della durata di 36 mesi, ai sensi dell'art. 24, comma 3, lett. a), Legge 240/10, con regime di impegno a tempo pieno, con scadenza per la presentazione delle istanze di partecipazione il giorno il 27 agosto 2020. Ciò premesso ed al fine di consentire alla U.O. Procedure concorsuali di poter predisporre i decreti di nomina delle Commissioni valutatrici, i Dipartimenti, in ottemperanza a quanto stabilito dall'art. 7 del "Regolamento per il reclutamento dei ricercatori con contratto a tempo determinato" di questa Università (D.R. n.506/2020 del 18.02.2020), dovranno individuare i nominativi dei componenti che dovranno far parte delle Commissioni. La relativa deliberazione dovrà essere assunta a partire dal 28.08.2020, giorno successivo allo scadere del predetto termine per la presentazione delle istanze di partecipazione.

Il Direttore evidenzia che le procedure relative a questo Dipartimento sono state bandite con decreti rettorali dal n. 1700 al n. 1708 del 13.07.2020 e che, in base al nuovo "Regolamento per il reclutamento di ricercatori a tempo determinato", sulla base del quale verranno effettuati gli odierni sorteggi, le commissioni devono essere composte da un membro interno designato, che può anche non essere un professore ordinario ma che deve avere i requisiti prescritti relativamente alla qualificazione scientifica, e due membri di sesso diverso sorteggiati in una rosa di 4 nominativi (2 maschi e 2 femmine) di professori ordinari. I due non sorteggiati utilmente resteranno come supplenti. Il Consiglio deve designare anche un altro membro interno supplente.

Il Direttore, quindi, in riferimento a ciascuna delle procedure bandite, enuclea la proposta di "rosa di nominativi" per il relativo settore scientifico disciplinare come pervenuta dai colleghi del medesimo settore i quali hanno assicurato che ciascuno dei docenti proposti possiede i requisiti richiesti.

I docenti del SSD BIO/11 propongono un'unica commissione per tutte le procedure bandite per tale settore scientifico disciplinare e cioè:

la procedura bandita con D.R. 1700 del 13/7/2020 Codice Pratica 1A32D6F0,

la procedura bandita con D.R. 1701 del 13/7/2020 Codice Pratica 856662FD,

la procedura bandita con D.R. 1707 del 13/7/2020 Codice Pratica C1A93B75.

Membro interno designato: Carmela Gissi, Professore Associato, BIO/11;

membro interno designato supplente: Ernesto Picardi, Professore Associato, BIO/11.

Rosa di professori ordinari esterni, del settore BIO/11, fra cui effettuare l'estrazione:

Vittorio Colantuoni (Università del Sannio),

Simone Ottonello (Università di Parma),

Manuela Helmer Citterich (Università di Roma Tor Vergata),

Valeria Poli (Università di Torino).

Il Consiglio, all'unanimità degli aventi diritto al voto, approva la proposta sopra esposta.

Si procede quindi al sorteggio. Sono stati preparati dei biglietti riportanti i nominativi dei docenti da estrarre e sono ripiegati in modo da non consentirne il riconoscimento. Viene invitata la Dott.ssa De Leo ad effettuare l'estrazione.

Il risultato dell'estrazione è il seguente:

1° estratto: Vittorio Colantuoni

2° estratto: Manuela Helmer Citterich

3° estratto: Simone Ottonello

4° estratto: Valeria Poli

Tenuto conto dei vincoli posti dal regolamento, la commissione risulta individuata nei termini seguenti:

membri effettivi:

Carmela Gissi, membro interno designato

Vittorio Colantuoni (Università del Sannio),

Manuela Helmer Citterich (Università di Roma Tor Vergata),

membri supplenti:

Ernesto Picardi, membro interno designato supplente

Simone Ottonello

Valeria Poli

Per la procedura bandita con D.R. 1702 del 13/7/2020, per il SSD BIO/09 Codice Pratica 4FC8E072:

Membro interno designato: Giuseppe Calamita, Professore Ordinario, BIO/09;

membro interno designato supplente: Grazia Paola Nicchia, Professore Ordinario, BIO/09.

Rosa di professori ordinari esterni, del settore BIO/09, fra cui effettuare l'estrazione:

Rosa Serio (Università degli Studi di Palermo);

Carla Perrone-Capano (Università degli Studi di Napoli Federico II)

Pasquale Pagliaro (Università degli Studi di Torino);

Massimo Dal Monte (Università degli Studi di Pisa)

Il Consiglio, all'unanimità degli aventi diritto al voto, approva la proposta sopra esposta.

Si procede quindi al sorteggio. Sono stati preparati dei biglietti riportanti i nominativi dei docenti da estrarre e sono ripiegati in modo da non consentirne il riconoscimento. Viene invitata la Dott.ssa De Leo ad effettuare l'estrazione.

Il risultato dell'estrazione è il seguente:

1° estratto: Pasquale Pagliaro

2° estratto: Rosa Serio

3° estratto: Massimo Dal Monte

4° estratto: Carla Perrone-Capano

Tenuto conto dei vincoli posti dal regolamento, la commissione risulta individuata nei termini seguenti:

membri effettivi:

Giuseppe Calamita, membro interno designato

Pasquale Pagliaro (Università degli Studi di Torino)

Rosa Serio (Università degli Studi di Palermo);

membri supplenti:

Grazia Paola Nicchia, membro interno designato supplente

Massimo Dal Monte

Carla Perrone-Capano

Per la procedura bandita con D.R. 1703 del 13/7/2020, per il SSD BIO/09 Codice Pratica 6F34D1BF:

membro interno designato: Grazia Paola Nicchia, Professore Ordinario, BIO/09;

membro interno designato supplente: Giuseppe Calamita, Professore Ordinario, BIO/09.

Rosa di professori ordinari esterni, del settore BIO/09, fra cui effettuare l'estrazione:

Giuseppe Cibelli, (Università di Foggia)

Massimo Dal Monte, (Università di Pisa)

Antonia Lanni, (Università degli Studi della Campania Luigi Vanvitelli)

Maria Carmela Cerra, (Università della Calabria)

Il Consiglio, all'unanimità degli aventi diritto al voto, approva la proposta sopra esposta.

Si procede quindi al sorteggio. Sono stati preparati dei biglietti riportanti i nominativi dei docenti da estrarre e sono ripiegati in modo da non consentirne il riconoscimento. Viene invitata la Dott.ssa De Leo ad effettuare l'estrazione.

Il risultato dell'estrazione è il seguente:

1° estratto: Maria Carmela Cerra

2° estratto: Antonia Lanni

3° estratto: Massimo Dal Monte

4° estratto: Giuseppe Cibelli

Tenuto conto dei vincoli posti dal regolamento, la commissione risulta individuata nei termini seguenti:

membri effettivi:

Grazia Paola Nicchia, membro interno designato

Maria Carmela Cerra, (Università della Calabria)

Massimo Dal Monte, (Università di Pisa)

membri supplenti:

Giuseppe Calamita, membro interno designato supplente

Antonia Lanni

Giuseppe Cibelli

Per la procedura bandita con D.R. 1704 del 13/7/2020, per il SSD MED/04 Codice Pratica 4FB2BCF8:

membro interno designato: Prof.ssa Giuseppina Barrera, Professore Associato, MED/04, Università degli Studi di Torino;

membro interno designato supplente: Prof. Massimo Conese Professore Ordinario, MED/04, Università degli Studi di Foggia.

Rosa di professori ordinari esterni, del settore MED/04, fra cui effettuare l'estrazione:

Alessandro Weisz (Università degli Studi di Salerno)

Maurizio Parola (Università degli Studi di Torino)

Maria Luisa Lavitrano (Università degli Studi di Milano Bicocca)

Maria Rescigno (Università Humanitas di Milano).

Il Consiglio, all'unanimità degli aventi diritto al voto, approva la proposta sopra esposta.

Si procede quindi al sorteggio. Sono stati preparati dei biglietti riportanti i nominativi dei docenti da estrarre e sono ripiegati in modo da non consentirne il riconoscimento. Viene invitata la Dott.ssa De Leo ad effettuare l'estrazione.

Il risultato dell'estrazione è il seguente:

1° estratto: Maurizio Parola

2° estratto: Alessandro Weisz

3° estratto: Maria Luisa Lavitrano

4° estratto: Maria Rescigno

Tenuto conto dei vincoli posti dal regolamento, la commissione risulta individuata nei termini seguenti:

membri effettivi:

Giuseppina Barrera (Università degli Studi di Torino) membro interno designato

Maurizio Parola (Università degli Studi di Torino)

Maria Luisa Lavitrano (Università degli Studi di Milano Bicocca)

membri supplenti:

Massimo Conese (Università degli Studi di Foggia) membro interno designato supplente

Alessandro Weisz

Maria Rescigno

Per la procedura bandita con D.R. 1705 del 13/7/2020, per il SSD BIO/09 Codice Pratica 091C54A8:

membro interno designato: Giovanna Valenti, Professore Ordinario, BIO/09;

membro interno designato supplente: Giuseppe Procino, Professore Associato, BIO/09.

Rosa di professori ordinari esterni, del settore BIO/09, fra cui effettuare l'estrazione:

Marco Narici (Università degli Studi di Padova)

Massimo Dal Monte (Università degli Studi di Pisa)

Maria Carmela Cerra (Università degli Studi di Cosenza)

Rosa Serio (Università degli Studi di Palermo).

Il Consiglio, all'unanimità degli aventi diritto al voto, approva la proposta sopra esposta.

Si procede quindi al sorteggio. Sono stati preparati dei biglietti riportanti i nominativi dei docenti da estrarre e sono ripiegati in modo da non consentirne il riconoscimento. Viene invitata la Dott.ssa De Leo ad effettuare l'estrazione.

Il risultato dell'estrazione è il seguente:

1° estratto: Rosa Serio

2° estratto: Maria Carmela Cerra

3° estratto: Massimo Dal Monte

4° estratto: Marco Narici

Tenuto conto dei vincoli posti dal regolamento, la commissione risulta individuata nei termini seguenti:

membri effettivi:

Giovanna Valenti, membro interno designato

Rosa Serio (Università degli Studi di Palermo).

Massimo Dal Monte (Università degli Studi di Pisa)

membri supplenti:

Giuseppe Procino, membro interno designato supplente

Maria Carmela Cerra

Marco Narici

Per la procedura bandita con D.R. 1706 del 13/7/2020, per il SSD BIO/10 Codice Pratica 41F10F22:

membro interno designato: Luigi Palmieri, Professore Ordinario, BIO/10;

membro interno designato supplente: Vito Pesce, Professore Associato, BIO/10.

Rosa di professori ordinari esterni, del settore BIO/10, fra cui effettuare l'estrazione:

Stefania Iammetti (Università degli Studi di Milano)

Maria Fiammetta Romano (Università degli Studi di Napoli Federico II)

Francesco Bonomi (Università degli Studi di Milano)

Marco Moracci (Università degli Studi di Napoli Federico II).

Il Consiglio, all'unanimità degli aventi diritto al voto, approva la proposta sopra esposta.

Si procede quindi al sorteggio. Sono stati preparati dei biglietti riportanti i nominativi dei docenti da estrarre e sono ripiegati in modo da non consentirne il riconoscimento. Viene invitata la Dott.ssa De Leo ad effettuare l'estrazione.

Il risultato dell'estrazione è il seguente:

1° estratto: Francesco Bonomi

2° estratto: Maria Fiammetta Romano

3° estratto: Marco Moracci

4° estratto: Stefania Iammetti

Tenuto conto dei vincoli posti dal regolamento, la commissione risulta individuata nei termini seguenti:

membri effettivi:

Luigi Palmieri, membro interno designato

Francesco Bonomi (Università degli Studi di Milano)

Maria Fiammetta Romano (Università degli Studi di Napoli Federico II)

membri supplenti:

Vito Pesce, membro interno designato supplente

Marco Moracci

Stefania Iammetti

Per la procedura bandita con D.R. 1708 del 13/7/2020, per il SSD BIO/09 Codice Pratica D14F94D6:

membro interno designato: Giuseppe Procino, Professore Associato, BIO/09;

membro interno designato supplente: Giovanna Valenti, Professore Ordinario, BIO/09.

Rosa di professori ordinari esterni, del settore BIO/09, fra cui effettuare l'estrazione:

Giuseppe Cibelli (Università di Foggia)

Massimo Dal Monte (Università di Pisa)

Antonia Lanni (Università degli Studi della Campania Luigi Vanvitelli)

Maria Carmela Cerra (Università della Calabria)

Il Consiglio, all'unanimità degli aventi diritto al voto, approva la proposta sopra esposta.

Si procede quindi al sorteggio. Sono stati preparati dei biglietti riportanti i nominativi dei docenti da estrarre e sono ripiegati in modo da non consentirne il riconoscimento. Viene invitata la Dott.ssa De Leo ad effettuare l'estrazione.

Il risultato dell'estrazione è il seguente:

1° estratto: Maria Carmela Cerra

2° estratto: Massimo Dal Monte

3° estratto: Antonia Lanni

4° estratto: Giuseppe Cibelli

Tenuto conto dei vincoli posti dal regolamento, la commissione risulta individuata nei termini seguenti:

membri effettivi:

Giuseppe Procino, membro interno designato

Maria Carmela Cerra (Università della Calabria)

Massimo Dal Monte (Università di Pisa)

membri supplenti:

Giovanna Valenti, membro interno designato supplente

Antonia Lanni

Giuseppe Cibelli

Il Consiglio unanime assevera la regolarità della procedura espletata.

Il presente dispositivo è approvato seduta stante.

Il Direttore passa alla discussione del secondo punto all'O.d.G.:

2. Predisposizione Offerta Formativa 2021-2022;

Il Direttore riferisce che con nota prot. n. 43740-III/2, del 31.07.2020 (ns. prot.A. n. 895-III/2, del 31.07.2020) della Sezione offerta formativa della Direzione offerta formativa e servizi agli studenti, come ogni anno, per le esigenze di espletamento dei controlli sulla esaustività delle determinazioni e dei contenuti della documentazione da predisporsi per la presentazione dell'Offerta Formativa 2021-2022, in

attesa delle scadenze ufficiali stabilite dal MIUR, al fine di avviare tempestivamente le procedure, è stato richiesto alle singole strutture dipartimentali di far pervenire, entro il 30.09.2020, all'indirizzo del responsabile della sezione Offerta Formativa (paola.amati@uniba.it) le proprie determinazioni su:

1) proposte di nuove istituzioni di corsi di studio;
2) accessi a numero programmato;
3) linee programmatiche della prossima offerta (conferma di attivazione dei corsi di studio, modifiche già programmate ed eventuali disattivazioni).

Il Direttore propone che la scheda SUA (Scheda Unica Annuale) sia aperta in modalità "modifica", per tutti i Corsi di Laurea del Dipartimento, sottolineando la reversibilità di questa opzione che potrebbe essere tramutata nelle modalità: "aggiorna" o "conferma". Occorre riprendere e mettere a frutto, infatti, il lavoro già svolto lo scorso anno nel tentativo di una complessiva revisione della proposta formativa del Dipartimento, la quale, come è emerso in quella sede, deve essere necessariamente considerata nel suo complesso per evitare duplicazioni e nello stesso tempo per mettere a frutto le competenze presenti nell'ateneo e con ciò fornire la migliore proposta formativa possibile. Si potrebbe, a suo parere, procedere in modalità "aggiorna" solo per il CLM in Scienze della nutrizione per la salute umana (LM61) che già lo scorso anno è stato interessato da importanti modifiche.

Il Consiglio, unanime, delibera che la SUA sia aperta in modalità "modifica" per tutti i Corsi di Studio gestiti dal Dipartimento, fatta eccezione per il CLM in Scienze della Nutrizione per la Salute Umana (LM61) per il quale si procederà in modalità "aggiorna".

Il Direttore passa alla discussione del terzo punto all'O.d.G.:

3. Nulla osta per assunzione di incarichi di insegnamento per corsi post-laurea;

Il Direttore illustra la richiesta avanzata dal Prof. Gennaro Agrimi, professore associato confermato presso questo Dipartimento, che, con nota del 02.09.2020 (ns. Prot.A. n. 933-VII/4 del 02.09.2020), chiede il nulla osta a svolgere il seguente incarico, a titolo retribuito: "due cicli di lezioni online 1) Cellulosic biomass pretreatment: Hydrolyse, fermentation, chimica treatment; 2) Biotechnologies for biomass conversion", a favore dell'Université de Lille – UFR de Chimie. L'istante dichiara che il suddetto impegno non confligge con l'assolvimento dei propri compiti istituzionali, né vi reca pregiudizio.

Il Direttore invita, quindi, il Consiglio a pronunciarsi in merito.

Il Consiglio, unanime, concede il nulla osta richiesto.

Il presente dispositivo è approvato seduta stante.

Il Direttore passa alla discussione del quarto punto all'O.d.G.:

4. Graduatoria definitiva Bando di mobilità studentesca Erasmus+ 2020/2021: ratifica del Decreto del Direttore n. 16 del 5 Agosto 2020;

Il Direttore dà lettura del proprio decreto n. 16 del 05.08.2020 con il quale, viste, tra le altre, la nota del 29.07.2020, a firma del Delegato alle Politiche Erasmus+, Prof.ssa Antonietta Ivona, con la quale è stato chiesto alle Commissioni Erasmus di Dipartimento/Scuola di provvedere allo scorrimento e/o

aggiornamento delle graduatorie relative al Bando di mobilità studentesca Erasmus+ 2020/2021 e la graduatoria aggiornata accessibile attraverso il collegamento di seguito riportato (http://uniba.llpmanager.it/docenti/logind.aspx), che assegna a ciascun studente il seguente status:

- RIONTINO Flavia, matricola 731255, corso di laurea magistrale in Scienze della Nutrizione per la Salute Umana; IDONEA
- TARRICONE Giorgia, matricola 730546, corso di laurea magistrale in Biotecnologie Mediche e Medicina Molecolare; RINUNCIATARIA
- PLASMATI Lisa, matricola 726281, corso di laurea magistrale in Scienze Biosanitarie; IDONEA
- MAGARELLI Vittoria, matricola 724218, corso di laurea triennale in Biotecnologie Mediche e Farmaceutiche; RINUNCIATARIA
- SASSI Maria, matricola 702392, corso di laurea triennale in Biotecnologie Mediche e Farmaceutiche; RINUNCIATARIA
- MENOLASCINA Carlo, matricola 702664, corso di laurea triennale in Biotecnologie Mediche e Farmaceutiche; RINUNCIATARIO
- CASTELLANO Giulia, matricola 683850, corso di laurea triennale in Biotecnologie Mediche e Farmaceutiche; IDONEA
- FACCILONGO Roberta, matricola 701169, corso di laurea triennale in Biotecnologie Industriali e Agro-Alimentari; IDONEA
- SPANÒ Elena, matricola 702579, corso di laurea triennale in Biotecnologie Mediche e Farmaceutiche. NON IDONEA
- PACE Giuseppe, matricola 719823, corso di laurea triennale in Biotecnologie Industriali e Agro-Alimentari; IDONEO
- VALENTE Nicla, matricola 720258, corso di laurea triennale in Biotecnologie Industriali e Agro-Alimentari IDONEA,

ravvisata l'urgenza di procedere, dovendo trasmettere, in tempi brevi, al Settore Internazionalizzazione - U.O. Mobilità Internazionale, lo scorrimento e/o aggiornamento della graduatoria definitiva relativa al Bando di mobilità studentesca Erasmus+ 2020/2021, al fine di consentire ai vincitori una ottimale accettazione e collocazione presso le varie istituzioni europee, e nell'impossibilità di procedere alla convocazione del Consiglio di Dipartimento, ha decretato di approvare le seguenti istituzioni partner presso le quali sarà svolto il periodo di mobilità Erasmus+ nell'A.A. 2020/2021 agli studenti riconosciuti come idonei:

- RIONTINO Flavia: P SANTARE01 - INSTITUTO POLITÉCNICO DE SANTARÉM (PORTOGALLO);
- PLASMATI Lisa: E CORDOBA01 - UNIVERSIDAD DE CÓRDOBA (SPAGNA);
- CASTELLANO Giulia: D ULM01 - UNIVERSITÄT ULM (GERMANIA);

- FACCILONGO Roberta: E MADRID03, UNIVERSIDAD COMPLUTENSE DE MADRID (SPAGNA);
- PACE Giuseppe: PL OLSZTYN01 - WARMIA AND MASURIA UNIVERSITY IN OLSZTYN (POLONIA);
- VALENTE Nicla: PL OLSZTYN01 - WARMIA AND MASURIA UNIVERSITY IN OLSZTYN (POLONIA).

Il Consiglio, unanime, ratifica il D.D. n. 16 del 05.08.2020.

Il Direttore altresì, data la eventualità di possibili variazioni nelle destinazioni assegnate legate alla situazione sanitaria che sono state rese possibili fino ad Ottobre, propone di delegare la loro approvazione alla Commissione Erasmus di Dipartimento.

Il Consiglio, unanime, approva tale delega.

Il presente dispositivo è approvato seduta stante.

Il Direttore passa alla discussione del quinto punto all'O.d.G.:

5. Ripresa degli esami di profitto in presenza: ratifica del Decreto del Direttore n. 17 del 31 Agosto 2020;

Il Direttore, in merito all'argomento indicato in oggetto, considerato che, tra le altre cose, in vista dell'organizzazione degli interventi di sanificazione, l'amministrazione ha chiesto ai Dipartimenti di comunicare la calendarizzazione delle attività didattiche in presenza per organizzare gli interventi di sanificazione degli ambienti al termine del loro utilizzo e considerata l'insufficiente disponibilità di aule di cui dispone il Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica per cui, ordinariamente, per far fronte alle attività didattiche relative ai corsi di studio di propria competenza, fa ricorso ad aule messe a disposizione da altri Dipartimenti, con ciò avendo bisogno di un tempo congruo per la redazione di un calendario completo con l'indicazione della sede di svolgimento per tutti gli esami dei CdS afferenti al Dipartimento, riferisce di aver decretato, con proprio D.D. n. 17 del 31.08.2020, che, per quanto riguarda i Corsi di laurea gestiti dal Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica, gli esami di profitto continuino ad essere svolti in modalità a distanza almeno fino al 14 Settembre 2020.

Il Direttore invita, quindi, il Consiglio a deliberare in merito.

Il Consiglio, unanime, ratifica il suddetto decreto.

Il Direttore riferisce che, con grande sforzo dei coordinatori dei corsi di studio e con il prezioso supporto della Dott.ssa Teresa Lorusso e della Sig.ra Roberta Gravina che ringrazia per il lavoro svolto, si è proceduto alla elaborazione di un calendario degli esami di profitto dal 15 settembre al 15 ottobre.

Alla luce delle linee guida emanate da questo ateneo per la ripresa delle attività didattiche in presenza, il Direttore ritiene che si debba procedere a riprendere lo svolgimento degli esami di profitto in presenza a partire dal 14 Settembre inviando, come era stato richiesto, il calendario relativo e chiedendo che l'amministrazione predisponga le misure necessarie (distributori di gel igienizzante e interventi di sanificazione soprattutto). Evidenzia che ci potranno essere delle eccezioni legate a situazioni di particolare "fragilità" di alcuni docenti. Il Ministero della Salute ha recentemente prodotto una circolare

in merito ai lavoratori c.d. “fragili” sulla base della quale la nostra amministrazione ha attivato gli accertamenti avvalendosi del medico competente. Ci potranno essere richieste anche da parte degli studenti impossibilitati a presenziare all’appello perché in quarantena o con familiari in quarantena o altro. Non è stabilita alcuna modalità di accertamento delle motivazioni addotte che però, a parere di chi parla, devono essere ragionevoli e non pretestuose. L’effettuazione della didattica in presenza, in ogni caso, ritiene il Direttore, deve tornare ad essere la regola. Gli studenti, infatti, evidenzia, hanno diritto ad avere docenti con cui interfacciarsi e il nostro non è un ateneo telematico.

Si apre una lunga discussione nella quale emergono, in particolare, le seguenti osservazioni:

- la Prof Nicchia fa notare che, secondo le Linee Guida, se uno studente richiede, per ragioni che non è tenuto ad esplicitare né nessuno a verificare, di svolgere l’esame nella modalità telematica, questo gli deve essere consentito senza alcuna valutazione di ragionevolezza della richiesta;
- il Prof. Debellis ritiene che le modalità telematiche per il sostenimento degli esami non rappresentino una regressione ma siano, al contrario, una modalità parallela aggiuntiva e, pertanto, arricchente che occorre conservare;
- il Prof. Pierri rappresenta la necessità di estendere l’accezione di “fragilità” per ricomprendervi i docenti che convivono con soggetti anziani e/o fragili;
- il Prof. Agrimi, favorevole a continuare a svolgere alcune attività didattiche in modalità telematica, evidenzia che per la ripresa delle attività scolastiche è stato disposto lo svolgimento di test sierologici sui docenti;
- il Dott. La Piana riporta la propria esperienza positiva di esami sostenuti brillantemente tramite piattaforma tecnologica e concorda nella necessità di tutelare i docenti a rischio per pregresse patologie;
- il Sig. Digregorio ritiene opportuno riprendere le attività in presenza per garantire un diritto degli studenti;
- il Sig. Galluzzi sottolinea le grandi opportunità delle modalità telematiche, auspicando la possibilità di sostenere gli esami in presenza, pur considerando tutte le situazioni di rischio per le quali occorre dare priorità alla tutela della salute;
- la Prof.ssa Dell’Aquila si associa a coloro che sono favorevoli alla ripresa degli esami in presenza;

Esce, alle ore 11,40, la Prof.ssa Liuzzi.

- il Dott. Vozza pone il problema in cui uno studente voglia sostenere l'esame in presenza ed un componente della commissione (per una fragilità) possa farlo soltanto a distanza;
- la Prof.ssa Gissi ritiene che prevalga il diritto della persona “fragile” indipendentemente dallo status di docente o studente, sottolineando come "Resta valida la possibilità di organizzare colloqui ed esami con modalità telematica a distanza in risposta a specifiche richieste di studenti e/o docenti che dovessero avere particolari esigenze (es. soggetti fragili, studenti stranieri impossibilitati a raggiungere l'Italia, ecc.).";

- il Prof. Fiermonte che ritiene opportuno posticipare la ripresa degli esami in presenza visto l'aumento del numero di persone positive;
- la Sig.ra Longo che pone il problema di chi controllerà l'osservanza delle misure previste nelle linee guida;
- la Prof. Barile che propone di rinviare la ripresa degli esami in presenza ad Ottobre per avere più tempo per organizzare la stessa e per non creare tra gli studenti dissapori per la diversa modalità nello stesso appello di settembre.

Al termine del dibattito, il Direttore, ribadisce che l'indicazione di riprendere con gli esami in presenza è dell'Ateneo, è stata ampiamente discussa e votata negli organi di governo ed è stata attuata prontamente da alcuni Dipartimenti. Per le particolari criticità evidenziate, egli ha già decretato uno slittamento che questo Consiglio ha fatto proprio. Evidenzia, inoltre, in aggiunta alle criticità evidenziate dai colleghi, che anche la ripresa in presenza del personale tecnico e amministrativo, necessaria anche per lo svolgimento delle attività didattiche, che era stata annunciata per metà settembre non è stata ancora disciplinata.

Egli quindi, raccogliendo tutte le osservazioni emerse, chiede al Consiglio di esprimersi circa la ripresa degli esami di profitto in presenza dal 15 settembre prossimo.

Risultano, al momento della votazione, 66 presenti.

La proposta è respinta con 31 voti contrari e 3 astensioni.

Il Direttore, quindi, pone ai voti la proposta, emersa durante la discussione, di procrastinare la ripresa degli esami in presenza al 1° ottobre 2020.

Risultano, al momento della votazione, 66 presenti.

La proposta è approvata a maggioranza con 2 voti contrari e 10 astensioni.

Il Direttore passa alla discussione del sesto punto all'O.d.G.:

6. Approvazione grant agreement progetto Marie Curie Nicchia;

Il Direttore illustra gli elementi salienti della proposta progettuale di cui all'oggetto identificata dal numero 956325 e denominata "ASTROTECH". Il coordinamento del progetto è affidato al CNR di Roma. Il progetto coinvolge, in totale, 11 partners beneficiari tra cui UNIBA. Responsabile scientifico per Uniba è la Prof. Nicchia. Il progetto prevede un finanziamento totale pari a € 3 980 625.48 e la quota di competenza di questo Dipartimento è di € 261.499,68. Non è previsto cofinanziamento. Il progetto avrà durata di 48 mesi. Il progetto contempla il reclutamento di un dottorando.

Il Direttore, nel congratularsi con la Prof. Nicchia per l'importante progetto, propone di richiedere al Rettore la sottoscrizione del grant agreement relativo. Il documento, trasmesso nei giorni scorsi a tutti i membri del Consiglio, è allegato al presente Verbale (**Allegato A**) e ne costituisce parte integrante.

Il Consiglio, unanime, approva.

Il Direttore passa alla discussione del settimo punto all'O.d.G.:

7. Ripartizione assegni di tutorato AA 19/20 per il nostro Dipartimento;

Il Direttore introduce l'argomento ricordando che è pervenuta via mail dalla Dott. Patrizia Cioce della Direzione Offerta Formativa e Servizi agli Studenti, la comunicazione della attribuzione a questo Dipartimento di n. 3 assegni di tutorato. Ai fini dell'emanazione del bando di tutorato 2019/20 viene richiesta la determinazione circa la ripartizione di tali assegni tra tutorato informativo e tutorato didattico integrativo, propedeutico e di recupero, il titolo d'accesso per la partecipazione alla selezione e la denominazione corso di studio o scuola di dottorato di ricerca di accesso.

Riferisce, quindi, che, la Dott.ssa Volpicella, referente per l'orientamento e il tutorato, con i coordinatori dei Corsi di Studio/ Interclasse e la Prof. Cotecchia, referente per la didattica, ha elaborato la seguente proposta di ripartizione assegni di tutorato per l'A.A. 2019/2020, che ora viene sottoposta all'esame del Consiglio:

Dipartimento/Scuola	**RIPAR.**	**Sede Di Servizio**	**TIPOLOGIA ATTIVITA'**	**TITOLO DI ACCESSO**	**DENOMINAZIONE CORSO DI STUDIO o SCUOLA DI DOTTORATO DI ACCESSO**
Bioscienze, Biotecnologie e Biofarmaceutica (DBBB)	1	Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica Segreteria Didattica Via G. Fanelli n. 204, Bari	Tutorato didattico integrativo e di recupero in Matematica	Studente o dottorando di ricerca.	i) Laurea Magistrale in Matematica della classe LM-40 (DM 270/2004) o 45/S (DM 509/99), ovvero di diploma di laurea equiparato ai sensi del D.L. 09/07/09. ii) Dottorato di Ricerca in Informatica e Matematica.
Bioscienze, Biotecnologie e Biofarmaceutica (DBBB)	1	Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica Segreteria Didattica Via G. Fanelli n. 204, Bari	Tutorato didattico integrativo e di recupero in Fisica	Studente o dottorando di ricerca.	i) Laurea Magistrale in Fisica della classe LM 17 (DM 270/2004) o 20/S (DM 509/99), ovvero di diploma di laurea equiparato ai sensi del D.L. 09/07/09. ii) Dottorato in Fisica
Bioscienze, Biotecnologie e Biofarmaceutica (DBBB)	1	Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica Segreteria Didattica Via G. Fanelli n. 204, Bari	Tutorato didattico integrativo e di recupero in Chimica Organica	Studente o dottorando di ricerca.	i) Laurea Magistrale in Scienze Chimiche della classe LM 54, ovvero di diploma di laurea equiparato ai sensi del D.L. 09/07/09. ii) Laurea Magistrale in Biotecnologie Industriali ed Ambientali, classe LM8, ovvero di diploma di laurea equiparato ai sensi

					del D.L. 09/07/09. iii) Dottorato in Scienze Chimiche e Molecolari.

Al termine dell'illustrazione, il Direttore invita il Consiglio a deliberare in merito.

Il Consiglio, unanime, approva la ripartizione degli assegni di tutorato , così come proposta.

Il Direttore passa alla discussione dell'ottavo punto all'O.d.G.:

8. Richiesta di riproposizione di bando per assegno di ricerca andato deserto (programma 05.129, richiedente Prof. Luigi Palmieri);

Il Direttore spiega che l'assegno da lui richiesto, approvato da questo Consiglio nella seduta del 29 aprile scorso, e bandito con DR n. 1513 del 15.06.2020 (codice assegno n. 05.129), risulta deserto.

Per le esigenze del progetto PON BIOMIS, sul quale l'assegno ricade, egli chiede che l'assegno sia nuovamente bandito.

Il Direttore invita, quindi, il Consiglio ad esprimersi circa la richiesta da lui stesso riproposta di bandire un assegno di tipo "B" sul progetto "BIOMIS Costituzione della biobanca del microbiota intestinale e salivare umano: dalla disbiosi alla simbiosi con il codice ARS01_01220 di cui è responsabile e titolare di fondi, della durata di 12 mesi, titolo del progetto "Valutazione del profilo metabolomico sierico di soggetti sani e affetti da patologie selezionate". - Settore scientifico disciplinare BIO/10. La spesa relativa graverà sui Fondi BIOMIS. L'importo annuale lordo al percipiente è di euro 20.200,00 ed il responsabile scientifico è il Prof. Luigi Palmieri. Il bando sarà aperto ai laureati, early stage researcher or 0-4 yrs (Post graduate).

Il Consiglio, all'unanimità, approva.

Il Direttore passa alla discussione del nono punto all'O.d.G.:

9. Nomina tutor per assegnisti di ricerca;

Il Direttore comunica che con nota prot. n. 49742-III/13, del 07.09.2020 (ns. prot.A. n. 943-III/13 del 07.09.2020), della Direzione Risorse Umane, ci è stata inviata copia del contratto di assegno di ricerca stipulato dalla **Dott.ssa Iolanda SPERA** (Bando D.R. n. 1096 del 24/04/2020 - programma n. 05.125 – Richiedente Prof.ssa Alessandra Castegna). Egli, nel comunicare che la Dott.ssa SPERA ha iniziato l'attività in data 01.09.2020, invita ora questo Consiglio, ai sensi dell'art. 13 del Regolamento relativo agli assegni di ricerca, a nominare il tutor per il succitato assegnista.

Il Consiglio, all'unanimità, nomina la Prof.ssa Alessandra Castegna, quale tutor per l'assegnista Dott.ssa Iolanda SPERA.

Il Direttore comunica che con nota prot. n. 50323-III/13, del 09.09.2020 (ns. prot.A. n. 953-III/13 del 09.09.2020), della Direzione Risorse Umane, ci è stata inviata copia del contratto di assegno di ricerca stipulato dal **Dott.ssa Piero LEONE** (Bando D.R. n. 1094 del 24/04/2020 - programma n. 05.123 – Richiedente Prof.ssa Maria Barile). Egli, nel comunicare che il Dott. LEONE ha iniziato l'attività in data

01.09.2020, invita ora questo Consiglio, ai sensi dell'art. 13 del Regolamento relativo agli assegni di ricerca, a nominare il tutor per il succitato assegnista.

Il Consiglio, all'unanimità, nomina la Prof.ssa Maria Barile, quale tutor per l'assegnista Dott. Piero LEONE.

Il suddetto dispositivo è approvato seduta stante.

Il Direttore passa alla discussione del decimo punto all'O.d.G.:

10. Proposta di contributo straordinario da avanzare al Consiglio di Amministrazione dell'Ateneo;

Il Direttore riferisce che il Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica dell'Università di Bari ha acquisito nel 2012, nell'ambito di un progetto Regionale PON "Reti di Laboratorio BioBOP", un Microscopio Confocale-Multifotone Leica TCS SP5 AOBS accessoriato di una testalaser a luce pulsata infrarossa (Chameleon Ultra II, 680-1080 nm, GDP.1001H.3364) prodotta dall'Azienda Coherent(Glasgow, Scozia).

Rispetto alla classica microscopia a fluorescenza confocale nel visibile, l'utilizzo della luce laser pulsata infrarossa permette sia una maggiore profondità di penetrazione della radiazione incidente all'interno dei campioni da analizzare, sia una forte riduzione del decadimento della fluorescenza (photobleaching). In virtù di queste eccellenti caratteristiche, la microscopia multi fotone consente di condurre misure dilive imaging, cioè di caratterizzare/osservare/studiare il movimento, le interazioni, la crescita, il differenziamento nel tempo di cellule eucariotiche in (1) preparati biologici spessi,quali organoidi, linfonodi, fettine/biopsie tissutali e/o (2) nell'animale in vivo.

Tuttavia, da qualche anno, il laser non è più funzionante e, in seguito ad una richiesta di intervento tecnico in situ, è stata condotta una valutazione preliminare del guasto, da cui è emersa la necessità di spedire il laser presso la stessa casa madre produttrice (Coherent) sita a Glasgow (Scozia) per una verifica più approfondita del problema tecnico. Al termine della suddetta valutazione, è stato inviato un preventivo di 18.430,00 € per poter procedere ad una riparazione, detta "major repair", che consiste nell'apertura del laser in camera pulita, dove verranno effettuate tutte le operazioni di pulizia, sostituzione/ripristino delle parti ammalorate, allineamento e ricalibrazione necessarie al suo completo ripristino funzionale. Prima di questa fase, verrà effettuata una completa pulizia - disostruzione dei canali della base della testa laser in cui circola il liquido di raffreddamento (che verrà sostituito con il nuovo CoolFlow, che sostituisce il precedente OptiShield).

Poiché il Dipartimento, al momento, non dispone dei fondi sufficienti per la riparazione della strumentazione vuole chiedere al CdA dell'Università degli Studi di Bari un contributo straordinario per procedere alla riparazione della strumentazione in oggetto. Il Microscopio Confocale-Multifotone rientrerebbe in una Piattaforma (Facility) Tecnologica di Imaging (Multifotonico) disponibile per le esigenze di ricerca di questo Ateneo. Tale piattaforma potrà essere soggetta a tariffario e potrà essere fruibile da tutti i gruppi di ricerca di Ateneo.

L'avvio della Facilility di ImagingMultifotonico permetterebbe/permetterà:

- di migliorare la produttività di docenti e ricercatori che necessitino di approcci di microscopia multi fotonica per lo sviluppo delle loro attività scientifiche/ di ricerca;
- di incrementare la competitività dei gruppi di ricerca del nostro Ateneo;
- ampliare la rete di collaborazioni con Istituzioni di Ricerca nazionale e internazionali per supportare la ricerca e la formazione (es. Corso di Dottorato);
- consolidare le interazioni già esistenti con realtà industriali in ambito regionale e nazionale (es. Distretto H-Bio);
- promuovere la partecipazione a progetti di ricerca competitivi transnazionali;
- rafforzare l'internazionalizzazione della ricerca di Ateneo, favorendo (i) la partecipazione dei docenti, ricercatori e dottorandi ai bandi di mobilità internazionale (es. azioni Marie Sklodowska Curie) e la presenza di visiting professors e visiting researchers; (ii) la stipula di convenzioni e collaborazioni con Istituzioni di ricerca straniere anche mediante il bando "visiting professor" e "visiting researcher" per lo scambio di dottorandi e ricercatori/docenti.

Al termine dell'illustrazione, il Direttore chiede al Consiglio di esprimersi sulla proposta in oggetto.

Il Consiglio, unanime, approva la proposta in oggetto.

Esce, alle ore 12,50, la Prof.ssa Paola Loguercio Polosa.

Il Direttore passa alla discussione dell'undicesimo punto all'O.d.G.:

11. Richieste di autorizzazione a frequentare il Dipartimento;

Il Direttore illustra le seguenti richieste:

- del 10.09.2020 (ns. Prot.A. n. 957-VII/16, del 10.09.2020), a firma della **Dott.ssa Ines Angelini**, e vistata dal docente tutor, **Marianna Ranieri**, con la quale la Dott.ssa Angelini, in possesso della laurea di II livello in Biologia Cellulare e Molecolare conseguita presso l'Università degli Studi di Bari Aldo Moro, chiede l'autorizzazione a frequentare il Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica dal 11.09.2020 al 10.09.2021, per un periodo di formazione e/o ricerca al fine di migliorare le proprie competenze professionali.

Il Consiglio, unanime, autorizza la suddetta richiesta ai sensi del Regolamento di ateneo per "laureati frequentatori".

Il suddetto dispositivo è approvato seduta stante.

Il Direttore passa alla discussione del dodicesimo punto all'O.d.G.:

12. Varie ed eventuali.

Non ci sono varie ed eventuali.

Non essendoci altri argomenti in discussione, il Direttore, alle 12,55, dichiara sciolta la seduta.

Il Coordinatore — Il Direttore

Dott.ssa Margherita Ardito — Prof. Luigi Palmieri

EUROPEAN COMMISSION
Research Executive Agency

Director

GRANT AGREEMENT

NUMBER 956325 — ASTROTECH

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, Marie Skłodowska-Curie Innovative Training Networks, Klaus HAUPT,

and

on the other part,

1. 'the coordinator':

CONSIGLIO NAZIONALE DELLE RICERCHE (CNR), established in PIAZZALE ALDO MORO 7, ROMA 00185, Italy, VAT number: IT02118311006, represented for the purposes of signing the Agreement by Director, ROBERTO ZAMBONI

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

2. **THE CHANCELLOR MASTERS AND SCHOLARSOF THE UNIVERSITY OF CAMBRIDGE (UCAM)**, established in TRINITY LANE THE OLD SCHOOLS, CAMBRIDGE CB2 1TN, United Kingdom, VAT number: GB823847609,

3. **USTAV EXPERIMENTALNI MEDICINY AKADEMIE VED CESKE REPUBLIKY VEREJNA VYZKUMNA INSTITUCE (UEM AVCR)**, established in VIDENSKA 1083, PRAHA 4 14220, Czech Republic, VAT number: CZ68378041,

4. **UNIVERSITE D'AIX MARSEILLE (AMU)**, established in Boulevard Charles Livon 58, Marseille 13284, France, VAT number: FR84130015332,

5. **BCAM - BASQUE CENTER FOR APPLIED MATHEMATICS (BCAM)**, established in AL MAZARREDO 14, BILBAO 48009, Spain, VAT number: ESG95543526,

6. **INEB-INSTITUTO NACIONAL DE ENGENHARIA BIOMEDICA (INEB)**, established in RUA ALFREDO ALLEN 208, PORTO 4200 135, Portugal, VAT number: PT502312220,

7. **UNIVERSITA DEGLI STUDI DI BARI ALDO MORO (UNIBA)**, established in PIAZZA UMBERTO I 1, BARI 70121, Italy, VAT number: IT01086760723,

8. **FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA (IIT)**, established in VIA MOREGO 30, GENOVA 16163, Italy, VAT number: IT09198791007,

9. **AGENCIA ESTATAL CONSEJO SUPERIOR DEINVESTIGACIONES CIENTIFICAS (CSIC)**, established in CALLE SERRANO 117, MADRID 28006, Spain, VAT number: ESQ2818002D,

10. **AVANZARE INNOVACION TECNOLOGICA SL (AVA)**, established in AVENIDA LENTISCARES 4 6, NAVARRETE 26370, Spain, VAT number: ESB26370908,

11. **OPTOCEUTICS APS (OPTOCEUTICS)**, established in DIPLOMVEJ 381, KONGENS LYNGBY 2800, Denmark, VAT number: DK39769689,

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 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

TERMS AND CONDITIONS

TABLE OF CONTENTS

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 '**Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces** ' — '**ASTROTECH**' **('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 November 2020 ('**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 beneficiaries.

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

However, no more than 40% of the maximum grant amount (see Article 5.1) may be allocated to beneficiaries located in the same country or to any one international European interest organisation or international organisation.

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 3 980 625.48** (three million nine hundred and eighty thousand six hundred and twenty five EURO and forty eight eurocents).

5.2 Form of grant, reimbursement rate and form of costs

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 **3 980 625.48** (three million nine hundred and eighty thousand six hundred and twenty five EURO and forty eight eurocents).

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

(a) for **costs for recruited researchers** (living, mobility and family allowances): 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 and 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 to the eligible costs

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 rates to the eligible costs

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

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:

(a) they are calculated as follows:

{amounts per unit set out in Annex 2

multiplied by

the number of actual units}.

(b) 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 for recruited researchers (A.1 Living allowance, A.2 Mobility allowance and A.3 Family allowance) are eligible, if:

(a) the number of units declared:

(i) corresponds to the actual number of months spent by the recruited researchers on the research training activities and

(ii) does not exceed 36 months (per researcher);

(b) the recruited researchers comply with the following conditions:

(i) be recruited by the beneficiary under an **employment contract** (or other direct contract with equivalent benefits, including social security coverage) or — if not otherwise possible under national law — under a fixed amount fellowship agreement with minimum social security coverage;

(ii) be employed for at least 3 months;

(iii) be employed full-time, unless the Agency has approved a part-time employment for personal or family reasons;

(iv) be working exclusively for the action;

(v) not have resided in the country of the recruiting beneficiary for more than 12 months in the 3 years immediately before the recruitment date (and not have carried out their main activity (work, studies, etc.) in that country) — unless as part of a procedure for obtaining refugee status under the Geneva Convention[1].

For beneficiaries that are international European interest organisations or international organisations: not have spent with the beneficiary more than 12 months in the 3 years immediately before the recruitment date.

(vi) be — at the date of recruitment — an '**early stage researcher**' (i.e. in the first four years of his/her research career and not have a doctoral degree).

(c) the costs have been fully incurred for the benefit of the recruited researchers.

This latter condition is met if:

{{{**total remuneration costs** (salaries, social security contributions, taxes and other costs included in the remuneration under the employment contract or other direct contract) or **total fixed-amount fellowship costs** for the researcher during the action

plus

total mobility costs (household, relocation and travel expenses and, if they must be paid under national law, taxes, duties and social security contributions) for the researcher during the action}

plus

total family costs for the researcher during the action}

divided by

the number of actual units}.

[1] 1951 Refugee Convention and the 1967 Protocol.

is equal to or higher than the following amount:

{{amount per unit cost set out in Annex 2 as living allowance

plus

amount per unit cost set out in Annex 2 as mobility allowance}

plus

if it is due, amount per unit cost set out in Annex 2 as family allowance}.

The family allowance is due if the researcher has a family at the time of recruitment.

'Family' means persons linked to the researcher by marriage (or a relationship with equivalent status to a marriage recognised by the legislation of the country where this relationship was formalised) or dependent children who are actually being maintained by the researcher.

B. Institutional costs (B.1 Research, training and networking costs and B.2 Management and indirect costs) are eligible if the costs for the recruited researchers (living allowance, mobility allowance, family allowance; 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), and 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 or Euratom 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, unless it can demonstrate that the operating grant does not cover any costs of the action.

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:

- call upon entities with a capital or legal link to the beneficiaries[2], to implement certain action tasks described in Annex 1 (i.e. hosting and training of researchers);
- call upon partner organisations to implement certain action tasks described in Annex 1 (i.e. hosting and training researchers during secondments).

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

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

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

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 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.

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 and that the costs for recruited researchers (living allowance, mobility allowance, family allowance) have been fully incurred for the benefit of the researchers.

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 one year from the starting date of the action;
- organise a '**mid-term meeting**' between the beneficiaries, entities with a capital or legal link, partner organisations and the Agency before the deadline for the submission of the report for RP 1 (reporting period 1);
- establish a **supervisory board** of the network;
- 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 recruitment of each researcher.

19.2 Consequences of non-compliance

If a beneficiary or the coordinator 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).

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.

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 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 **3 184 500.38** (three million one hundred and eighty four thousand five hundred EURO and thirty eight eurocents).

The Agency will — except if Article 48 applies — make the pre-financing payment to the coordinator within 30 days 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).

An amount of EUR **199 031.27** (one hundred and ninety nine thousand thirty one EURO and twenty seven eurocents), 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.

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:

- 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: BANCA NAZIONALE DEL LAVORO S.P.A.
Full name of the account holder: CONSIGLIO NAZIONALE DELLE RICERCHE
IBAN code: IT75N0100503392000000218150

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 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.

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[3] and No 2185/96[4] (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)

Under Article 287 of the Treaty on the Functioning of the European Union (TFEU) and Article 161 of the Financial Regulation No 966/2012[5], 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).

[3] 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).

[4] 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).

[5] 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).

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).

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

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.

If the Agency or the Commission accepts the alternative flat-rate proposed by the beneficiary concerned, it will formally notify the application of the accepted 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[6].

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

The beneficiaries must ensure that the researchers, entities with a capital or legal link and partner organisations 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

[6] Commission Recommendation C (2008) 1329 of 10.4.2008 on the management of intellectual property in knowledge transfer activities and the Code of Practice for universities and other public research institutions attached to this recommendation.

(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 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[7]established in an EU Member State or '**associated country**'[8], 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.

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 researchers

The beneficiaries must — on a royalty-free basis — give access to the recruited researchers to background necessary for their research training 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

[7] For the definition, see Article 2.1(2) 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): '**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.

[8] For the definition, see Article 2.1(3) 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.

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 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 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 956325".

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

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 956325".

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 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:

“This project has received funding from the European Union’s Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 956325”.

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:

(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.

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 researchers

The beneficiaries must — on a royalty-free basis — give access to the recruited researchers to results necessary for their research training 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 RECRUITED RESEARCHERS

32.1 Obligations towards recruited researchers

The beneficiaries must respect the following recruitment and working conditions for the researchers recruited 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[9] and ensure that the researchers are aware of them;

(b) advertise and publish vacancies internationally, including on the web-sites requested by the Agency;

(c) recruit the researchers, following an open, transparent, impartial and equitable recruitment procedure, on the basis of:

  (i) their scientific skills and the relevance of their research experience;

  (ii) the impact of the proposed training on the researcher's career;

  (iii) a fair gender representation (by promoting genuine equal access opportunities between men and women throughout the recruitment process);

(d) ensure that no conflict of interest exists in or arises from the recruitment;

(e) ensure that the researchers enjoy at the place of the implementation at least the same standards and working conditions as those applicable to local researchers holding a similar position;

(f) ensure that the employment contract, other direct contract or fixed amount-fellowship agreement (see Article 6) specifies :

  (i) the starting date and duration of the research training activities under the action;

  (ii) the monthly support for the researcher under this Agreement (in euro and, if relevant, in the currency in which the remuneration is paid);

  (iii) the obligation of the researcher to work exclusively for the action;

  (iv) the obligation of the researcher not to receive for activities carried out in the frame of the action, other incomes than those received from the beneficiary (or other entity mentioned in Annex 1);

  (v) the obligation of the researcher to inform the beneficiary as soon as possible of any events or circumstances likely to affect the Agreement (see Article 17);

[9] Commission Recommendation 2005/251/EC of 11 March 2005 on the European Charter for Researchers and on a Code of Conduct for the Recruitment of Researchers (OJ L 75, 22.3.2005, p.67).

(vi) the arrangements related to the intellectual property rights between the beneficiary and the researcher — during implementation of the action and afterwards;

(vii) the obligation of the researcher to maintain confidentiality (see Article 36);

(viii) the obligation of the researcher 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);

(g) assist the researchers in the administrative procedures related to their recruitment;

(h) inform the researchers about:

- the description, conditions, location and the timetable for the implementation of the research training activities under the action and the name of the supervisor;
- the rights and obligations of the beneficiary toward the researcher under this Agreement;
- the obligation of the researcher to complete and submit — at the end of the training — the evaluation questionnaire and — two years later — follow-up questionnaire provided by the Agency;

(i) ensure that the researchers do not receive, for activities carried out in the frame of the action, other incomes than those received from the beneficiaries (or other entity mentioned in Annex 1);

(j) ensure that the researchers do not have to bear any costs for the implementation of the action as described in Annex 1;

(k) host the researchers at their premises (or at the premises of an entity with a capital or legal link);

(l) provide training and the necessary means for implementing the action (or ensure that such training and means are provided by entities with a capital or legal link);

(m) ensure that the researchers are adequately supervised;

(n) ensure that a career development plan is established and support its implementation;

(o) ensure an appropriate exposure to the non-academic sector;

(p) limit secondments to a maximum of 30% of the actual months spent implementing the research training activities under the action.

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

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.

In addition, the beneficiaries must respect the fundamental principle of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity[10].

This implies compliance with the following fundamental principles:

- **reliability** in ensuring the quality of research reflected in the design, the methodology, the analysis and the use of resources;

[10] European Code of Conduct for Research Integrity of ALLEA (All European Academies) http://ec.europa.eu/research/participants/data/ref/h2020/other/hi/h2020-ethics_code-of-conduct_en.pdf

- **honesty** in developing, undertaking, reviewing, reporting and communicating research in a transparent, fair and unbiased way;

- **respect** for colleagues, research participants, society, ecosystems, cultural heritage and the environment;

- **accountability** for the research from idea to publication, for its management and organisation, for training, supervision and mentoring, and for its wider impacts

and means that beneficiaries must ensure that persons carrying out research tasks follow the good research practices and refrain from the research integrity violations described in this Code.

This does not change the other obligations under this Agreement or obligations under applicable international, EU or national law, all of which still apply.

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:

- 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, entities with a capital or legal link or partner organisations only if they:

(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[11], 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

37.3 ctivities 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

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

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 956325".

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 956325".

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 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[13], 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.

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."

[13] 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.

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[14] 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.

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

[14] 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).

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 Article 44.

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:

- 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 entities with a capital or legal link and partner organisations).

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;
- 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 **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 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.

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).

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 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 or the Commission 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.

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[15] 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

the final grant amount (see Article 5.3)},

minus

[15] 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).

{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 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 or the Commission 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:

{{{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 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 or the Commission 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

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, prizes 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.

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 interim payments or the payment of the balance 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. 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);

(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:

- 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 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 — 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 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.

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 an 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);

(m) a beneficiary (or the 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 an 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.

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 — 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 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.

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

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

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

All communication must be made through the Participant Portal **electronic** exchange system and using the forms and templates provided there.

If — after the payment of the balance — the Agency finds that a formal notification was not accessed, a second formal notification will be made by registered post with proof of delivery ('formal notification on **paper**'). Deadlines will be calculated from the moment of the second notification.

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/info/funding-tenders/opportunities/portal/screen/myarea/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 official mailing address indicated on the Agency's website.

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[16], 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).

The request for amendment must include:

- the reasons why;
- the appropriate supporting documents, and

[16] 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).

- 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

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).

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 offsetting and 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

For the Agency

EUROPEAN COMMISSION
Research Executive Agency

The Director

ANNEX 1 (part A)

European Training Networks

NUMBER — 956325 — ASTROTECH

Table of Contents

1.1. The project summary

Project Number [1]	956325	Project Acronym [2]	ASTROTECH

One form per project

General information	
Project title [3]	Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces
Starting date [4]	01/11/2020
Duration in months [5]	48
Call (part) identifier [6]	H2020-MSCA-ITN-2020
Topic	MSCA-ITN-2020 Innovative Training Networks
Fixed EC Keywords	Cell differentiation, physiology and dynamics, Materials engineering, Nano-materials: oxides, alloys, composite, organic-inorganic hybrid, nanoparticles
Free keywords	Advanced biomaterials; flexible electronics; optogenetics; Neurostimulation; Computational Neuroscience; Neuron-Glial-Vascular Unit; Neuron-Astrocyte interaction;

Abstract [7]

The past four decades demonstrated that non-neuronal cells, called astrocytesare emerging as crucial players for brain function & dysfunction. A major obstacle of previous and current initiatives on Neurotechnologiesis a lack of focus on astrocytesand most of the tools used to probe and sense astrocytes are derived from those developed to study neurons. ASTROTECH will create and develop the field of Glial Engineering, to provide a consistent range of tools to record, study, and manipulate astrocytes in the healthy and diseased brain. ASTROTECH will train 15 Early Stage Researchers (ESRs) on research, training and complimentary skills aiming at: engineering biomaterials and nanostructured interfaces to provide in vivo-like in vitro models for controlled & reliable studies of astrocytes in vitro; fabrication and characterization of nanostructured devices for stimulation, recording and biosensing of astrocytes; optogenetics tools, optoelectronic device &photonic methods for precice and cell selective stimulation of astrocytes; computationalapproaches to describe and predict neuron-astrocytes interactions.The training on state-of-the-art biomaterials interfaces, electronic, photonic devices will be combined with in depth knowledge on optogenetics, neuroscience, glial physiology and biology and computational methodsto validate the developed tools in vitro, ex vivo, in silico & in pathological models of glioma, ischemia, epilepsy and depression.The ASTROTECH network combines 11 beneficiaries and 14 partners belonging to 9 European and Non-EU countries Academia, Public Research Centersand industrial labs, that combines interdisciplinary, intersectoral and soft skills knowledges where the private sector is highly representedand covers every step “from benchside to bedside” of the value chain. ASTROTECH Glial Engineeringto provide a more complete understanding of brain health and disorders.

1.2. List of Beneficiaries

Project Number [1]	956325	Project Acronym [2]	ASTROTECH

List of Beneficiaries

No	Name	Short name	Country	Project entry month[8]	Project exit month
1	CONSIGLIO NAZIONALE DELLE RICERCHE	CNR	Italy	1	48
2	THE CHANCELLOR MASTERS AND SCHOLARSOF THE UNIVERSITY OF CAMBRIDGE	UCAM	United Kingdom	1	48
3	USTAV EXPERIMENTALNI MEDICINY AKADEMIE VED CESKE REPUBLIKY VEREJNA VYZKUMNA INSTITUCE	UEM AVCR	Czech Republic	1	48
4	UNIVERSITE D'AIX MARSEILLE	AMU	France	1	48
5	BCAM - BASQUE CENTER FOR APPLIED MATHEMATICS	BCAM	Spain	1	48
6	INEB-INSTITUTO NACIONAL DE ENGENHARIA BIOMEDICA	INEB	Portugal	1	48
7	UNIVERSITA DEGLI STUDI DI BARI ALDO MORO	UNIBA	Italy	1	48
8	FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA	IIT	Italy	1	48
9	AGENCIA ESTATAL CONSEJO SUPERIOR DEINVESTIGACIONES CIENTIFICAS	CSIC	Spain	1	48
10	AVANZARE INNOVACION TECNOLOGICA SL	AVA	Spain	1	48
11	OPTOCEUTICS APS	OPTOCEUTICS	Denmark	1	48

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	Project management, coordination and quality control	1 - CNR	1	48
WP2	Glioelectronic device development fabrication and validation in vitro, ex vivo	2 - UCAM	7	39
WP3	Gliophotonic device and optogenetics approaches development and validation in vitro, ex vivo and in vivo	8 - IIT	7	39
WP4	Gliomaterials interfaces for in vitro-like -in vivo healthy and gliotic astrocyte culture model	6 - INEB	7	43
WP5	Validation in vivo of electronic, optogenetics, photonic astrotechnologies	9 - CSIC	24	48
WP6	Validation of astrotechnologies in pathological models	4 - AMU	24	48
WP7	Computational glioscience	5 - BCAM	12	48
WP8	Dissemination, communication, exploitation and public engagement	1 - CNR	1	48
WP9	Ethics requirements	1 - CNR	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	Consortium Agreement	WP1	1 - CNR	Report	Confidential, only for members of the consortium (including the Commission Services)	2
D1.2	Report on the common training standards and recruitment plans and policies	WP1	1 - CNR	Report	Public	3
D1.3	Definition of ASTROTECH Management Guidelines AGM	WP1	1 - CNR	Report	Public	5
D1.4	Report on recruitment; Collection of all PDCP	WP1	1 - CNR	Report	Public	12
D1.5	Progress report	WP1	1 - CNR	Report	Confidential, only for members of the consortium (including the Commission Services)	13
D1.6	Supervisory Board of the network	WP1	1 - CNR	Report	Confidential, only for members of the consortium (including the Commission Services)	2
D2.1	Protocols for glioelectronic device fabrication and characterization	WP2	2 - UCAM	Report	Confidential, only for members of the consortium (including the Commission Services)	25
D2.2	Validated glioelectronic AuSiNws device providing stimulation and recording of astrocytes in vitro	WP2	1 - CNR	Report	Public	25
D2.3	Validated glioelectronic carbon based and hybrid device providing stimulation and recording of astrocytes in vitro	WP2	1 - CNR	Report	Public	30
D2.4	Validated glioelectronic carbon based and	WP2	3 - UEM AVCR	Report	Public	39

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
	hybrid device providing stimulation and recording of astrocytes ex-vivo					
D3.1	Optoceutic device providing stimulation of astrocytes function in vitro and ex vivo	WP3	1 - CNR	Report	Public	39
D3.2	Optoelectronic devices providing stimulation of astrocytes function in vitro and ex vivo	WP3	8 - IIT	Report	Public	30
D3.3	Validated optogenetic approaches for stimulation and recording of astrocytes function ex vivo	WP3	9 - CSIC	Report	Public	39
D4.1	Chemico-physical features of ASTROTECH materials interface	WP4	1 - CNR	Report	Public	30
D4.2	Properties (viability, structural and functional) of primary astrocytes and co-cultures models in ASTROTECH scaffold	WP4	7 - UNIBA	Report	Public	39
D4.3	Properties of gliotic astrocytes in ASTROTECH scaffold	WP4	6 - INEB	Report	Public	43
D5.1	Fabrication and assessment of glioelectronic device efficacy and efficiency in vivo	WP5	4 - AMU	Report	Public	48
D5.2	Assessment of gliophotonic device efficacy in vivo and protocols for testing in humans	WP5	11 - OPTOCEUTICS	Report	Public	48
D6.1	Assessment of ASTROTECH in vitro model for the study of glioma	WP6	7 - UNIBA	Report	Public	48
D6.2	Assessment of glioelectronic device in epileptic model in vivo and pilot in human	WP6	4 - AMU	Report	Public	48

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D6.3	Assessment of glioelectronic device in MCAO model ex vivo/ optogenetic approach in depression ex vivo	WP6	11 - OPTOCEUTICS	Report	Confidential, only for members of the consortium (including the Commission Services)	48
D7.1	Biophysical model of astrocytic bioelectricity	WP7	5 - BCAM	Report	Public	28
D7.2	Design and Validation of multi-scale models of volume transmission in the NGVU	WP7	5 - BCAM	Report	Public	36
D7.3	Design and implementation of glial-based clamping simulations	WP7	4 - AMU	Report	Public	48
D7.4	Scalable NGVU model and integration in TVB and clinical technology	WP7	4 - AMU	Report	Public	48
D8.1	ASTROTECH website	WP8	1 - CNR	Websites, patents filling, etc.	Public	2
D8.2	Dissemination, communication and exploitation Plan	WP8	1 - CNR	Report	Public	8
D8.3	Internationalization Plan of project outcomes	WP8	1 - CNR	Report	Confidential, only for members of the consortium (including the Commission Services)	36
D8.4	Final Dissemination, communication and exploitation Plan	WP8	1 - CNR	Report	Public	48
D9.1	H - Requirement No. 1	WP9	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.2	HCT - Requirement No. 2	WP9	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.3	POPD - Requirement No. 3	WP9	1 - CNR	Ethics	Confidential, only for members	12

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
					of the consortium (including the Commission Services)	
D9.4	EPQ - Requirement No. 4	WP9	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.5	A - Requirement No. 5	WP9	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.6	NEC - Requirement No. 6	WP9	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12

1.3.3. WT3 Work package descriptions

Work package number [9]	WP1	**Lead beneficiary** [10]	1 - CNR
Work package title	Project management, coordination and quality control		
Start month	1	**End month**	48

Objectives

A) To ensure that research, training and dissemination objectives are pursued B) To monitor use of committed resources in terms of staff, facilities time and funding. B) Monitoring of alignment of the implementation with communication and decision-making procedures agreed among all network participants. C) Monitoring of deliverable technical consistency and submission deadline. D) Ensure proper internal communication within the consortium. E) Control of full respect of the H2020 financial and reporting rules.

Description of work and role of partners

WP1 - Project management, coordination and quality control [Months: 1-48]
CNR
Task 1.1: (Leader: CNR; M4, all): Definition of Consortium Agreement.
Task 1.2: (Leader: CNR; M1, 24, 48): Organization of the kick-off, mid- term, project meetings and final conference meeting and appointment of members to form the project management boards, project meetings and final conference.
Task 1.3: (Leader: CNR; M5): Definition of ASTROTECH Management Guidelines (AMG). The AMG will be a “how to” document intended to support ASTROTECH participants the management and will include templates, guidelines and standards for the deliverables and for financial management.
Task 1.4: (Leader: CNR; M5) definition of ASTROTECH Website and cloud data base for information flow and data sharing.
Task 1.5: (Leader: CNR; in cooperation with all partners; M12; M24; M36; M48): Compilation of joint periodic management reports and financial cost statements.

Participation per Partner

Partner number and short name [10]
1 - CNR
2 - UCAM
3 - UEM AVCR
4 - AMU
5 - BCAM
6 - INEB
7 - UNIBA
8 - IIT
9 - CSIC
10 - AVA
11 - OPTOCEUTICS

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D1.1	Consortium Agreement	1 - CNR	Report	Confidential, only for members of the consortium (including the Commission Services)	2
D1.2	Report on the common training standards and recruitment plans and policies	1 - CNR	Report	Public	3
D1.3	Definition of ASTROTECH Management Guidelines AGM	1 - CNR	Report	Public	5
D1.4	Report on recruitment; Collection of all PDCP	1 - CNR	Report	Public	12
D1.5	Progress report	1 - CNR	Report	Confidential, only for members of the consortium (including the Commission Services)	13
D1.6	Supervisory Board of the network	1 - CNR	Report	Confidential, only for members of the consortium (including the Commission Services)	2

Description of deliverables

D1.1: Consortium Agreement (CNR, M2). D1.2: Report on the common training standards and recruitment plans and policies (CNR and all partners, M3). D1.3: ASTROTECH Management Guidelines (AMG). D1.4: Report on recruitment; Collection of all Declarations on Conformity (CNR, M12). D1.5-D1.10: Progress Reports and Periodic Reports (M12, M24, M36, M48)

D1.1 : Consortium Agreement [2]

Consortium Agreement

D1.2 : Report on the common training standards and recruitment plans and policies [3]

Report on the common training standards and recruitment plans and policies

D1.3 : Definition of ASTROTECH Management Guidelines AGM [5]

Definition of ASTROTECH Management Guidelines AGM

D1.4 : Report on recruitment; Collection of all PDCP [12]

Report on recruitment; Collection of all PDCP

D1.5 : Progress report [13]

First progress report

D1.6 : Supervisory Board of the network [2]

supervisory Board of the network

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS1	Recruitment finalization	1 - CNR	12	Recruitment finalization
MS9	Project Mid term check	1 - CNR	15	Meeting between REA and consortium

Work package number [9]	WP2	Lead beneficiary [10]	2 - UCAM
Work package title	Glioelectronic device development fabrication and validation in vitro, ex vivo		
Start month	7	End month	39

Objectives

A) Glioelectronic device development, fabrication and characterization B) Validation of Glioelectronic device for stimulation and recording of astrocytes bioelectrical activity in vitro and ex vivo.

Description of work and role of partners

WP2 - Glioelectronic device development fabrication and validation in vitro, ex vivo [Months: 7-39]
UCAM
Task 2.1: (Leader:ESR4-UCAM; Participants:ESR-13-AVA;ESR-2-CNR-IMM,M7-M25): Fabrication and characterization of nanostructured carbon based and hybrid bioelectronic device for stimulation and read-out of astrocytes bioelectrical activity in vitro: Patterning of PEDOT-PSS and conductive polymers based on graphene loaded thermoplastics for active microelectrode array by nanoimprinting lithography, laser microfabrication, pulsed laser deposition, ink-jet printing patterning techniques, over multiple spatial scales for controlled growth of astrocytes cells and to maximize signal transduction/cell stimulation (ESR-4-UCAM, AVA, D 2.1). Fabrication and characterization of silicon nanowire and hybrid based bioelectronic device for stimulation and read-out of astrocytes bioelectrical activity in vitro (ESR-2-CNR-IMM). Identification of the best nanostructured material for inducing the natural differentiation in cultured astrocyte (D 2.2). Fabrication of nanostructures grown by large area techniques (PECVD, Hydrothermal growth, etc.); fabrication of nanostructured ultra-flexible microelectrode array on poly imide; electrical and electrochemical characterization of smart devices for astrocytes recording. Novel graphene-based nanostructures in order to design devices for in-vitro astrocytes stimulatin and recording and optimization of the performance of the electronic conductors to reduce impedance and improve ratio signal/noise (ESR-13-AVA). Electronic characterization of glioelectronic device by electrical and electrochemical techniques and AFM, UFM, SEM, contact angle morphology, topography and mechanical properties of devices (ESR-4-UCAM, ESR-2-CNR-IMM)
Task 2.2: (Leader: ESR-1-CNR-ISOF; Participants: ESR-5-INEM; M9-M15): Impact of glioelectronic /material interface on primary astrocytes and co-culture structure and function in vitro. Elucidate the impact of glial device provided by ESR-2-CNR-IMM and ESR-4-UCAM on adhesion, proliferation of astrocytes. Morphological examination by means of immunocytochemistry and fluorescence microscopy and cell viability via Alalmar Blue Assay. At UNIBO and CNR, ESR-1-CNR-ISOF will evaluateof the impact of the growth of cells on device on electrophysiological properties of neurons and astrocytes by patch-clamp and calcium imaging in vitro, while ESR-5-INEM will verify the impact of device in slices (D 2.3).
Task 2.3: Validation of glioelectronic device for the recording and stimulation of primary astrocytes and co-culture: (Leader: ESR-1-CNR-ISOF; ESR-5-INEM, ESR-2-CNR-IMM and ESR-4-CNR UCAM; M15-M30): definition of protocols for continuous and long-term recording and for electrical stimulation of primary astrocytes and co-cultures of astrocytes and neurons on glioelectronic devices (carbon based and Au/SiNWs) provided by ESR-2-CNR-IMM and ESR-4-UCAM. Verification of impact of stimulation on whole-cell currents and calcium signaling of astrocytes primary culture and neuron-astrocytes co-culture by coupling glioelectronic device to patch-clamp and calcium imaging. Investigation of astrocytes-neuron cross-talk by glioelectronic devices. (ESR-1-CNR-ISOF, ESR-5-INEM, D 2.3).
Task 2.4: Validation of glioelectronic device for the recording and stimulation of astrocytes ex vivo: (Leader: ESR-5-INEM Participants: ESR-6, AMU, M15-M40): Verification of impact of stimulation on whole-cell current of astrocytes, NG2 and neurons ex vivo. Pharmacological and genetic manipulation (GFAP/GFP+, NG2/GFP+, TRPV4 KO, AQP-4 KO mice) for evaluation of electrical contribution of astrocytes, NG2 and neurons by coupling glioelectronic device to patch-clamp and calcium imaging. Evaluation of the role of ion channels, such as Transient Receptor Potential (TRPs), aquaporin 4 channels, potassium channels and others (ESR-5-INEM, D2.4). Investigation of astrocytes-neuron cross-talk by glioelectronic devices, and parallel recording of synaptic transmission and plasticity (LTP, LTD, ESR-6-AMU, D2.4). (Figure 7).
Task 2.5: Fabrication of astrocytes interfaces and smart devices for electrical stimulation and read-out in vivo (Leader: UCAM; Participants: CNR-IMM; M24-M40). Integration of smart materials in astrocyte interface together with flexible electronics circuitry for in vivo measurements. Fabrication of flexible devices for astrocytes recording using both carbon-based and polycrystalline silicon active materials for the integration of thin film transistors. (ESR-4-UCAM, ESR-2-CNR-IMM, ESR-13-AVA D5.1).

Participation per Partner

Partner number and short name [10]
1 - CNR
3 - UEM AVCR
4 - AMU
10 - AVA

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D2.1	Protocols for glioelectronic device fabrication and characterization	2 - UCAM	Report	Confidential, only for members of the consortium (including the Commission Services)	25
D2.2	Validated glioelectronic AuSiNws device providing stimulation and recording of astrocytes in vitro	1 - CNR	Report	Public	25
D2.3	Validated glioelectronic carbon based and hybrid device providing stimulation and recording of astrocytes in vitro	1 - CNR	Report	Public	30
D2.4	Validated glioelectronic carbon based and hybrid device providing stimulation and recording of astrocytes ex-vivo	3 - UEM AVCR	Report	Public	39

Description of deliverables

D2.1 Protocols for glioelectronic device fabrication and characterization (UCAM, M25); D2.2 Validated glioelectronic AuSiNws device providing stimulation and recording of astrocytes in vitro (CNR-IMM, M25); D2.3 Validated glioelectronic carbon based and hybrid device providing stimulation and recording of astrocytes in vitro (CNR-ISOF, M30), D2.4 Validated glioelectronic carbon-based and hybrid device providing stimulation and recording of astrocytes ex-vivo (INEM, M40);

D2.1 : Protocols for glioelectronic device fabrication and characterization [25]

Protocols for glioelectronic device fabrication and characterization

D2.2 : Validated glioelectronic AuSiNws device providing stimulation and recording of astrocytes in vitro [25]

Validated glioelectronic AuSiNws device providing stimulation and recording of astrocytes in vitro

D2.3 : Validated glioelectronic carbon based and hybrid device providing stimulation and recording of astrocytes in vitro [30]

Validated glioelectronic carbon based and hybrid device providing stimulation and recording of astrocytes in vitro

D2.4 : Validated glioelectronic carbon based and hybrid device providing stimulation and recording of astrocytes ex-vivo [39]

Validated glioelectronic carbon based and hybrid device providing stimulation and recording of astrocytes ex-vivo

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS2	Glioectronic devices fabrication and validated and efficient for stimulation and recording of astrocytes in vitro and ex vivo	2 - UCAM	39	Glioectronic devices fabrication and validated and efficient for stimulation and recording of astrocytes in vitro and ex vivo

Work package number [9]	WP3	Lead beneficiary [10]	8 - IIT
Work package title	Gliophotonic device and optogenetics approaches development and validation in vitro, ex vivo and in vivo		
Start month	7	End month	39

Objectives

A) Light source for optogenetic stimulation of astrocytes calcium signal and currents in vitro and ex vivo. B) Optical fibers devices for gene-less, spatially and temporally selective excitation of astrocytes C) Photo modulation of astrocytes activity by organic and hybrid optoelectronic device D) Investigation of astrocytes physiology and neuron-crosstalk by optogenetic stimulation of astrocytes calcium signaling.

Description of work and role of partners

WP3 - Gliophotonic device and optogenetics approaches development and validation in vitro, ex vivo and in vivo [Months: 7-39]

IIT

Task 3.1 (Leader: ESR-1-CNR-ISOF; Participants: ESR-14-OPTO; ESR-10-UNIBA, ESR-12-CSIC M12-M39): label free stimulation of astrocytes by low size optical fiber at precise and fast wavelength Optimization of low size optical fiber capable of delivering a wide range of wavelengths of light (infrared and visible) at precise intensities and frequency (ESR-14-OPTO, D3.1). Integration to optical fibers at different wavelength in high resolution calcium imaging and patch-clamp set up and water perlmeability measurement, for gene free stimulation of astrocytes primary culture (ESR-10-UNIBA, CNR-ISOF, D3.1). Definition of photostimulation protocols that change ion time and frequency and verification of the impact on astrocytes signaling and membrane current. Use of pharmacological and genetic manipulation to uncover the mechanism underpinning the response of astrocytes to light. (CNR-ISOF, UNIBA, D3.1) Identification of protocols for photostimulation ex vivo. Validation of the findings in ex vivo preparations (ESR-12-CSIC. D3.1)

Task 3.2 (Leader ESR-11-IIT, Participants: ESR-1-CNR, ESR-12-CSIC; M8-M30): Organic and hybrid organic/ inorganic bioactuators for spatio-temporally resolved modulation of the cellular activity of astrocytes in vitro and ex vivo: development and optimization light-sensitive, nanostructured actuators for efficient photomodulation of astrocytes activity (ESR-11-IIT, D3.2). Characterization of phototransduction mechanisms in dependence on photoexcitation protocols parameters and device architecture (ESR-11-IIT, D3.2). Identification of photo-activated biological pathways and assessment of temporal and spatial resolution of astrocytes optical modulation, at the supra-, sub- and cellular level (ESR-11-IIT, ESR-1-CNR-ISOF D3.2).

Task 3.3 (Leader: ESR-12-CSIC; Participants: ESR-14-OPTO; M8-M39): Optogenetic and gene-free sti mulation of astrocytes calcium signal and currents ex vivo. Integration to optical fibers at different wavelength in high resolution calcium imaging and patch clamp set up for touchless, gene free photostimulation of astrocytes primary culture (ESR-14-OPTO, D3.3). Definition of photostimulation protocols that change ion time and frequency and verification of the impact on astrocytes signaling and membrane current in Wild Type and Melanopsin transfected astrocytes. Use of pharmacological and genetic manipulation to uncover the mechanism underpinning the response of astrocytes to light in in WT and Melanopsin transfected astrocytes (ESR-12-CSIC, OPTO D3.3) Protocols definition and validation of the findings in ex vivo preparations for photostimulation ex vivo. (Figure 9, ESR-12-CSIC, D3.3)

Participation per Partner

Partner number and short name [10]
1 - CNR
7 - UNIBA
9 - CSIC
11 - OPTOCEUTICS

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D3.1	Optoceutic device providing stimulation of astrocytes function in vitro and ex vivo	1 - CNR	Report	Public	39
D3.2	Optoelectronic devices providing stimulation of astrocytes function in vitro and ex vivo	8 - IIT	Report	Public	30
D3.3	Validated optogenetic approaches for stimulation and recording of astrocytes function ex vivo	9 - CSIC	Report	Public	39

Description of deliverables

D3.1 Optoceutic device providing stimulation of astrocytes function in vitro and ex vivo (CNR-ISOF, M39). D3.2, Optoelectronic devices providing stimulation of astrocytes function in vitro and ex vivo (IIT, M30); D3.3 Validated optogenetic approaches for stimulation and recording of astrocytes function ex vivo (CSIC, M39)

D3.1 : Optoceutic device providing stimulation of astrocytes function in vitro and ex vivo [39]

Optoceutic device providing stimulation of astrocytes function in vitro and ex vivo

D3.2 : Optoelectronic devices providing stimulation of astrocytes function in vitro and ex vivo [30]

Optoelectronic devices providing stimulation of astrocytes function in vitro and ex vivo

D3.3 : Validated optogenetic approaches for stimulation and recording of astrocytes function ex vivo [39]

Validated optogenetic approaches for stimulation and recording of astrocytes function ex vivo

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS3	Gliophotonic device and optogenetics approaches validated for efficient photostimulation of astrocytes in vitro, ex vivo	8 - IIT	39	Gliophotonic device and optogenetics approaches validated for efficient photostimulation of astrocytes in vitro, ex vivo

Work package number [9]	WP4	Lead beneficiary [10]	6 - INEB
Work package title	Gliomaterials interfaces for in vitro-like -in vivo healthy and gliotic astrocyte culture model		
Start month	7	End month	43

Objectives

A) To design and characterize nano-structured biomaterials that can assure in vitro the phenotype of astrocytic cultures in the context of healthy and gliotic tissue; B) To increase the level of complexity of the proposed model with the integration of spheroids models. C) Identification of molecular and functional cues mediating astrocytes matrix interaction in homeostasis and disease to infer the impact of the matrix on astroglial phenotype.

Description of work and role of partners

WP4 - Gliomaterials interfaces for in vitro-like -in vivo healthy and gliotic astrocyte culture model [Months: 7-43]

INEB

Task 4.1 (Leader: ESR-3-CNR-IPCB; Participants: INEB; M7-M30): Design and synthesis of ASTROTECH fibrous biomaterial interfaces and scaffold for in vivo-like in vitro model.The activity of the ESR-3 at IPCB-CNR will be aimed at designing fibrous biomaterials by the use of electrospinning for the fabrication of instructive interfaces suitable to investigate in vitro glioma interactions (ESR-3-CNR-IPCB, D4.1). During this activity, materials and process conditions will be selected in order to optimize the morphology at the level of single fibre (defects occurrence, surface roughness) and fibre assembly (size distribution, fibre orientation). Chemical/physical properties of fibres (i.e., wettability, surface. porosity) will be investigated in order to validate their use as gliomaterial interfaces (ESR-3-CNR-IPCB, ESR-9-INEB, D4.1)

Task 4.2 (Leader: ESR-9-INEB; Participants:ESR-1-CNR-ISOF, ESR-5-INEM, ESR-3-CNR-IPCB;M9-M39): Design, preparation and characterization of alginate-based hydrogels for astrocytic tissue engineering. The use of peptide modified alginate will facilitate cell adhesion (through RGD and other cell-adhesion motifs) and matrix remodeling (through metalloproteinase-9 sensitive peptide – PVGLIG – or other sensitive sequences) (ESR-9-INEB D4.1). The stiffness of the hydrogels will also be tunned by altering alginate molecular weight and cross-linking degree. The prepared hydrogels will be characterized by rheology (ESR-3-CNR-IPCB, INEB D4.1). An astrocyte cell line and primary rat astrocytes will be mixed in the alginate matrices and cultured within the hydrogel either in the absence or presence of pro-inflammatory stimulus to simulate homeostasis and pathological conditions, respectively. Astrocytic status of activation will be assessed by microscopy (GFAP/GFP+ astrocytes provided by INEM), genetic and protein expression of glial fibrillary acidic protein, vimentin, collagen type IV and chondroitin sulphate proteoglycan. (ESR-1-CNR-ISOF, D4.3)

Task 4.3 (Leader: ESR-10-UNIBA; Participants: ESR-1-CNR-ISOF, ESR-9-INEM, ESR-3-CNR-IPCB, M12-M39): Characterization of molecular and functional properties of primary astrocytes and co-cultures models in the ASTROTECH scaffold. Optical, confocal and time lapse microscopy to verify impact on astrocytes morphological arrangement and differentiation. Verifying the impact of glial interface on adhesion, proliferation of astrocytes Morphological examination by means of immunocytochemistry and fluorescence microscopy and cell viability via Alalmar Blue Assay (CNR-ISOF). Evaluation of the impact of the growth of cells on device on electrophysiological properties of neurons and astrocytes by water permeability assay and calcium imaging (ESR-10-UNIBA D4.2). Super resolution microscopy to study the expression pattern of AQP-4 and ion channels such as Transient Receptor Potential (TRPs). Evaluation of the impact of the growth on ASTROTECH scaffold actin cytoskeleton (CNR-ISOF, UNIBA, UMD, D4.2). Identification of the role of AQP4 in cell-biomaterial interaction. Task 4.4 (Leader: ESR-10-UNIBA; Participants:CNR-ISOF, INEB, CNR-IPCB; M24-M44): Study the impact of the gliomaterials on molecular and functional properties of organoids and neurospheres in the ASTROTECH scaffold. The same approaches described above will be implemented to study the interaction of hydrogels and electrospun nanofibers on organids preparation and neurospheres as models of mixed population of nervous cells with particular focuse on astrocytes. Morphological examination by means of immunocytochemistry and fluorescence microscopy and cell viability via Alalmar Blue Assay (ESR-1-CNR-ISOF, D4.2). Evaluation of the impact of the materials on calcium signalling and analysis of water permeability and calcium signalling (UNIBA). Super resolution microscopy to study the expression pattern of AQP-4 and ion channels such as Transient Receptor Potential (TRPs). Evaluation of the impact of the growth on ASTROTECH scaffold actin cytoskeleton (ESR-1-CNR-ISOF, ESR-10-UNIBA, UMD). Identification of the role of AQP4 in cell-biomaterial interaction (UNIBA, D4.2)

Task 4.5 Impact of the gliomaterials physico-chemical properties on gliotic astrocytes (Leader: ESR-9-INEB;Participants: ESR-10-UNIBA, M36-M48): Modification of gliomaterial interface through biofunctionalization and matrix stiffness changes, and analyses of the impact on astrocyte genetic modifications. Identification of possible role of ion channels and AQP4 mechanotransduction signaling pathways inducing gliotic process (ESR-9, D4.3)

Participation per Partner

Partner number and short name [10]
1 - CNR
3 - UEM AVCR
6 - INEB
7 - UNIBA

List of deliverables

Deliverable Number[14]	**Deliverable Title**	**Lead beneficiary**	**Type**[15]	**Dissemination level**[16]	**Due Date (in months)**[17]
D4.1	Chemico-physical features of ASTROTECH materials interface	1 - CNR	Report	Public	30
D4.2	Properties (viability, structural and functional) of primary astrocytes and co-cultures models in ASTROTECH scaffold	7 - UNIBA	Report	Public	39
D4.3	Properties of gliotic astrocytes in ASTROTECH scaffold	6 - INEB	Report	Public	43

Description of deliverables

D4.1 Chemico-physical features of ASTROTECH materials interface (CNR-IPCB, M30). D4.2 Properties (viability, structural and functional) of primary astrocytes and co-cultures models in ASTROTECH scaffold (UNIBA, M39). D4.3 Properties (viability, structural and functional) of gliotic astrocytes in ASTROTECH scaffold (INEB, M46).

D4.1 : Chemico-physical features of ASTROTECH materials interface [30]

Chemico-physical features of ASTROTECH materials interface

D4.2 : Properties (viability, structural and functional) of primary astrocytes and co-cultures models in ASTROTECH scaffold [39]

Properties (viability, structural and functional) of primary astrocytes and co-cultures models in ASTROTECH scaffold

D4.3 : Properties of gliotic astrocytes in ASTROTECH scaffold [43]

Properties (viability, structural and functional) of gliotic astrocytes in ASTROTECH scaffold

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS4	ASTROTECH in vitro model validated for in-vivo like in vitro testing of astrocytes	6 - INEB	43	ASTROTECH in vitro model validated for in-vivo like in vitro testing of astrocytes

Work package number [9]	WP5	Lead beneficiary [10]	9 - CSIC
Work package title	Validation in vivo of electronic, optogenetics, photonic astrotechnologies		
Start month	24	End month	48

Objectives

A) Investigation of astrocytes-neuron cross-talk by optogenetic stimulation of astrocytes in vivo; B) organic and hybrid optoelectronic device for photostimulation of astrocytes in vivo; C) effective low invasive light source for optoceutics stimulation of astrocytes Ca2+ signal and currents in vivo

Description of work and role of partners

WP5 - Validation in vivo of electronic, optogenetics, photonic astrotechnologies [Months: 24-48]
CSIC
Task 5.1 (Leader: ESR-6-AMU; Participants: ESR-4-UCAM, ESR-2-CNR-IMM, ESR-13-AVA, M24-M48): Protocol testing and assesment of stimulation and recording protocols for a closed loop stimulation and recording device in vivo (ESR-6-AMU, ESR-4-UCAM, ESR-2-CNR-IMM, D5.1). This will allow to verify the potential of glioelectronic device for investigation of astrocytes-neuron crosstalk by electric stimulation and recording and to set the parameters to be used in WP6.
Task 5.2 (Leader: ESR-12-CSIC; Participants: ESR-6-AMU, ESR-4-UCAM, ESR-2-CNR-IMM, ESR-14-OPTO; M24-M48): Investigation of astrocytes-neuron crosstalk by optogenetic stimulation with ad hoc generated optical fiber of astrocytes in vivo and recording by means of glioelectronic device. The validation of above mentioned optogenetics and optical and photonic methods will be performed with methodologies described in task 3.1 in wildtype mice and in Ip3r2-/- mice to clarify the contribution of such important biochemical path in the light evoked stimulation of astrocytes. (Figure 10). Nonetheless the activity of this task will define protocols of stimulation frequency and duration to be used for either optogenetically transfected and label-free cells. The extracellular recordings will be performed also by means of flexible glioelectronic devices D5.2
Task 5.3 (Leader: ESR-15-OPTO; Participants, ESR-11-IIT, ZUH; UCPH; M24-M48): Investigation of light induced neurostimulation by gliophotonic devices measured by electroencephalogram (EEG) and Functional magnetic resonance imaging fMRI (fMRI) in humans, ESR-11-IIT ESR-14 and ESR-15-OPTO-D5.2
Task 5.4 (Leader: ESR-6-AMU; Participants, ESR-2-CNR-IMM, ESR-12-CSIC, ESR-11-IIT, ESR-14-OPTO, ESR-15-OPTO, ESR-13-AVA; M24-M48): Physiological information gained regarding astriocyte function will be sent to ESR-7. Predictions generated by the model will be tested experimentally D 7.3

Participation per Partner

Partner number and short name [10]
1 - CNR
2 - UCAM
8 - IIT
10 - AVA
11 - OPTOCEUTICS

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D5.1	Fabrication and assessment of glioelectronic device efficacy and efficiency in vivo	4 - AMU	Report	Public	48
D5.2	Assessment of gliophotonic device efficacy in vivo and protocols for testing in humans	11 - OPTOCEUTICS	Report	Public	48

Description of deliverables

D5.1 Fabrication and assesment of glioelectronic device efficacy and efficiency in vivo (AMU, M48);
D5.2Assesment of gliophotonic device efficacy in vivo and protocols for tesing in humans (OPTO, M48)

D5.1 : Fabrication and assessment of glioelectronic device efficacy and efficiency in vivo [48]

Fabrication and assessment of glioelectronic device efficacy and efficiency in vivo

D5.2 : Assessment of gliophotonic device efficacy in vivo and protocols for testing in humans [48]

Assessment of gliophotonic device efficacy in vivo and protocols for testing in humans

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS5	Astrotechnologies validated in vivo	9 - CSIC	48	Astrotechnologies validated in vivo

Work package number [9]	WP6	Lead beneficiary [10]	4 - AMU
Work package title	Validation of astrotechnologies in pathological models		
Start month	24	End month	48

Objectives

A) Study of the potential of gliomaterials interface for the study of glioma in vitro model B) Unsing glioelectronic device in MCAO model ex vivo C) Unsing glioelectronic device optogenetic approach in depression ex vivo (IEM, M44); D) Assesment of glioelectronic device in epileptic model in vivo and pilot data in human (OPTO, M48)

Description of work and role of partners

WP6 - Validation of astrotechnologies in pathological models [Months: 24-48]
AMU
Task 6.1 (Leader: ESR-10-UNIBA; Participants: ESR-9-INEB, ESR-3-CNR-IPCB; M24-M48): Glioma cell growth, migration in ASTROTECH in vitro model. Evaluation of the role of aquaporins and ion channels. The effect of ASTROTECH devices provided by ESR-9-INEB and ESR-3-CNR-IPCB on the bahaviour of glioma cells will be detailed. In particular, specific assays will be performed to investigate if Astrotech devices can influence the fate of glioma cells toward apoptosis or invasiveness. Invasion, migration and proliferation assays will be performed together with the analysis of methalloproteinase and DNA fragmentation. Apoptotis and Necrosis assay will be performed in parallel as well as patch clamp and water transport to characterize potential alteration of ion and water fluxes (UNIBA, D6.1).
Task 6.2 (Leader: ESR-6-AMU; Participants: ESR-2-CNR-IMM, ESR-4-UCAM; M24-M48): Glioelectronic device recording in vivo in experimental epilepsy. ESR-6-AMU will use glioelectronic device provided by ESR-4-UCAM and ESR-2-CNR-IMM and implant them in a focal model of epilepsy (intrahippocampal injection of tetanus toxin, a transient model of spontaneous seizures). Each animal will be used at its own control, from a non-epilepsy state, epilepsy, back to a non-epilepsy state. Testing of the hypothesis that astrocytic dysfunction will manifest before seizure onset (predictive biomarker) and that is possibly causally related to seizure genesis (mechanism, and target identification) (D6.2). While waiting for the devices to be ready ESR-6 will use commercial technology (DC and extracellular K+ recordings), and Ca2+ recordings from astrocytes (AMU uses miniscope and 2-photon in vivo recordings techniques) (Figure 11).
Task 6.3 (Leader: ESR-12-CSIC; Participants: ESR-5-INEM, ESR-2-CNR-IMM, ESR-4-UCAM, ESR-15-OPTO; M24-M28): Optical Stimulation and Glioelectronic device recording in brain slices from hippocampus and cortex of mouse model of depression and of ischemia. Induction of depression by using the unpredictable chronic mild stress (UCMS) protocol, one of the most realistic and well validated models of depression for the major depressive disorder (MDD) core symptom, called anhedonia (in humans) or anhedonia-like behavior (in animals). Evaluation of the role of astrocytes in serotonergic modulation of synaptic transmission by electrophysiological recordings by means of glioelectronic devfices providsed by UCAM. Excitatory and inhibitory synaptic activity modulated by serotonergic system will be analyzed in cortex and hippocampus by neuronal whole cell recordings, then the contribution of optical stimulation of astrocytes by optical system provided by ESR-15-OPTO and optimized in WP4 and WP5, to such modulation will be evaluated in naive and depressed-like mice. The glioelectronic device recording in brain slice from MCAO induced ischemia. Evaluation of the role of ion channels and water channels and calcium signaling in ischemia by methodologies described in task 2.5 (INEM, UNIBA, D6.3)

Participation per Partner

Partner number and short name [10]
1 - CNR
2 - UCAM
3 - UEM AVCR
6 - INEB
7 - UNIBA

Partner number and short name [10]
8 - IIT
9 - CSIC
11 - OPTOCEUTICS

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D6.1	Assessment of ASTROTECH in vitro model for the study of glioma	7 - UNIBA	Report	Public	48
D6.2	Assessment of glioelectronic device in epileptic model in vivo and pilot in human	4 - AMU	Report	Public	48
D6.3	Assessment of glioelectronic device in MCAO model ex vivo/ optogenetic approach in depression ex vivo	11 - OPTOCEUTICS	Report	Confidential, only for members of the consortium (including the Commission Services)	48

Description of deliverables

D6.1 Assesment of ASTROTECH in vitro model for the study of glioma (UNIBA, 48); D6. 2 Assesment of glioelectronic device in epileptic model (AMU, M48). D6.3 Assessment of glioelectronic device in MCAO model ex vivo /optogenetic approach in depression ex vivo (OPTO, M48);

D6.1 : Assessment of ASTROTECH in vitro model for the study of glioma [48]

Assessment of ASTROTECH in vitro model for the study of glioma

D6.2 : Assessment of glioelectronic device in epileptic model in vivo and pilot in human [48]

Assessment of glioelectronic device in epileptic model in vivo and pilot in human

D6.3 : Assessment of glioelectronic device in MCAO model ex vivo/optogenetic approach in depression ex vivo [48]

Assessment of glioelectronic device in MCAO model ex vivo/optogenetic approach in depression ex vivo

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS6	Astrotechnologies proof of principle for use in pathological condition	4 - AMU	48	Astrotechnologies proof of principle for use in pathological condition

Work package number [9]	WP7	**Lead beneficiary** [10]	5 - BCAM
Work package title	Computational glioscience		
Start month	12	**End month**	48

Objectives

A) Develop theoretical and computational tools to the analysis of neuron-glial interactions at different spatial and temporal scales of brain function. B) Modeling & testing of in silico models of astrocyte's bioelectricity; C) Development of diagnostic tools informed by the biophysics of neuron-astrocyte interactions. D) Production and dissemination of algorithms & scalable models for neuron-glial interactions for large simulating platforms

Description of work and role of partners

WP7 - Computational glioscience [Months: 12-48]
BCAM
astrocytic bioelectric and water transport phenomena and development of in silico tools to record and probe glial bioelectricity. The development of such tools aims at prototyping new experimental paradigms to engineer astrocytic signaling and its interactions with the neuropile (BCAM, CNR-ISOF). The task relies on the synergy of competences in the Consortium in neuroengineering and computational glioscience, pioneering training in (i) principles of design and implementation of new-generation brain-machine interfaces (BMIs) heavily relying on astrocyte physiology; (ii) development experimental protocols that exploit glioelectronic devices used to record and stimulate astrocytes in conditions of voltage or /current /clamping of dynamic clamping of ions fluxes and water diffusion (ESR-8-BCAM, ESR-1-CNR-ISOF, ESR-10-UNIBA, D7.1).
Task 7.2: (Leader: ESR-8-BCAM; Participants: CNR-ISOF, UNIBA, AMU, M12-M36). Analysis of neuron-glial interactions in the context of the neuron-glial-vascular unit (NGVU), with emphasis on volume/system processes. This step relies on characterization of volume regulation in vitro models provided by ASTROTECH partners and envisages three training objectives: (i) learning physiology of volume regulation by astrocytes, (ii) developing the ability to translate physiological data into biophysical models with emphasis on diffusion and reaction-diffusion processes; (iii) implementing models based on principles of neuromorphic engineering to design effective probes for diagnostics tasks based on biophysical principles of neuron-glial interactions (ESR-8-BCAM, ESR-1-CNR-ISOF, ESR-10-UNIBA D7.1)
Task 7.3: (Leader: ESR-7-AMU, Participants: ESR-8-BCAM, CODEMART M12-M36). ESR-7 will produce generative mathematical models for each node to incorporate the neuron-glial-vascular unit. The model will be incorporated in The Virtual Mouse Brain, and its predictions value will be tested using the dataset of already virtualized 19 mice. The validation will be provided by the ability to mimic experimental resting state fMRI data from the 19 mice. ESR-7 will work closely with ESR-8 to construct the best formalism. Some model predictions will be tested in vivo within WP 7. ESR-7 will work with CODEMART for translational applications within The Virtual Brain framework. The task foresees two complementary directions of pursuit and training: (i) integration of algorithms developed specifically for the task along with those resulting from Task 7.1 in The Virtual Brain simulator environment; and (ii) development of a strong synergy with stakeholders represented by CODEMART to build a middleware that enables smooth translation of discoveries to diagnostic tools or related technology of clinical relevance (ESR-8-BCAM, ESR-7-AMU, CODEMART, D7.3) AMU runs a multicenter clinical trial with TVB to improve neurosurgery outcome for drug-resistant patients. Knowledge generated in Task 7.3 will be included in TVB, and we will test whether the new generative model improves the predictive power (using a retrospective cohort).
Task 7.4: (Leader: ESR-7-AMU, Participants: ESR-8-BCAM, CODEMART, M12-M36). Role of astrocytes in epilepsy at the whole brain scale: AMU has proposed a comprehensive mathematical framework to explain seizure dynamics. The model predicts that a state variable evolving slowly in time is required to explain seizure onset, time course and offset. Identification of the role of astrocytes ion and water homeostasis, metabolism and energy supply, which evolve slowly in time, are integral components of this state variable. At AMU ESR-7 will closely work with ESR-6. Both approaches are complementary (ESR-6 in a focal model and ESR-7 at the whole brain scale). (ESR-8-BCAM, ESR-7-AMU, CODEMART, D7.3)

Participation per Partner

Partner number and short name [10]
1 - CNR
4 - AMU
7 - UNIBA

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D7.1	Biophysical model of astrocytic bioelectricity	5 - BCAM	Report	Public	28
D7.2	Design and Validation of multi-scale models of volume transmission in the NGVU	5 - BCAM	Report	Public	36
D7.3	Design and implementation of glial-based clamping simulations	4 - AMU	Report	Public	48
D7.4	Scalable NGVU model and integration in TVB and clinical technology	4 - AMU	Report	Public	48

Description of deliverables

D7.1: Biophysical model of astrocytic bioelectricity (BCAM, M28); D7.2: Design and Validation of multi-scale models of volume transmission in the NGVU (BCAM, M36); D7.3: New generative model including astrocytes in TVMB (AMU, M48); D7.4: Scalable NGVU model and integration in TVB and clinical technology (AMU, M48).

D7.1 : Biophysical model of astrocytic bioelectricity [28]

Biophysical model of astrocytic bioelectricity

D7.2 : Design and Validation of multi-scale models of volume transmission in the NGVU [36]

Design and Validation of multi-scale models of volume transmission in the NGVU

D7.3 : Design and implementation of glial-based clamping simulations [48]

Design and implementation of glial-based clamping simulations

D7.4 : Scalable NGVU model and integration in TVB and clinical technology [48]

Scalable NGVU model and integration in TVB and clinical technology

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS7	Data integration in Computational methods and in TVB	5 - BCAM	48	Data integration in Computational methods and in TVB

Work package number [9]	WP8	Lead beneficiary [10]	1 - CNR
Work package title	Dissemination, communication, exploitation and public engagement		
Start month	1	End month	48

Objectives

A) Dissemination of research and training results to aware the academic research community at a multidimensional level: Intra consortium, Consortium Wide (Global) B) Dissemination to stakeholders including industrial partners and the general public C) Maximize Potential Exploitation of ASTROTECH results, including IPRs.

Description of work and role of partners

WP8 - Dissemination, communication, exploitation and public engagement [Months: 1-48]
CNR
Task 8.1 (Leader: CNR; in cooperation with all partners; M2): Set-up and maintenance of the ASTROTECH website, for presentations of results outside the network.
Task 8.2 (Leader: CNR; in cooperation with all partners; M8-M48): Definition of IPR management set forth in the Consortium Agreement. Development and implementation of the exploitation and usage plan.
Task 8.3 (Leader: CNR; in cooperation with all partners; M48): Case study analyses for clinical application of successful ASTROTECHNOLOGY
Task 8.4 (all partners; M4-M48): Implementation of outreaching activities for increasing globally ASTROTECH network and subsidiary projects.
Task 8.5 (Leader: CNR in cooperation with all partners: M44-M48) Organization of the ASTROTECH final conference.

Participation per Partner

Partner number and short name [10]
1 - CNR
2 - UCAM
3 - UEM AVCR
4 - AMU
5 - BCAM
6 - INEB
7 - UNIBA
8 - IIT
9 - CSIC
10 - AVA
11 - OPTOCEUTICS

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D8.1	ASTROTECH website	1 - CNR	Websites, patents filling, etc.	Public	2
D8.2	Dissemination, communication and exploitation Plan	1 - CNR	Report	Public	8
D8.3	Internationalization Plan of project outcomes	1 - CNR	Report	Confidential, only for members of the consortium (including the Commission Services)	36
D8.4	Final Dissemination, communication and exploitation Plan	1 - CNR	Report	Public	48

Description of deliverables

D8.1: ASTROTECH website (CNR, M2). D8.2: Dissemination, communication and exploitation Plan (CNR, M8); D8.3: Internationalization Plan of project outcomes (CNR, M36). D8.4: Final Dissemination, communication and exploitation Plan (CNR, M48)

D8.1 : ASTROTECH website [2]

ASTROTECH website

D8.2 : Dissemination, communication and exploitation Plan [8]

Dissemination, communication and exploitation Plan

D8.3 : Internationalization Plan of project outcomes [36]

Internationalization Plan of project outcomes

D8.4 : Final Dissemination, communication and exploitation Plan [48]

Final Dissemination, communication and exploitation Plan

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS8	ASTROTECH website	1 - CNR	2	ASTROTECH website

Work package number [9]	WP9	Lead beneficiary [10]	1 - CNR
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

WP9 - Ethics requirements [Months: 1-48]
CNR
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]
D9.1	H - Requirement No. 1	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.2	HCT - Requirement No. 2	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.3	POPD - Requirement No. 3	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.4	EPQ - Requirement No. 4	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.5	A - Requirement No. 5	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12
D9.6	NEC - Requirement No. 6	1 - CNR	Ethics	Confidential, only for members of the consortium (including the Commission Services)	12

Description of deliverables

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

D9.1 : H - Requirement No. 1 [12]

Before the beginning of activities involving human participants: - The procedures and criteria that will be used to identify/recruit research participants must be submitted as a deliverable. - The informed consent procedures that will be implemented for the participation of humans must be submitted as a deliverable. - Templates of the informed consent/assent forms and information sheets (in language and terms intelligible to the participants) must be kept on file (to be specified in the grant agreement before signature). - The applicant must clarify whether vulnerable individuals/groups will be involved. The measures to protect them and minimise the risk of their stigmatisation must be provided. - Details on incidental findings policy must be provided. - Copies of opinions/approvals by ethics committees and/or competent authorities for the research with humans must be submitted as a deliverable. - For each clinical study, the following documents/information must be submitted as a deliverable (in one package) prior to enrolment of first study subject: (i) Final version of study protocol as submitted to regulators/ethics committee(s), (ii) Registration number of clinical study in a WHO-or ICMJE- approved registry (with the possibility to post results), (iii) Approvals (ethics committees and national competent authority if applicable) required for invitation/enrolment of first subject in at least one clinical centre. - For each clinical study, a report on the status of posting results in the study registry(s) must be submitted as a deliverable, including timelines if/when final posting of results is scheduled after end of funding period.

D9.2 : HCT - Requirement No. 2 [12]

Before the beginning of activities involving human cells: - Copies of relevant documents for using, producing or collecting human cells or tissues (e.g., ethics approval, import licence, accreditation/designation/authorisation/ licensing) must be kept on file (to be specified in the grant agreement).

D9.3 : POPD - Requirement No. 3 [12]

Before the beginning of activities involving personal data: - The beneficiary must check if special derogations pertaining to the rights of data subjects or the processing of genetic, biometric and/or health data have been established under the national legislation of the country where the research takes place and submit a declaration of compliance with respective national legal framework(s). - The host institution must confirm that it has appointed a Data Protection Officer (DPO) and the contact details of the DPO are made available to all data subjects involved in the research. For host institutions not required to appoint a DPO under the GDPR a detailed data protection policy for the project must be kept on file (to be specified in the grant agreement). - The beneficiary must explain how all of the data they intend to process is relevant and limited to the purposes of the research project (in accordance with the ‘data minimisation ‘principle). This must be submitted as a deliverable. - A description of the technical and organisational measures that will be implemented to safeguard the rights and freedoms of the data subjects/research participants must be submitted as a deliverable. - A description of the security measures that will be implemented to prevent unauthorised access to personal data or the equipment used for processing must be submitted as a deliverable. - Description of the anonymysation/pseudonymisation techniques that will be implemented must be submitted as a deliverable. - Detailed information on the informed consent procedures in regard to data processing must be submitted as a deliverable. - Templates of the informed consent forms and information sheets (in language and terms intelligible to the participants) must be kept on file (to be specified in the grant agreement).

D9.4 : EPQ - Requirement No. 4 [12]

Before the beginning of activities potentially involving health and safety for staff involved: - The applicant must demonstrate that appropriate health and safety procedures conforming to relevant local/national guidelines/ legislation are followed for staff involved in this project. This must be confirmed in the grant agreement before signature. - The applicant must confirm that recommendations of EU-OSHA on safety in the workplace while using nanomaterials will be ensured (https://osha.europa.eu/en/tools-and-publications/publications/e-facts/e-fact-72-toolsfor-themanagement-of-nanomaterials-in-the-workplace-and-prevention-measures).

D9.5 : A - Requirement No. 5 [12]

Before the beginning of animal experiments: - Copies of relevant authorisations for animal experiments (covering also the work with genetically modified animals, if applicable) must be kept on file (to be specified in the grant agreement). - If applicable, copies of training certificates/personal licenses of the staff involved in animal experiments must be kept on file (to be specified in the grant agreement).

D9.6 : NEC - Requirement No. 6 [12]

- In case activities undertaken in non-EU countries raise ethics issues, the applicants must ensure that the research conducted outside the EU is legal in at least one EU Member State. This must be specified in the grant agreement.

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification

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	Recruitment finalization	WP1	1 - CNR	12	Recruitment finalization
MS2	Glioectronic devices fabrication and validated and efficient for stimulation and recording of astrocytes in vitro and ex vivo	WP2	2 - UCAM	39	Glioectronic devices fabrication and validated and efficient for stimulation and recording of astrocytes in vitro and ex vivo
MS3	Gliophotonic device and optogenetics approaches validated for efficient photostimulation of astrocytes in vitro, ex vivo	WP3	8 - IIT	39	Gliophotonic device and optogenetics approaches validated for efficient photostimulation of astrocytes in vitro, ex vivo
MS4	ASTROTECH in vitro model validated for in-vivo like in vitro testing of astrocytes	WP4	6 - INEB	43	ASTROTECH in vitro model validated for in-vivo like in vitro testing of astrocytes
MS5	Astrotechnologies validated in vivo	WP5	9 - CSIC	48	Astrotechnologies validated in vivo
MS6	Astrotechnologies proof of principle for use in pathological condition	WP6	4 - AMU	48	Astrotechnologies proof of principle for use in pathological condition
MS7	Data integration in Computational methods and in TVB	WP7	5 - BCAM	48	Data integration in Computational methods and in TVB
MS8	ASTROTECH website	WP8	1 - CNR	2	ASTROTECH website
MS9	Project Mid term check	WP1	1 - CNR	15	Meeting between REA and consortium

1.3.5. WT5 Critical Implementation risks and mitigation actions

Risk number	Description of risk	WP Number	Proposed risk-mitigation measures
1	Conflicts within the consortium (I= Me; P=L)	WP1	The Project Coordinator will contact involved parts and identify problems, finding a suitable solution before a possible escalation.
2	Conflicts over IPs (I= Me; P=L)	WP1, WP2, WP3, WP4, WP5, WP6, WP7, WP8, WP9	Negotiations will be conducted by the Coordinator among the participants in dispute, according the norms and rules ratified in the CA.
3	Beneficiary withdrawing from the consortium (I= Me; P=L)	WP1	a) Identify other colleagues within the same Institution or find a new beneficiary with similar profile and competencies. b) If not available: training and research activities and tasks will be redistributed over the consortium. c) The involved ESRs will be recruited by the new beneficiary or by a beneficiary within the ASTROTECH consortium.
4	Beneficiary not signing the Grant Agreement (I= Me; P=L)	WP1	Identify a new Beneficiary with similar profile and competencies. If not available training and research activities and tasks will be redistributed over the consortium
5	Change in ownership of a private beneficiary/partner (I= Me; P=L)	WP1	If the new owner does not intend or cannot (for example, the new owner is located in a Third Country) carry on the research and training activities of ASTROTECH, a new beneficiary will be sought, or tasks and activities redistributed within the consortium.
6	One of the supervisors cannot guarantee adequate involvement or decides/has to leave the project (I= Me; P=Me)	WP2, WP3, WP4, WP5, WP6, WP7	The supervisors will be replaced by a new supervisor, possibly within the same institution, with similar competencies and experience.
7	The Coordinator decides/has to leave the project (I= H; P=L)	WP1	The co-coordinator will be in charge for this position.
8	Delay in recruitment; lack of qualified applicants (I= H; P=L)	WP1, WP2, WP3, WP4, WP5, WP6, WP7, WP8	Research activities linked to that or those ESRs will be developed locally to not delay deliverables/milestones achievements.
9	ESR on maternity/paternity leave(I= Me; P=L)	WP1, WP2, WP3, WP4, WP5, WP6, WP7	Provisions in the GA will oblige the ESRs to inform the employer and the coordinator about circumstances affecting the implementation. Training and research activities will be rescheduled accordingly.
10	One of the ESRs resigns (I= Me; P=Me)	WP1	A new ESR will be recruited with similar competence and experience. If lapsing time will occur between ERS leave and new ESR entry, training and research activities will be rescheduled among partners to ensure project milestones achievement.
11	Training not meeting the expected standards or	WP1, WP2, WP3, WP4, WP5, WP6, WP7	The TTB will control the quality of the training through a series of evaluating procedures (self-

Risk number	Description of risk	WP Number	Proposed risk-mitigation measures
	Training provided by non-academic partners due to internal re-organization (I= H; P=Me)		evaluation tests, student questionnaires, trainer evaluation, etc.). In case of training failure, additional training program will be provided by the beneficiaries.
12	ESRs do not complete the academic Ph.D program within the duration of ASTROTECH activities (I= H; P=H)	WP1	Beneficiaries are committed to support the completion of the PhD program also after the end of the project.
13	Issues between the ESRs and the supervisor (I= H; P=Me)		The co-supervisor will be involved to mediate and solve issues between the ESR and the supervisor by amicable solutions, to support and assist the supervision of the ESR. In the worst cases (unsolvable issues, harassment, mobbing) the ESR will be transferred to another beneficiary with complementary expertise.
14	Materials and devices for optogenetics and electrophysiology do not satisfy the expected requirements. Failure of equipment to perform the experiments (I= H; P=Me)	WP2, WP3, WP4, WP5, WP6	The risks can rely on: 1) lack of advanced materials: unavailability of newly synthesized materials will be overcome by using commercially available ones. 2) Failure of equipment supply: temporary unavailability of access at facilities at a partner sites will be mitigated by the secondment of ESRs at a beneficiary or partner with similar expertise. Whereas beneficiaries have partial overlap in labs and facilities (clean rooms, chemical labs, enclosures, etc.) these structures can be made available for a certain period to other ESR.
15	Unavailability of biological materials (animals, cell cultures) (impact: H; probability: L)	WP2, WP3, WP4, WP5, WP6	If primary cell cultures or animals are unavailable at partner sites (contamination, failure of breeding procedures), biological materials will be purchased from other providers.
16	Failure in devices and prototypes fabrication for interfacing astrocytes (I= H; P=Me)	WP2, WP3	Redefinition and prototyping of current devices available at the beneficiary lab with the innovative materials. Integration of commercial components in the new platform (hybrid solution).
17	Failure of equipment and/ or unavailability of ad hoc electronics for cell signaling readout (impact: H; probability: L)	WP2	ASTROTECH proposed electronics relies on previous knowledge of past projects. In case of electronics failure, standard bulky electronics will be used or multiple commercial equipment will be interconnected to accomplish the dedicated task.
18	Failure in the validation of prototypes of electronic/ optoelectronic devices (I= H; P=Me)	WP3	Experiments will performed with hybrid solutions, merging commercial parts with successful components developed in ASTROTECH.
19	Project overall timeline and milestone deadlines not respected (I= H; P=Me)	WP1, WP2, WP3, WP4, WP5, WP6, WP7	If the workload results unbalanced, leading to possible deviations of the expected milestone timeline, task distribution will be adjusted among ESRs and research units.

1.3.6. WT6 Summary of project effort contribution

	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9
1 - CNR	✓	✓	✓	✓	✓	✓	✓	✓	✓
2 - UCAM	✓				✓	✓		✓	
3 - UEM AVCR	✓	✓		✓		✓		✓	
4 - AMU	✓	✓					✓	✓	
5 - BCAM	✓							✓	
6 - INEB	✓			✓		✓		✓	
7 - UNIBA	✓		✓	✓		✓	✓	✓	
8 - IIT	✓				✓	✓		✓	
9 - CSIC	✓		✓			✓		✓	
10 - AVA	✓	✓			✓			✓	
11 - OPTOCEUTICS	✓		✓		✓	✓		✓	

1.3.7. WT7 Tentative schedule of project reviews

No project reviews indicated

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 Agency). 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
DATA	data sets, microdata, etc.

16. Dissemination level

Please indicate the dissemination level using one of the following codes:

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.

Marie Skłodowska-Curie Actions (MSCA)
Innovative Training Networks (ITN)
H2020-MSCA-ITN-2020

Annex 1 to the Grant Agreement (Description of the Action) Part B

GAP-956325
"Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards Glial interfaces -ASTROTECH"

History of changes

• The required cover page has been added which replaced the previous start page

• The table of contents has been updated

• The following sections have been deleted:
- Work Packages description
- List of major deliverables
- List of major milestones
- Risks management at consortium level
- Capacities of the Participating Organisations
- Letters of Commitment

• Information regarding Ethics has been updated

LIST OF PARTICIPATING ORGANIZATIONS

R=Research; T=Training; S=Hosting Secondments; TEO=Training Event Organization; DD=Delivering Doctoral Degree.

Consortium Member	Legal Entity Short Name	Academic	Non-academic	Awards Doctoral Degrees	Country	Dept./ Division / Laboratory	Scientist-in-Charge	
Beneficiaries								
Consiglio Nazionale delle Ricerche	CNR	✓			IT	Institute for Organic Synthesis and Photoreactivity (ISOF), Institute for Microelectronics and Microsystems (IMM), Institute of Polymers, Composites and Biomaterials (IPCB)	Valentina Benfenati (Coordinator) Luca Maiolo (Co-Coordinator) Vincenzo Guarino (IPCB-Unit Responsible)	
University of Cambridge	UCAM	✓		✓	UK	Dept. Engineering (ENG)	George Malliaras	
The Czech Academy of Sciences	UEM AVCR (IEM)	✓			CZ	Institute of Experimental Medicine	Miroslava Anderova	
AMU-Marseille Université	AMU	✓		✓	FR	Institut de Neurosciences des Systèmes	Christophe Bernard	
Basque Center for Applied Mathematics	BCAM	✓			ES	Group of Mathematical, Computational and Experimental Neuroscience (MCEN)	Maurizio De Pittà	
Instituto Nacional de Engenharia Biomédica	INEB	✓			PT	nanoBiomaterials for Targeted Therapies Group	Ana Pego	
Università degli Studi di Bari	UNIBA	✓		✓	IT	Dipartimento Di Bioscienze, Biotecnologie e Biofarmaceutica	Grazia Paola Nicchia	
Fondazione Istituto Italiano di Tecnologia	IIT	✓			IT	Center for Nanoscience and Technology (CNST)	Maria Rosa Antognazza	
Spanish National Research Council	CSIC	✓			ES	The Cajal Institute	Gertrudis Perea	
Avanzare srl	AVA		✓		ES	R&D Department	Julio Gomez	
Optoceutics ApS	OPTO		✓		DK	R&D Department	Marcus S. Carstensen	
Partner Organizations								**Role**
CODEMART	CODEMA				RM		Lia Domide Jochen Mersmann	T, S, TEO
MEDTRONIC	MEDTR		✓		IT	The MC2 Study & Scientific Solutions division	Francesco De Seta Dafni Carmina	T, S, TEO
University of La Rioja	UR	✓		✓	ES	PhD in Chemistry	Jesús Berenguer	T; DD
National Council of University Research Administrators	NCURA		✓		US		Claire Cheng	T, TEO
University of Bologna	UNIBO	✓		✓	IT	Dept. of Chemistry Dept. Pharmacy & Biotechnologies (FABIT) Dept of Electrical, Electronics & Information Engineering (DEI)	Matteo Calvaresi Marco Caprini Mauro Ursino	T; R; S; DD
Politecnico di Milano	POLIMI	✓		✓	IT	Dept. Physics	Guglielmo Lanzani	T; DD
University of Madrid	UMAD	✓		✓	IT	Dept. Anatomy, Histology and Neuroscience	Lucia Prensa	T; DD

University of Porto	UPORTO - ICBAS	✓		✓	IT	Instituto de Ciencias Biomédicas Abel Salazar of the University of Porto	Mario Barbosa	T; DD
Charles University	CUNI	✓		✓	CZ	Dept of Neuroscience	Lydia Vargova	T; DD
Università Federico II	UNINA	✓			IT	Dept. Industrial Products and Process Engineering	Andrea D'Anna	DD
University of Basque Country	UPV/EHU	✓			ES	Dept. Neuroscience	Jose Luis Martin	DD
University of Copenhagen	UCPH	✓		✓	DK	Dept. Clinical Medicine	Troels Wesenberg Kjær	T, DD
Zealand University Hospital	ZUH	✓			DK	Dept. Neurology	Troels Wesenberg Kjær	T, S
Technical University of Denmark	DTU	✓		✓	DK	Dept. Photonics Engineering	Paul Michael Petersen	T, DD

Data for non-academic beneficiaries:

Name	Location of research premises (city / country)	Type of R&D activities	No. of full-time employees	No. of employees in R&D	Web site	Annual turnover (in Euro)	Enterprise status (Yes/No)	SME status (Yes/No)
Avanzare (AVA)	Navarrete / Spain	Nanomaterial products development	32	29	www.avanzarematerials.com	2.369.578	Yes	Yes
Optoceutics (OPTO)	**Kongens Lyngby Denmark**	**Photonics, optics, electronics**	**10**	**8**	www.Optoceutics.com	**50.000 €**	**No**	**Yes**

1. Excellence

1.1 Quality, innovative aspects and credibility of the research programme

- **Introduction, objectives and overview of the research programme**

Despite decades of research, including heavily funded Human Brain Project (EU) and BRAIN (NIH) initiatives, our understanding of the big picture of brain functions is still incomplete and insights on neuro-pathophysiological conditions and diseases (such as cerebral ischemia, glioma, epilepsy and depression) are very limited. This lack of knowledge inhibits our ability to provide the proper treatment of neurological conditions and meet this major societal challenge. It was estimated that there were 127 million Europeans living with a brain disorder and disease out of a population of 466 million. The total annual cost in healthcare of brain disorders in Europe was estimated in a range between €386 to 700 billion in 2010[1]. The frequency of epilepsy alone in Europe in 2004 was 4.3-7.8 per 1,000, leading to an estimated total cost of €15.5 billion in 2010. This societal challenge call for an **urgent action to develop better diagnostic tools and treatments, which require major technological and conceptual advances**[1]. A major obstacle of previous and current initiatives on *Neurotechnologies* is a lack of interest in **non-neuronal brain cells, called** glia, which are as numerous as neurons. Glial cells are tightly linked to neurons and blood vessels, thus forming the neuron-glia-vascular unit. Although cutting-edge tools have been developed to study neurons, which are electrogenic cells, no tool has been specifically developed to study glial cell function. **ASTROTECH** will fill this gap. Glial cells were once considered to provide trophic and mechanical support to the neuronal network. Studies over the past four decades have revealed that **astrocytes** display a variety of activities, that are crucial for brain function at the synaptic, cell network and organ scales[2,3]. For example, astrocytes regulate the concentration of ions and neurotransmitters, they participate to communication between neural cells and exerting a central role in the brainvolume homeostasis, cerebro-vascular neurovascular coupling which critically supersede and cognitive functions and information process.[2,3] Neurological disorders are invariably associated with astrocyte dysregulation, raising the possibility of causal links, in particular in cerebral ischemia, glioma, epilepsy or depression[4,5]. The

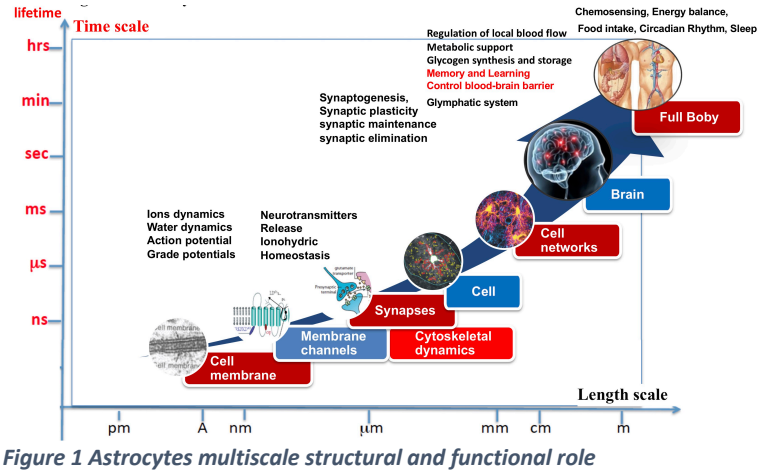


Figure 1 Astrocytes multiscale structural and functional role

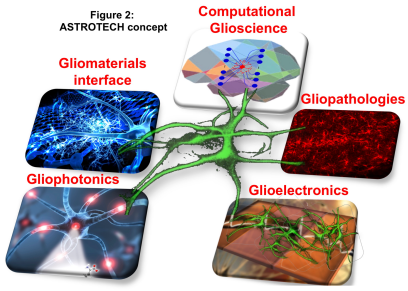
complex signalling dynamics underpinning astrocytes functions remain unclear as most of the technologies and tools used to probe and sense astrocytes are derived from those developed to study neurons.

ASTROTECH is a multidisciplinary European Training Network aiming at obtaining a more complete understanding of brain function and dysfunction, leveraging on the fast-growing recognition of the importance of glial signaling. ASTROTECH will implement "training-through-research" by the **development and application of innovative technologies & methodologies**, targeting the monitoring, the study, and the manipulation of the function of **glial cells called astrocytes** and their role and interaction with neurons at multiple scales: from intracellular and subcellular synaptic level, to cellular and neural circuits to behaviour, in both time and space.

ASTROTECH will create and develop the field of Glial Engineering, to provide a consistent range of tools to record, study, and manipulate astrocytes in the healthy and diseased brain. **ASTROTECH** will train the next generation of brain scientists with the required skills in the supradisciplinary field of **Glial Engineering**.

ASTROTECH will combine imaging, neurophysiology and biology to state-of-the-art nanostructured material processing, biotechnological probes, photonic and electronic device development and fabrication, computational approaches and software development to develop **glial interfaces, glial electronics, gliophotonic and computational glioscience**. Technologies and approaches will be validated with experiments *in vitro*, *ex vivo*, *in vivo* and *in silico* in normal and pathological conditions including epilepsy, ischemia, glioma and depression, which represent a selection of conditions that affect large populationss worldwide[6]. Protocols for studies in humans will be assessed to exploit the clinical potential of selected technologies.

The **ASTROTECH** network combines **11** beneficiaries and **14** partners belonging to **9** European and Non-EU countries Academia, Public Research Centers and industrial labs, gathers all complementary expertise needed to explore the several venues for **glial interfacing** offered by advanced materials, device architectures and operation as well as for their validation to manipulate glial cells function. The 9 academic and public research Beneficiaries (**CNR, IIT, CSIC, UCAM, AMU, UNIBA, INEB, IEM, BCAM**) are internationally renowned for their research and training activities in the fields that they represent within **ASTROTECH**. The **contribution of the private sector** in the research & training program is pivotal for the training network, as it makes available the know-how for nanomaterial processing and device fabrication, covering advanced materials for electronic (**AVANZARE**) and light emitting devices (**OPTOCEUTICS**) as well as computational tools (**CODEMART**) and for expertise in translating research knowledge and technology into clinical practice (**MEDTRONIC**) and finally on professional development, knowledge and leadership in research management and administration (**NCURA**).



- **Research Training Objectives**

The main objective of ASTROTECH is to boost the career success of Early Stage Researchers (ESR) by a training network at the forefront of research in the supradisciplinary field of **Glial engineering.** In particular, ASTROTECH aims:

- **To provide personalized individual training** though Individual Research Projects and a Complementary Skills Training Program that fulfills the requirements for transfer of relevant knowledge and gaining of skills in the field of **Glial Engineering**.
- **To provide researchers with high quality network-wide** training (e.g. organization of training and transfer of knowledge, workshops, summer schools) and local training (training opportunities such as PhD programs, local courses, tutorials, specialized symposia and modules), aimed at synchronizing integration of research activities performed by the 15 enrolled ESRs within local research teams, reinforcing **complementary skill training** and disseminating knowledge and results, thereby fully exploiting the network potential and complementarities.
- **To transfer existing and new knowledge between the participating institutions** thus catalyzing the creation or reinforcement, when already existing, of a long-lasting collaboration **for the formation of a European and Global network of knowledge on Glial Engineering**. In this sense, all the ESRs will be encouraged to perform at least one secondment in a different node, giving priority to the multidisciplinary and intersectoral character of these secondments. Oversea secondments are also encouraged by existing collaboration with US and Australia.

ASTROTECH will spawn a new generation of researchers with a unique **hybridization of scientific skills** that immerse ESRs in inter-disciplinary and multi-sectorial research and training programs. ESRs will benefit from a broader view of the research issues and will improve their career possibilities by working at private partner facilities and being trained on state-of-the-art **biomaterial processing** and **bioelectronic** and **biophotonic** device fabrication protocols as well as on methodologies for results exploitation as for example bioelectronic device clinical testing, or software development for big data analyses. ESRs will benefit of the interdisciplinarity and intersectoral excellence of the ASTROTECH training network that covers every step **"from benchside to bedside"** of the value chain of the emerging **Glial Engineering, which no single partner in the network can provide as such**. ESRs will be trained and will contribute to research program of the most advanced level on i) advanced materials development and

characterization (**CNR, INEB, IIT, UCAM, AVA**), ii) electronic and optoelectronic device fabrication and studies (**CNR, UCAM, IIT, AVA, OPTO**), iii) biological validation at a multiple scale: in vitro (**CNR, UNIBA**), ex vivo (**AMU, IEM, CSIC**) in vivo (**AMU, IEM, CSIC**), iv) validation in pathological models (**UNIBA, AMU, CSIC, IEM, OPTO**), being developed and available at the beneficiaries; v) Computational studies and software development integrate combined with experimental validation to understand the roles of astrocytes at the molecular, cellular, network and organ levels (**BCAM, CODEMART, AMU**). ESR training will include **intersectoral aspects** of research on materials and devices validation in industrial environment (**AVA**), photonic device for low invasive brain disease therapy (**OPTO**) complementary soft skills commercial software validation (**CODEMART**) and service providing on study & scientific solutions (**MEDTRONIC**). The training offered by Partner **MEDTRONIC** support the development of clinical studies as well as provide operational and analytical support. The latter soft skill is essential to support and translate results obtained within **ASTROTECH** into effective clinical solutions and practice and to really impact on patient healthcare. Internationalization is also a peculiar aspect of the **high-level advanced education offered by ASTROTECH. NCURA** will train European ESRs on topics as **funding opportunities and proposal development, research capacity building, and partnership development overseas** to provide a global dimension that will maximize the impact of **ASTROTECH** training network, ESRs career development, and market applicability of the research result.

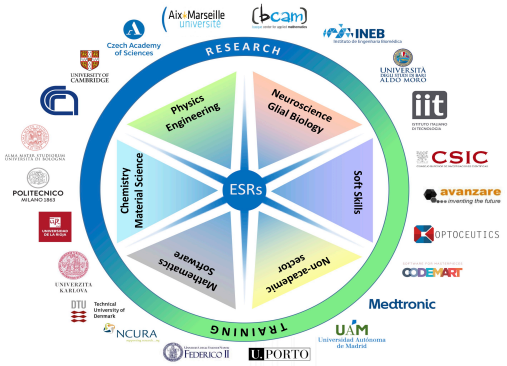


Figure 3: ASTROTECH multidisciplinarity and intersectoral knowledges

- **Objective of the research program**

ASTROTECH consortium offers an inter-disciplinary and intersectoral (–academic/industrial-) training program approach based on a bottom-up research model that will open the way for this **novel supra-disciplinary field of Glial Engineering** as the key for generating innovations and ideas that may result in reliable product applications appealing for biomedical, pharmaceutical and technological industry for the ultimate benefit of public health. In particular the research objectives will be:

i) **Development of biomaterials and nanostructured interface that** models how healthy or reactive astroglial cells in vitro are structured and **express molecular and functional properties similar to those expressed in vivo**.

ii) **Design, fabrication and characterization of nanostructured** devices for **stimulation, recording and biosensing** of astrocytes (simultaneously with neurons) at different spatiotemporal scales *in vitro ex vivo* and *in vivo*.

iii) **Validation of optogenetics tools, photonic devices and optical methods** to uncover the role of astroglial cells in neural circuits *in vitro ex vivo* and *in vivo*, in animals and possibly in humans (for selected technologies).

iv) **Explore the potential of these new technologies in pathological models** of ischemia, epilepsy, glioma and depression, to explore new research avenues for the treatment of these conditions.

v) Definition of computational approaches and inspired by Control Theory that can reverse-engineer, describe and predict neuron-astrocytes interactions.

ASTROTECHNOLOGIES will complement *Neurotechnologies* while providing tools that will open new domains of knowledge on brain function and neurological disorders.

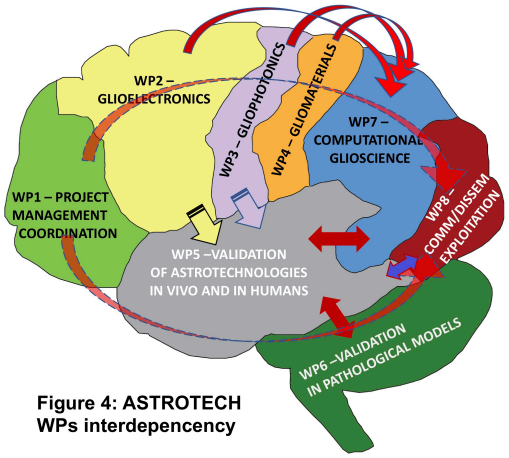


Figure 4: ASTROTECH WPs interdepencency

1.2 Research methodology and approach

Since astrocytes are an integral part of brain circuits, constantly interacting with neurons and blood vessels, it is important to develop materials and technologies able to interface with astrocytes together with those already available for neurons to probe further brain function and possibly treat brain disorders.

Astrocytes cannot generate action potentials, but they can sense and respond to **mechanical, electrical and photonic stimuli**. **ASTROTECH** will develop disruptive and **ad-hoc tailored technologies in biomaterials, electronics, photonics and optogenetics**. Astrocyte membrane proteins can form channels and receptors that generate ionic (ion flux generating a current, intracellular Ca^{2+} changes) and molecular (e.g. water flux) signals, that will be captured by the **ASTROTECH** electronic devices, simultaneously with state-of the art electrophysiology and high-resolution imaging approaches. **ASTROTECH** will attempt to decode the language between neurons, astrocytes and blood vessels using a reverse engineering approach. We will create an **open-source platform** for the neuroscience community, providing tools for simulating and analyzing astrocyte/neuron function at the whole brain level.

The overall workplan is arranged into 8 Workpackages (WPs), 6 WPs (WP2-WP7) are devoted to research/training activities, while **WP1** will pertains to coordination and management and ***WP8*** focus on dissemination and result exploitation. Each WP contains specific Tasks in which the ESRs at each Research Unit will be deeply involved (see section 3). In **WP2**, we will fabricate and characterize (glio)electronic devices based on metal/silicon nanowires, graphene-graphite/nanostructured blends and conducting polymers together with flexible electronics solutions for recording and stimulating astrocytes in vitro in primary culture, in co-cultures with neurons, and on brain slices from rodents. In **WP3** we will study the ability of optogenetics approaches, optical and photonic tools to provide precise and fast control of ions and water dynamics in astrocytes and to study the cellular and molecular mechanisms of astrocyte function in primary cultures, in co-cultures and *ex vivo*. In **WP4** we will study the interactions and mutual influence of healthy and astrogliotic cells with nanostructured biomaterials interface and evaluate the impact of such structures on astrocyte morphology, viability, migration, as well as on molecular and functional expression for ion channels and water channels expressed in vivo. In **WP5** we will test **ASTROTECH** technologies for electrical, optogenetic and photonic stimulation, manipulation of astrocytes ions and water dynamics and recording of astrocytes bioelectrical activity *in vivo* in transgenic animal models, allowing to selectively target the stimulation of astrocytes and to analyze their contribution to the recorded signal. Protocols for trials of selected technologies in Humans will be defined. **WP6** will evaluate the potential translational applications of *ASTROTECHNOLOGIES* for: i) the study of glioma and gliosis in vitro and in in vivo, ii) neuropathological models such as ischemia epilepsy and depression where astrocyte physiology is highly altered and iii) possible restoration of glial function in pathological conditions. In particular, we will try to identify astrocytic events that predict the occurrence of a spontaneous seizure, the involvement of ion channels and water channels and calcium signaling in ischemia and glioma, as well as the role of astrocytes signaling in rescuing from depression. Finally, **WP7** will use a computational approach, intergrating electrophysiological recording and calcium imaging in vitro, ex vivo and in vivo from WP 3-6, in order to understand and possibly predict the role of astrocytes in normal and pathological conditions. **WP1** and **WP8** will be dedicated to management and dissemination/exploitation, respectively. The original and innovative aspects of the research and training program are listed below.

Table 1.1. ASTROTECH Work Package LB = Lead Beneficiary; S = Start Month; E = End Month; R = Research; T = Training; DISS = Dissemination; OUT = Outreach; EXP = Exploitation; MGT = Management.

WP	WP Title	LB No.	S	E	Activity	LB	ESR involvement
1	Project management, coordination and quality control	1	1	48	MGT	CNR	all
2	Glioelectronic device development fabrication and validation in vitro, ex vivo	2	7	36	R, T	UCAM	CNR-IMM, CNR-ISOF, AVA, IEM, BCAM, AMU
3	Gliophotonic device and optogenetics approaches development and validation in vitro, ex vivo	8	7	36	R, T	IIT	OPTO, CSIC, UNIBA, CNR-ISOF
4	Gliomaterials interfaces for in vitro-like -in vivo healthy and gliotic astrocytes model	6	1	48	R, T	INEB	UNIBA, CNR-IPCB, IEM
5	Validation in vivo of electronic, optogenetics, photonic astrotechnologies	9	24	48	R, T	CSIC	CNR-IMM, AMU, IIT, OPTO, AVA
6	Validation of astrotechnologies in pathological models	4	24	48	R, T	AMU	IEM, UCAM, CNR, INEB, UNIBA, IIT, OPTO, CSIC
7	Computational glioscience	5	1	48	R, T	BCAM	AMU, CNR-IMM, CNR-ISOF, CODEMA, UCAM, UNIBA
8	Dissemination, communication, exploitation and public engagement	1	1	48	DISS, OUT, EXP, T	CNR	all

- **Originality and innovative aspects of the training program**

It is essential to take into account astrocytic functions and develop ad hoc devices. Although they are incapable of generating and propagating action potentials, astrocytes display bioelectrical activiy mediated by ion channel proteins, which are transmembrane movement of ions and organic molecules[1]. In particular, local transmembrane K^+, Na^+ and Ca^{2+} dynamics at astrocytic process are critical for brain function, from synaptic function to memory and learning. Gap junctional communication channels also allow astrocytes to form a network[5]. Cell volume regulation is also an essential function for astrocytes. **Measuring ionic and water dynamics is highly demanded and requires the development of bioelectronic tools allowing analyses of events occurring at different spatial and temporal scales with high resolution capabilities.** In the traditional patch-clamp method the spatial resolution is limited to the electrical signal recorded from the cell body of the single astrocyte and the probe invasiveness reduces the monitoring to minutes. In addition, extracellular recording systems based on planar microelectrode arrays (MEAs) suffer from critical limitations for the recording of astroglial signaling.

ASTROTECH-ITN *will develop and validate* ***glial electronic interface and devices*** *ideally suited for the recording, stimulation and modulation of ionic, molecular and electrical activity in astrocytes***.** In this view, we will investigate the use of devices based on both organic and inorganic nanostructures[7-9]. In case of inorganic materials, silicon nanowires (SiNWs) are a promising neural interface allowing real-time, spatial-resolved recording and manipulation of neuronal bioelectrical activity[10,11], promoting interactions with micro/nanoscale features of cell surface[12,13]. Moreover, surface chemistry engineering makes SiNWs suitable for probing and sensing different types of cells. In

addition, the "soft" nature of organic materials offers improved mechanical compatibility may also support conduction of ions, in addition to electron and hole transport, offering a broad spectrum of possibility for interaction and communication with astrocytes[14,15]. This technology has been translated to the clinic[15b]. A step further in terms of performance has been achieved through the use of organic electrochemical transistors, which were shown to record neuronal activity with record-high signal-to-noise ratio.[16-19] Organic conducting polymers and small molecules such as poly(3,4-ethylenedioxythiophene) doped with poly(styrene sulfonate) (PEDOT:PSS), P3HT: PCBM, or perylene dimmide derivatives have been shown to be biocompatible with a variety of different cells including astrocytes *in vitro*.[20] However, the ability of organic devices to sense gliotransmitters or molecule released from astrocytes as well as to record astrocytes biolelectrical activity have never been reported. **In WP2, ESR-2** at **CNR-IMM** will develop and validate interface and electrode device based on gold coated SiNWs (Au/SiNWs), randomly organized and not-homogeneous sized (nano-forest). **ESR-13** at **AVA** will develop new nanocomposite materials with low impedance based on organic materials and graphene printing technique, in order to simplify glio interface fabrication process. **ESR-4** at **UCAM** will develop and fabricate flexible organic device, including electrodes and electrochemical transistors. Both devices types will be engineered to interface astrocytes in vitro and to record and modulate their functionality *in vivo*. **ESR-1** at **CNR_ISOF** will study the bioelectrical activity of astrocytes coupled to the device based on Au/SiNWs and on Carbon based devices *in vitro* while **ESR-5** *at* **IEM** and **ESR-6** at **AMU** will validate **ASTROTECH** electronic device capability to record astrocytes signals respectively on brain slices *ex vivo* and *in vivo*. *In situ* (brain rodent slices) **in WP2** and *in vivo,* **in WP5**, experiments will be performed on genetically modified animal models where astrocytes will be selectively fluorescently labeled (GFAP/EGFP+). Thus, by coupling **ASTROTECH** with standard electrophysiological recording with state-of-the art confocal microscopy and two photon imaging, we will be able to perform a multiscale, comparative analysis and to distinguish and uncover the contribution of astrocytes and glial cells such as NG2 cells, to the bioelectrical activity recorded.

Intracellular calcium variations are another important readout of astrocyte activity and function. Astrocytes are capable to respond to different extracellular chemo-physical stimuli (such as neurotransmitters, temperature, osmostic gradient, mechanical stimulus) with changes in their cytosolic Ca^{2+} concentrations ($[Ca2^{+}]_i$).[21,22]In vivo studies indicated that $[Ca^{2+}]_i$ oscillations and dynamics can occur in restricted spatial domains (microdomains) or spread between astroglial cells through gap junctions (Ca^{2+} waves). [23,24] The increase in $[Ca^{2+}]_i$ can be caused by the entry of extracellular $[Ca^{2+}]_i$ or by the mobilization of the $[Ca^{2+}]_i$ stored in the endoplasmic reticulum. Uncovering the mechanisms of intracellular Ca^{2+} dynamics is essential to understand the role of astrocytes. The limited set of tools currently available to modulate ion fluxes, calcium signaling and water dynamics, and numerous receptors and channels expressed in astrocytes have limited our ability to effectively study their importance in normal and pathological conditions. Classical methods include pharmacology, genetic manipulation, fluorescence imaging of molecular sensors, and electrophysiology. [25-29] Despite recent advances in optogenetics and optoelectronics for neurons,[28] **optogenetic methods** and label-free **optical control** of ion flux and water dynamics remain to be developed for astrocytes[39].

ASTROTECH ESRs *will develop optogenetics and photonic stimulation methods with low energy, high temporal and spatial resolution for selective stimulation/modulation of astrocytes, measuring ionic/molecular activity, and validate the approaches in vitro, ex vivo, in vivo and in various mouse models.* Recent results from ASTROTECH consortium members pioneer using GPCRs optogenetics based on melanopsin in astrocytes.[39] **In WP3, ESR-12** at **CSIC** will use the new tool to provide insights of the role of astrocytes for the adjacent synapses, local circuits and animal behavior. To this end **ESR-12** will work also with **ESR-2 (CNR**) to demonstrate the ability of a Au/SiNWs platform to record *ex vivo* signals elicited using an optogenetic approach. **ESR-14** at **OPTO** will provide engineered optical fibers for reliable optogenetics experiments and will work with **ESR-12** at **CSIC** to validate it for its use in brain slices and in vivo. Finally, **ESR-15** will work with **ESR-10** at **UNIBA** to verify the possibility of photostimulation of astrocytes in ASTROTECH in vitro **(WP4)**. Previous study from IIT demonstrated that hybrid devices based on organic semiconductors are a highly efficient and reliable tool to optically modulate the electrical and metabolic activity of living cells, as proven in primary cells (neurons and astrocytes), progenitor cells (endothelial precursors), tissues, up to the complexity level of animal models. **ESR-11** at **IIT** will focus on the understanding and exploitation of phototransduction mechanisms, and on the optimization of functional devices in vitro and ex vivo in collaboration with **ESR-5** at **IEM. ESR-15 at OPTO** will be dedicated to the development of light technologies to improve cognitive function, with applications in neurological disorders. **In WP5**, the validation of the above mentioned optogenetics, optical and photonic methods will be performed *in vivo* wildtype mice and in *Ip3r2*$^{-/-}$ mice, which show downregulation of calcium signaling in astrocyte. Primary cell cultures are ideal to unravel basic mechanisms in neuroscience as they allow high throughput, they are easily controlled and provide high spatio-temporal resolution. They constitute an essential step before validation in brain slices and then in vivo. However, primary cultures grown on flat substrates lose structural and functional features, which play key roles in vivo.[36-40] Hence, it is crucial to improve the technology in order to make the technique more relevant to the in vivo situation. Recent results currently allow manipulating natural and synthetic biomaterials by finely controlling chemo-physical

properties (i.e., in vitro degradation, fluid transport and permeability, mechanical response), architecture at micro and sub-micrometric scale (inner pore structures and features) and bio functionality to preserve/improve the ability of the biomaterial to modulate/activate/inhibit proper cell-to-cell interactions mechanisms.

ASTROTECH ESRs *will develop nanostructured interfaces, biomaterials and bio-nanocomposites as a scaffolding support for the development of in vitro models to study astrocytes biology and physiology in a manner that is more controlled and more relevant to in vivo conditions*. Due to the lack of a screening platform, which would allow in vitro simultaneous testing of several variables, no comprehensive study has addressed and clarified how different microenvironmental properties affect astrocyte behaviour in homeostasis and disease (astrogliosis and gliomas). In **WP4**, **ESR-9** at **INEB** and **ESR-1** at **CNR-IOSF**, will develop and explore 3D instructive nanostructured biomaterials (developed by **ESR-1 and -3** at **CNR-ISOF** and **CNR-IMM** respectively and **ESR-13** at **AVA**) to culture astrocytes and study, in a reproducible way, its behaviour under different conditions. **ESR-3** at **CNR-IPCB** will be aimed at designing fibrous biomaterials by the use of electrospinning for the fabrication of instructive interfaces suitable to investigate in vitro glioma interactions. During this activity, materials and process conditions will be selected in order to optimize the morphology at the level of single fibre (i.e., defects occurrence, surface roughness) and fibre assembly (i.e., size distribution, fibre orientation). Chemical/physical properties of fibres (i.e., wettability, surface porosity, etc) will also be investigated to validate their use as gliomaterial interfaces. **ESR-10** at **UNIBA** and **ESR-5** at **IEM** will evaluate the molecular and functional features of primary rodent astrocyte/neuron primary co-cultures in the developed system, with a particular attention to the expression and function of ion channels and water channels aquaporins essential for astrocytes function in vivo. For these purposes, they will be trained and use state-of-the-art gene and protein expression analyses as well as confocal and high Resolution STED microscopy. ASTROTECH will bridge the knowledge gap that exists between the current in vitro models and in vivo approaches. In such models, the response[45] of astrocytes, neurons and of their dialogue in response to photonic or electrical stimuli will be studied and controlled at different time and spatial scales.
Glial cells play also a key role in pathological conditions. In response to insults, disorders or injuries, glial cells undergo a dramatic reaction, named gliosis, that include hypertrophic proliferation and release of toxic molecules (i.e. glutamate and cytokines). Alterations of astrocyte ion channel structure and function, occurring during astrogliosis, is causally linked to phenotypes and represent a major obstacle to brain recovery in pathologies such as ischemia, epilepsy and glioma[4]. Devices can be implanted in the brain to study/treat pathologies. Dysfunction of bioelectrical properties of astrogliotic cells surrounding brain implants facilitates the spread of inflammation and formation of gliotic scar leading to decreased performance.[40b] Over time, the astrocytes and microglia begin to accumulate, forming a sheet surrounding the array that extends tens of micrometres around the device. The resulting effects are neuronal cell loss, glial scarring, and a drop in the number of functioning electrodes. It is thus very difficult to disentangle the effects due to the pathology from the effects due to the implantation of a device in the brain.

ASTROTECH will build a simple, controllable, culture system for the culture of astrogliotic astrocytes. **In WP4** using astrocytes cultured in biofunctionalized alginate hydrogels,[41,] and electrospun nanofibers **ESR-9, and ESR-3** respectively at **INEB** and **CNR**, will develop tissue engineered constructs to study, in a reproducible way, the behaviour of astrocytes mimicking many features of the glial scar. At the same time, the *in vitro* model will be validated by growing astrocytes, organoids and neurospheres. At UNIBA, and at CNR, ESR-10 and ESR-1 will study molecular and functional aspects by performing patch-clamp (where possible) and calcium imaging. The analyses at the submolecular level will be performed using STED and confocal microscopy in order to uncover the mechanisms underpinning gliotic scar formation.
According to WP6, **ESR-6** at **AMU** will study seizure mechanisms and predictive biomarkers. Despite decades of research, the mechanisms underlying seizure genesis are not fully understood, which may explain why 30% of patients are drug-resistant since 1850. Beyond the mechanistic insight, which would open the way to new therapeutic approaches, it would be crucial for uncontrolled patients to receive reliable warnings of incoming seizures, if only to place themselves in safe conditions and warn others. In addition, reliable predictive biomarkers may open the way to the implantation of closed loop systems using neurostimulation, or possibly optogenetics, to abort seizures before their occurrence. AMU has proposed a comprehensive mathematical framework [42]to explain seizure dynamics. The model predicts that a state variable evolving slowly in time is required to explain seizure onset, time course and offset. Preliminary data show that molecular events such as those related to ion homeostasis, metabolism and energy supply, which evolve slowly in time, are integral components of this state variable. Such events are directly controlled by astrocytes. Most (at least 70%) seizures recorded in patients and animal models start with a DC shift, which is associated with a rise in extracellular K^+, suggesting a dysfunction of astrocytes in buffering K^+. AMU uses a focal model of epilepsy (intrahippocampal injection of tetanus toxin), which has several advantages. The contralateral side can be used as a control. The model is transient, spontaneous seizures start to appear 2-3 weeks after injection and disappear 2-3 weeks later. Each animal can thus be used at its own control, from a non-epilepsy state, epilepsy, back to a non-epilepsy state. We hypothesize that astrocytic dysfunction will manifest before seizure onset (predictive

biomarker), possibly causally related to seizure genesis (mechanism, and target identification). **ESR-6** will use classical (e.g. Ca^{2+} imaging of astrocytes, DC recordings) and novel combinations of devices developed in ASTROTECH to get a complete electro-molecular picture of the events leading to seizures. There will be close links between **ESR-2** at **CNR-IMM** and **ESR-4** at **UCAM** for the development, testing and refienement of new devices. This project is highly original since most classical approaches focus on electrophysiological signatures only (action potentials, field oscillations).
Finally, the information gained in this project will be used to refine theoretical approaches developed hereafter.
Gliomas account for ~80% of malignant brain tumors. The incidence of glioma is highest in Northern Europe and higher in males compared to females. Although important advances related to glioma prognosis, treatment response and treatment targets, results for patients currently diagnosed with glioblastoma are poor, indicating the need to pursue new approaches. UNIBA has recently demonstrated a new perspective on the role of water channel proteins, called aquaporins, in brain tumors, not necessarily associated with edema formation. In particular, UNIBA has demonstrated that the molecular dynamics of water channel protein (aquaporin-4, AQP4) assembly occurring at the plasma membrane of glioblastoma cells, and their link with actin cytoskeleton are important determinant in orienting glioma cells to potentiate its invasiveness potential or activate its apoptotic path.
*The developed technologies and approaches within **ASTROTECH** will be validated to study mechanisms beyond **glioma** proliferation and invasion, as well on **ischemia, epilepsy and depression**, providing knowledge and setting the scene for innovative diagnostic and therapeutic tools.* Accordingly, in **WP6, ESR-10**, **5**, **6** and **12**, respectively at **UNIBA, IEM, AMU** and **CSIC** will be also trained to perform electrophysiological measurements, electric/optical stimulation, recordings in pathophysiological animal models. Additionally, ESRs will be involved in the analysis of electrophysiological/biochemical/ and cell volume properties of astrocytes using pathological mouse models for focal cerebral ischemia, employing the middle cerebral artery occlusion (MCAO) model in mice, as well as mouse models for epilepsy and depression, where mice will be treated with an intrahippocampal injection of tetanus toxin and with an unpredictable chronic mild stress (UCMS) protocol, respectively.[43],[44]In ischemic injury we will mainly focus on the role ion channels/receptors, such as TRPV4 and water channels (AQP4), in edema formation, their role in chronic gliosis and NG2 cell differentiation towards reactive astrocytes and oligodendrocytes (**IEM, UNIBA**). At UNIBA, **ESR-10** will seek to investigate the role of AQP4 assembly occurring at the plasma membrane of glioma cells, and their link with actin cytoskeleton in the ASTROTECH model to determine its relevance in glioma cells proliferation and invasiveness.

A major originality of ***ASTROTECH*** is to include advanced mathematica and computational approaches to explore mechanisms *in silico* and generate predictions that can be tested experimentally with the network.

***ASTROTECH** will allow the emergence of "**computational glioscience",** which aims to adapt and develop theoretical and computational tools for the analysis of neuron-glial-blood vessels*. **In WP7**, **ESR-8** at **BCAM** and **ESR-7** at **AMU** will work on the design and study of in silico models of neuron-glial-blood vessel signaling. **BCAM** expertise is in the biophysics of neuron-glial interactions, with emphasis on reverse-engineering of intracellular calcium signaling, gliotransmission and astrocytic reactivity, in the context of learning and memory, and cortical activity in the healthy and diseased brain. **AMU** expertise lies on whole brain simulations with The Virtual Brain (TVB) platform (http://www.thevirtualbrain.org), which is an open access platform (included in the Human Brain Project), with an emphasis on translationable deliverables. Computational models provide mechanistic insights and testable predictions. Although detailed biophysical models developed to study brain stimulation at the microcircuit scale, provide useful information at the local scale, they need to be complemented with whole brain approaches. Large-scale models use coupled neural masses or neural fields, but they do include detailed modeling of astrocytes. TVB uses as inputs anatomical MRI and structural dMRI data of an individual to create a brain avatar. Generative models can produce brain-imaging signals such as EEG, MEG and BOLD, which enable exploring whole-brain dynamics *in silico* to obtain predictions. AMU is running a large multicentric clinical trial using TVB to improve neurosurgery outcome in patients with drug-resistant epilepsy. AMU has expanded TVB to the mouse brain (The Virtual Mouse Brain -TVMB), and recently provided the proof-of-concept of the validity of whole brain modeling for personalized medicine.[46]TVMB includes a pipeline to input diffusion MRI data and virtualize individual mouse brain. Each brain region (or node) includes a mathematical model that, integrated in time, describes the neural activity of that area. **ESR-7** at **AMU** in collaboration with ESR-8 at BCAM and with secondments at CODEMART will develop a mathematical model of the neuron-astrocyte-vascular unit to be incorporated into TVMB exploiting an existing experimental database of diffusion and resting state functional MRI of 19 mice.[46] We hypothesize that a model including astrocytes will improve the predictive power of the simulations.

1.2 Quality and innovative aspects of the training programme

- **Overview and content structure of the training**

ASTROTECH is offering an unprecedented combination of complementarities of skills, competences and know-hows among disciplines and sectors. The ESRs will be enrolled in PhD programmes from diverse disciplines such as

materials science, chemistry, engineering, physics, nanotechnology, neuroscience, computational neuroscience, as detailed in Tab. 1.2a. ASTROTECH complements other EU-Funded initiatives, within the ITN-call-FP7, such as NEUROGLIA, EDUGLIA or BrainTrain, that were focused on the use of model systems and research equipment. ASTROTECH is proposing both training on the most advanced and sophisticated research on technological development as well as on the most promising research approaches for the study of astrocytes in health and disease with possible translation to the clinic. ASTROTECH pioneers a training network of unprecedented breadth in terms of multidisciplinary and cutting-edge technologies and relies on strong synergies with potential for long-term structuring effects. The global dimension offered by ASTROTECH training program makes it uniquely suited to respond to challenges posed by a better understanding, monitoring and treatment of brain disorders. Among the innovative aspects of ASTROTECH, we highlight the *Internationalization and globalization* of the training action. The Coordinator Unit is also managing large initiatives such as the Graphene Flagship and the EU-KICK on Raw materials, AMU, via TVB, is an integral part of the Human Brain Project Flagship, thus providing ESRs with interaction non onlywith large EU-initiatives and empowering the possibility to relate with international excellence. ASTROTECH Beneficiaries and Partners have strong connection with Institutions overseas such as the University of Maryland (USA) and the University of Adelaide in Australia, (CNBP). The activities proposed are within the strategy proposed by the US-Italian Joint Commission on Advance Materials & Technologies and relies on results also supported by International Funding Agencies such as Air Force Office of Scientific Research[36]. Among actions to implement the peculiar aspect of internationalization and globalization is the network wide workshop organized by Partner NCURA. The latter will be a 2-day workshop on regarding topics such as U.S. research funding opportunities for non-U.S. organizations, applying for and managing U.S. federal research grants, sharing best practices in global research management and administration. The training proposed in the network event organized by Partner NCURA will tremendously increase the institution's capacity for internationalization, partnerships, and maximize the impact of research collaboration for ESRs. The intersectoral aspect of the ASTROTECH research approach relies on the strong competence and commitment of industrial participants in several fields related to the research programme: advanced materials for electronics (AVANZARE), light emitting devices (OPTOCEUTICS), computational tools (CODEMART), translation of research knowledge and technology into clinical practice (MEDTRONIC), as well as professional development, knowledge and leadership in research management and administration (NCURA).

The classical neurocentric vision has generated research results and products focused on neurons and founded disciplines such as Neural Engineering and Neural Interfacing. Thus, the most ambitious aspect for ASTROTECH network is in the training of young researchers to make them interdisciplinary and the next generation leaders experts in the disruptive field of Glial Engineering. European, Global research institutes and industry both need researchers with such multidisciplinary experience and a broad perspective, who are able to understand what the targeted end products are, when investigating novel materials or device configurations that interface with the brain. To achieve such ambitious goal the following specific actions and training elements will be implemented:

a) Realization of a personalized individual training via Individual Research Projects and Complementary Skills Training. **ASTROTECH** will offer a **large-scale** training program and research opportunities locally, within the Network and Network wide (including Internationalization and Globalization).

b) Beneficiary institutions will offer **Local Research** Training that will follow a "***training-through-research***" approach with a focus on individual research programmes in line with the activities planned in the WP and taking advantage of all the available expertise, resources and facilities of the hosting institution. The PhD programme (lectures, courses, seminaries, etc.) of the related graduate schools will complement the research Training and will ensure **high-quality academic training on scientific core and complementary skills**. The research and training programme **will naturally cover interdisciplinary aspects** demanded by the research and offered by know-how of PIs & Staff working in the **ASTROTECH** Consortium.

c) **Cross-fertilization of multidisciplinary aspect,** synchronization and integration **between local and network activity** will be promoted by i) open seminars to ASTROTECH members with streaming or webinar module. ii) **Trimestral web conference** with ESRs, PIs of the implementing WPs and Supervisory Board to check progress on Research & Training. iii) Online website and database to share knowledge, protocols with **on-line chat that will allow fast trouble shooting** when technical or theorical issues will be encountered by ERSs. The website will be updated with event list of mandatory & complementary Intra Network & Network Wide Event. iv) **Mutual help in bibliographic research.** Each ESR will be invited to continuously monitor the current literature, being updated on the most recent results, through the creation of an ***on-line journal club*****:** every 2 month he/she will report to the network (in the intranet section of the website) on published papers (outside the network), related to main topics of the project. This action will ensure continuous personal updating and correct training in bibliographic research means, as well as direct interactions and useful discussions on the research hot-topics with other researchers. We will create an online group by Doodle, or Tweelo to have a network-wide schedule and have the students to contribute to it automatically. The mailing list of the ETN will be created so that students can be directly supervised by the whole

partners of the ETN at their convenience and promoting synergies and real-time interactions. A Slack channel will be created for ESRs and PIs. This tool is particularly efficient for fast communication and exchanges.

d) **Development of network-wide training activities.** ASTROTECH will provide researchers with high quality **network-wide** training (e.g. organization of training and transfer of knowledge, workshops, summer schools, specialized sessions at conferences). Given the high inter-disciplinary and inter-sectorial nature of ASTROTECH initiative, we will have one network-wide training event every **4 months**. We will organise summer or winter schools and thematic workshop and periodic meetings (**every 8 month**) in a way that **three** events are well planned over the year time. Thematic workshops will *be on* ***technical topics and on soft skills*** and will be held in conjunction with the planned summer/winter schools or yearly meetings. Each event will be coherently integrated in the wider scope of the research implementation and will have a practical hands-on approach focussing on topics that parallel the evolution of the research programme. Network-wide events will take place at different beneficiary premises and will be organized by hosting institution with the **active participation of ESRs in the organization and coordination** of related activities and the supervision of the Supervisory Board. Lectures, courses and seminars held as webinars or e-learning modules, and the documentation related to network-wide events will be available in the Online database. An ASTROTECH ***YouTube Channel will be opened where, we will regularly update videos from meetings and conferencing directly linked with activities of the ETN.***

e) **ASTROTECH** will provide a peculiar set of **transferable skills including** local training opportunities skills through local PhD programmes and dedicated Workshops within network-wide activities organized by the consortium Beneficiaries OPTO and AVA and partners MEDTRONIC, NCURA and CODEMART. These workshops will be related to the private sector expertise and know-how and on transferable skills including research funding development, IPR and patent management and entrepreneurship, in the context of industrial environments. The complementary skills training will be instrumental to the overall research & training programme. **A**mong others **transferable skills** dedicated network wide event will be on:

(i) Ethics in Glial Engineering. There are a wide array of ethical issues that relate to ASTROTECH technologies and their applications on diagnostics & therapy of neurological diseases, which include informed consent, research ethics, the conundrum that needs to be addressed when altering the brain such as the issues of autonomy and free beneficence and social justice. Targeted delivery and organic-optoelectronic-neural interfaced applications also raise complex ethical problems. The goal is to heighten awareness on ethical issues, legal/social aspects, and to create an environment for the socially acceptable and economically successful development of **Glioelectronic, Gliophotonic** and **Glial interface** medicine research, diagnostic and therapy.

ii) ASTROTECH ESRs & Consortium will benefit of the expertise by **Medtronic** Partner team which specializes in generating, collecting and applying clinical and economic evidence to optimize health and improve outcomes. The workshop organized by Medtronic, with cooperation of CNR- ESRs aims to provide training on performing **Study Support** that helps generate the high-quality, reliable evidence needed to serve patients, physicians, and stakeholders. The workshop will aim at describing how to translate technologies and approaches into effective clinical solutions including all regulatory aspects for translation of technologies to clinical research.

iii) **Management and Exploitation**. In full collaboration with our industrial partners, ASTROTECH will offer specialized Workshops on Project Management, IP fundamentals, models and procedure to generate a technology start-up, and analyses of start-up Business Models. In addition to providing the fundamentals of entrepreneurship, the workshops will analyse in depth practical cases of technology-based start-up companies funded by ASTROTECH partners, like, e.g., OPTO and AVA.

iv) **Internationalization** & **Globalization**. The opportunities for trans-European networking in research and innovation will be covered in a workshop organized in collaboration with the Partner National Council of University Research Administrators (NCURA, USA). A *grant-writing competition* is planned, with the proposal, preparation and real submission of specific research projects (either on a European or international funding mechanism) related to the ASTROTECH main framework: ESRs will actively collaborate in setting-up proposals, with help from their local supervisors and administrative teams. In agreement with **Open Science modus operandi,** ESRs in ASTROTECH will be challenged and trained to disseminate, share, explore and maximize the impact of their research and to collaborate with the global scientific community. The digital tool available as well as instruction and expertise of NCURA will be instrumental to facilitate global research collaboration of ESRs. In addition to Ethics, training on **personal skills and attitudes,** such as research integrity, Open science, **honesty, teamwork, working under pressure, self-motivation,** gender issues, presentation skills, story-telling, communication and outreach will be delivered during the Network Wide workshop implementation.

vi) Editorial skills: Christophe Bernard is in Chief of eNeuron, and will organize a session on how to write and review papers, as well as on Editorial skills demanded to manage a scientific jornal.

f) Invitation of visiting researchers: Visiting researcher at Beneficiary site will be invited within **the training period as leading experts in different disciplines converging in ASTROTECH.** Anita Mahadevan-Jansen, Vanderbilt University, that pioneered infrared neural stimulation, Prof Wolfgang Losert, University of Maryland,

expert in analysis tool, Prof Mark Hutchinson, Director of CNBP, University of Adelaide, expert in Biophotonics, Prof Alfonso Araque, expert in glial biology, Prof David Spray, Albert Einstein College, expert on astrocytes physiology, Mahmood Amiry-Moghaddam, expert on water channels and brain Edema, Prof. Ivan Soltesz (Stanford) expert in optogenetic control of seizures, Prof. Viktor Jirsa co-inventor of TVB.

g) Each recruited researcher will establish, together with her/his personal supervisor(s) in the host organization/s, **a personal Career Development Plan**. PCDP will be an open document, reflect data reported in the proposal and in the Grant agreement and will include: i)the specific research objective of each ESR; ii)the research activities correlated and the specific tasks the researcher's training skills and career needs; iii) planning for publications and participation in conferences; iv) the supervisor and co-supervisor mentoring arrangements and career objectives and guidance; v) The list of visits and secondments to other partners. vi) The list of conference and training events ESR plan to participate; vii) Soft skills ESR will be trained including those provided by during PhD courses.

h) Secondments. Particular attention will be paid that all researchers have exposure via secondments to other research and private sectors environments, and at least in one other laboratory of ASTROTECH.Multidisciplinarity and transdisciplinary expertise will be gained by ESRS that will be exposed to all the aspect of the value chain for a technology intended for brain Interface: Basic Research in vitro, ex-vivo, in situ, in humans, and regulatory. International aspects are considered in the plan secondments as mobility will occur also Overseas with US collaborator UMD.

Table 1.2a. Recruitment Deliverables per Beneficiary

RP= Recruiting Participant; PhD Awarding Entities= (PhDAwE); Start m=Start month; d=Duration

ESR No.	Participant	PhDAwE	Start m	D	Project Title
1. ESR-CNR-ISOF	CNR	UNIBO	9	36	Glial interface impact on astrocytes physiology and validation of Glioelectronic devices for stimulation and read-out of astrocytes *in vitro*
2. ESR-CNR-IMM	CNR	UNIBO	7	36	Design, fabrication and characterization of Glioelectronic devices for stimulation and read-out of astrocytes *in vitro and in vivo*
3. ESR-CNR-IPCB	CNR	FED II	7	36	Design and fabrication of micro/nano structured platforms as organic polymers to study in neural cells response *in vitro*
4. ESR-UCAM	UCAM	UCAM	7	36	Development of electrophysiology devices for the *in vitro* and *in vivo* detection of electrical activity of astrocytes
5. ESR-IEM	IEM	CUNI	12	36	Electrophysiological recordings on astrocytes/glial cells by glioelectronic device and identification of astrocytes functions *ex vivo*
6. ESR-AMU	AMU	AMU	10	36	Disruption of K^+ clearance and metabolic processes in astrocytes at seizure onset
7. ESR-AMU	AMU	AMU	12	36	Integration of astrocytes function in computational model for the Neuron-Glial-Vascular Unit
8. ESR-BCAM	BCAM	UPV/EHU	12	36	Computational glioscience approach of volume signaling transmission in the in the Neuron-Glial-Vascular Unit in TVB
9. ESR-INEB	INEB	UPORTO	9	36	Astrocytic Tissue Engineered Models – Dissecting the role of the extracellular matrix mechanical properties towards the astrocytes' phenotype
10. ESR-UNIBA	UNIBA	UNIBA	12	36	Monitoring of astroglial water channel proteins structure and function
11. ESR-IIT	IIT-CNST	POLIMI	8	36	Photoceutic devices for gene-less, spatially and temporally selective excitation of astrocytes
12. ESR-CSIC	CSIC	UAM	8	36	Modulation of astrocyte-neuron signalling properties by optogenetic and photonic devices in control and a depression mouse model
13. ESR-AVA	AVA	UR	7	36	Advanced nanomaterials for developing glioectronic device
14. ESR-OPTO	OPTO	UCOPEN	12	36	Neurostimulation with non-invasive light source
15. ESR-OPTO	OPTO	DTU	12	36	Light induced neurostimulation with measurements of the modulation of neural activity and astrocytes physiology
Total 15				540	

Table 1.2 b Main Network-Wide Training Events, Conferences and Contribution of Beneficiaries

	Main Training Events & Conferences	ECTS	Lead Institution	Month
1	**Kick-off meeting (2 days). Day 1 - Overview of the project goals – Presentation of beneficiaries and partners – Consortium Agreement ratification – Appointment of boards – Financial issues-** ASTROTECH selection procedures, documentation to be submitted, evaluation rules.	-	CNR	M3
2	**Day 1-2: Orientation workshop for ESRs (3 days)**: **School** on Pathological Models and Astrocyte role in Edema Formation, **Day 3:** Transferable skills conflict resolution, mentoring, presentation/lecturing/communication skills	-	IEM	M9
3	**Day 1-2: School** on Glioelectronic device development fabrication and validation in vitro, ex vivo. **Day 3- Practical course; Day 4 - Transferable skills**: **regulation and ethics & research integrity**	3	UCAM	M12
4	**Day 1: First year full meeting; presentation of individual project progress. Day 2-3: NCURA Workshop Day 4 - Transferable skills**: grant proposal writing; scientific writing, EU Research Funding policies and overview of the main funding programmes; International and trans European funding opportunities. MEDTRONIC- Regulatory aspects for translation of technologies to clinical research	3	CNR/ NCURA MEDTRONIC	M16
5	**Day 1-2: School** on Gliophotonic device and optogenetics approaches development and validation in vitro, ex vivo **D Day 3: Practical course; Transferable skills**: Gender issues inclusivity ethnical diversity and sexual orientation in science and research.	3	IIT	M20
6	**Day 1-3: School** on Gliomaterials interfaces for in vitro-like -in vivo healthy and gliotic astrocytes model; **Transferable skills:** Techonological approaches on astrocytes sensing and imaging. Cell modelling.	3	INEB	M24
7	**Day 1**: **Second year full meeting;** Presentation of individual projects progress. Mid-term review meeting preparation. **Day 2:** Transferable skills: Open access journals, Editorial skills, editorial management, the review	2	AMU/CODE	M28

	process: rights and policies, conflicts of interest. Day 3: **Mid-term review meeting**			
8	**Day 1-3: School** "Fundamentals of material printing technologies and smart composites integration in tools for neural cell cultures". **Day 4 - Transferable skills**: Career Management, Entrepreneurial skills (leadership, lateral thinking).	3	AVA	M32
9	**Day 1-2: Technical Workshop** on Validation in vivo of electronic, optogenetics, photonic astrotechnologies; **Day 3 - Transferable skills:** Ethical issues: animal use in neuroscience and bioethics in therapeutic application: protection of individuals from fundamental investigation to clinical research.	2	CSIC	M36
10	**Day 1-2: School** on photonic device for low-invasive brain stimulation. **Day 3: Transferable skills:** Scientific communication of results, how to write an article, how to prepare a pitch	3	OPTO	M40
11	**Day 1-2: School** on materials and techniques for sensing ion channels and water channel biophysics **Day 3: Transferable skills:** team building, stress management, problem solving	2	UNIBA	M44
12	Day 1-4: School on Computational Glioscience and Glioelectronics. Day 5: Transferable skills: Conflict resolution and building resilience techniques / LGBT+ in STEM / Leadership skills	2	BCAM/CODE	M48
13	**Day 1-2: ASTROTECH Final Open Conference on Glial Engineering. Multi-INT network day** **Final meeting: overview of results;**	-	CNR	M48

- **Role of non-academic sector in the training programme**

The private sector, represented by the presence of **5** private entities (2 as Beneficiaries and 3 as partners), is actively and deeply involved in ASTROTECH. AVA and OPTO as beneficiaries will not only train researchers locally on specific research and training topics, such as nanostructured devices and optoelectronics, photonic device design and fabrication, but they will also be very active in hosting ESRs, for a limited period of time, from **all** academic partners. Private secors Beneficiaries and Partners will update ESRs with the most advanced technological platforms and techniques, industrial research methods, applied research constraints, making them familiar with an entrepreneurial context. **OPTO, AVA** will each host an ESR, giving them the opportunity to complete PhD course in an entrepreneurial context. Partners will also be very active: **CODEMART will host secondments ESRs on** Computational studies and software development integration in a private company context. **MEDTRONIC** will train ESRs on clinical translation, supporting the development of clinical studies as well as provide operational and analytical support. **NCURA** will train European ESRs on topics as **funding opportunities and proposal development, research capacity building, and partnership development overseas** to provide a global dimension that will maximize the impact of **ASTROTECH** training network, ESRs career development, and market applicability of the research result. The added value of the private sector Beneficiaries relates to essentially four aspects:1) direct access to state-of-the-art know-how, technologies and best practices in material science and biophotonics; 2) bridge the world of industry and academia; 3) hosting secondments; and 4) Organization of Technical and complementary skills workshops regarding project management, technology transfer methodologies, IPR principles and best practices, and other peculiar aspects (see above). The training capacity of the non-academic partners is also evident by oinformations reported in Partners Organization Table in B2 Section.

1.3 Quality of the supervision

- **Qualifications and supervision experience of supervisors**

The full scientific profile of ASTROTECH supervisors is detailed in Sec. 5. The persons in charge of supervision and co-supervisors of ESRs are fully qualified and experienced on tutoring and training at academic, research, and private sector level. The overall number of students trained is larger than 120. Supervisors and co-supervisor at Beneficiaries and Partner sites are appointed as full or associate or adjunct professors (G. Malliaras, C. Bernard, P. Nicchia, A.P. Pego, V. Benfenati, Ursino, Capri, Calvaresi, Ambrosio, Lanzanoi) at the Universities or senior scientist (Benfenati, Maiolo, Guarino, Pego, Antognazza, de Pittà, Perea) and Directors of Departments (Anderova, Malliaras) as well as CEO and funders of private sector (J.Gomez; Carstensen). They have already participated in several ITNs, and they are also part of committee in PhD schools and programmes. They are also experienced in the organization of training events such as workshops and summer schools, as part of intranetwork or network wide activities (see session 5). **Local supervisors** have an internationally recognized experience and have a solid track record (**see Tab. Part 5**). The mandatory role of the supervisor will be: i) to assist the integration at the hosting research institution, ii) to monitor training and research activities, iii) to ensure proper conditions to carry out the planned research work, and iv) to ensure enrollment in PhD programs, according to national and/or local regulations. Partner institutions will offer PhD enrolment to ESRs hosted by non-academic beneficiaries in line with agreements, as reported in the letters of commitment. ASTROTECH will integrate postgraduate courses offered locally to ESRs through an analysis of local programmes, carried out by the Training Tutoring Board (TTB, see below), at the beginning of the ESR activity, and by drafting a **joint syllabus**, which will allow ESRs to select complementary training activities according to their needs. Supervisors will dedicate adequate time to provide appropriate support to the training of ESRs and for the necessary progress and feedback mechanisms after review procedures by meeting on regular basis. The supervisor will inform the TTB every **six months** about the progress of ESR activities.

- **Quality of the joint supervision arrangements**

A joint supervision of each of the ESRs will be realized by appointing a **co-supervisor**, from academic and non-academic researchers on the basis of multidisciplinary, intersectoral expertise and **gender-balance** criteria with

respect to that of the supervisor. Each supervisor and co-supervisor will share information on the progress on ESR research and training activities with the TTB on a six months basis at Workshop meetings and by electronic means.

1.4 Quality of the proposed interaction between the participating organizations

- **Contribution of all participating organizations to the research and training programme.**

The Beneficiaries and partners of the Project have been selected by CU on the basis of complementarieties of knowledges, multidisciplinary of the conceived action, and intersectionality needs for implementing ASTROTECH vision, research training and innovation activities. The contribution of each beneficiary to the research and training WPs, while the interaction among beneficiaries and partners is described in section 1.2 and in the Research implementation (see Tab1.3). All participants (beneficiaries and partners) will contribute to all

TAB 1.3 – ESR interaction: S =secondement, 1…8 for WP number

ESR No.	ESR1	ESR2	ESR 3	ESR4	ESR5	ESR6	ESR7	ESR8	ESR9	ESR1 0	ESR1 1	ESR1 2	ESR1 3	ESR1 4	ESR1 5	Partner
ESR-1-CNR		2			S	2		7-S	4	3-4	3	3		3		CODE
ESR-2-CNR	2										5	5	5-S	5		MEDTRO
ESR-3-CNR	4				4				4-S	S			S			FED II
ESR-4-UCAM		2-5			2	5-S		S				5	2-S			MEDTRO
ESR-5-IEM	4-2-S	2-6	4	2		2		S		4		6			6	ZUH
ESR-6-AMU	S	5-6		5-6-S	6							5	5	5		CODE
ESR-7-AMU	S			S				7-S								CODE
ESR-8-BCAM	S						7			S						CODE
ESR-9-INEB	4		4-6-S		4					4-6-S						AVA
ESR-10-UNIBA	3-4-7		4-6			7		7	3-9-S			3		3-S		UMD
ESR-11-IIT	3-S	5	3	S								3-S	S		5-S	UPCH
ESR-12-CSIC	3-S	5-6		5-6	6	5				3	3-5-S		5	3-5	5-6-S	
ESR-13-AVA		2,5-S	S	2-5-S		5					5	5		5	5	
ESR-14-OPTO	3	5				5				3-S	5	3-5-S	5		5	ZUH
ESR-15-OPTO	S	5-6		6	6	5-S					5	5-6	5	5		ZUH

aspects of ASTROTECH, participating in WPs activities, hosting secondments, offering **scientific** (**research**) training opportunities, combined with ESR enrolment in PhD (**academic**) enrolment and transferable skills (**soft skills**) and organising network-wide events. The strongly multidisciplinary nature of ASTROTECH requires the commitment of ESRs to interdisciplinary and intersectoral secondments that will be offered by all institutions and private partners. ASTROTECH will foster collaborative work among ESRs and institutions on several aspects, from the exchange of expertise, protocols and know-how to the realization of joint experiments during secondments. The research WPs involve all ESRs that will develop their work at Beneficiary sites having access to a variety of local dedicated research facilities, and infrastructures, from large clean room for device fabrication to microscopy to animal facility and big data analysis see table 3.3. All beneficiaries and partners will organize a network-wide event at each respective site (**Tab. 1.2b**). ESRs working in the same WPs will be involved in the organization of the network-wide events.

- **Synergies between participating organizations.**

The overall program reflects existing and planned collaboration between partners on training and research topics of the proposal, as shown by events organized in the recent past by the coordinator and beneficiaries of the ASTROTECH Consortium: 1)Workshop at the 10th FENS forum for European Neuroscience, July 2016: , chaired by: **V. Benfenati,** invited speaker belonging to ASTROTECH Consortium: **C. Bernard**. 2) Workshop at 12th FENS forum for European Neuroscience, July 2020, chaired by: **V. Benfenati**, invited speaker from ASTROTECH Consortium: **A.P. Pego, M. de Pittà**. 3) Workshop at BMES meeting, Philadelphia, October 2019, chaired by **L. Maiolo**, invited speaker from ASTROTECH **V. Benfenati** 4) Biophysics Program AFOSR meeting, chaired by Dr Sofi Bin-Salamon, May 2019, Invited **V. Benfenati, G.P. Nicchia, V. Guarino, A. Pego, A. Convertino.** SPYWATCH Summer School on Water Channels and Ion Channels Biophysics, Chaired **G.P Nicchia**, Invited Speaker **V. Benfenati** 5) Workshop at Italian Embassy, "How diplomacy can help research", December 2018, chaired by: L. Ambrosio (CNR-IPCB), invited **V. Benfenati, L. Maiolo.** Consortium members have already collaborated within previous National, EU-supported as well as US-Funded projects in fields related to ASTROTECH (among others, ITNs OLIMPIA, ASTROMAT, 3D NEUROGLIA, ASTRONIR, FIRB-Miur, M-Gate, etc., see Part 5)[47] or collaborate on ASTROTECH research topics as proved by joint publications[2, 18, 21-27,35,36]. These different competences, merged within all WPs, will advance the state-of-the-art in existing discipline such as Neural Engineering, Organic Bioelectronic, Neurosciences, both experimental and theoretical, and Glial pathophysiology,

Glial Biology, Glial Physiology allowing ESRs to obtain the background necessary to develop successful career in academina or in the private sector. The existing synergies within the consortium will be further consolidated through i) collaborations within and across WPs, ii) knowledge flow among partners, online database, on line seminars, documents sharing, iii) secondments, iv) analyses and discussion of data through web calls, meetings, and deliverables preparation, v) preparation and submission of joint publications, vi) joint organization of intra network and network wide events, and vii) joint participations to international conferences and schools (e.g. GRCs), covering multidisciplinary aspects of ASTROTECH. In addition, collaboration with other ITNs will be pursued. We will contact ITNs dealing with complimentary topics, such as M-Gate (Bernard is a beneficiary).

- **Exposure of recruited researchers to different (research) environments, and the complementarity thereof.**

ESRs will benefit from the variety of competences related to the multidisciplinary nature of **ASTROTECH**, ranging from nanomaterials synthesis and characterization, device engineering and fabrication techniques, spectroscopy, optics and photonics, to different aspects of neuroscience including biotechnology, optogenetics neuroscience, neurophysiology, computational neuroscience, to animal handling, ethics, as well as translation to the clinic. The ESRs will also benefit from exposure to intersectoral environments, providing insight in both academic and entrepreneurial aspects of scientific research. Secondments and collaborative research work will be the primary tools to promote cross-fertilization and strong interaction of enrolled ESRs among Beneficiary and partners of ASTROTECH networks. Joint organization and participation to network-wide events will also ensure exposure of the ESRs to the complementarity of research fields, disciplines and sectors converging in the ASTROTECH consortium.

2. Impact

2.1 Enhancing the career perspectives and employability of researchers and contribution to their skills development.

ASTROTECH training will shed a new light on the role of glial cells in the brain in physio-pathological conditions. This, in turn, will maximize ESR carrier opportunities both in academic and industrial institutions. Neuroscience and specifically Glial Engineering is expected to gain potential breakthrough in medicine (developing novel treatment in severe pathologies such as depression, glioma, epilepsy), in engineering (providing non-invasive neural interface or ultra-flexible long-term implants) as well as biology (3D nano-scaffold and diagnostic tools) up to whole brain modelling for personalized medicine. ASTROTECH offers a wide network of companies and public institutions in Europe with strong collaborations with overseas partners (in the US and Australia). The most important aspects of impact are listed below (see Tab2.1).

Table 2.1 ASTROTECH Impact Summary

Challenge	Impact	Indicator/quantifier	Barriers/obstacles
Providing excellence in glioscience	Find novel tools for explaining brain functions and dysfunction	N. of published papers and invited talk	Acceptance of glioscience from neuroscientist
Providing transferable soft skills	Increase ESR communication, project management, Lateral thinking, etc.	N. of hand-on training, Self-evaluation tests, Pitch contest, etc.	Reluctance by ESR in recognizing the value of soft skills
Employability in R&D	Adding disruptive research ideas in the comprehension of brain functions	N. of ESR employed in academy in the next 5 years	None
Employability in private sector	Offering new diagnostic tools in glioma, epilepsy, etc.	N. of ESR employed in industry in the next 5 years	Large time to market of glio-products
Internationalization	Establish valuable networks with countries overseas	N. of established collaborations with Non-EU partners, N. of joint projects	Lack of specific funds, difficulties in task scheduling
Good communication strategy of project outcomes	Create the conditions for increasing the community of scientists and stakeholders	N. of stakeholders involved in side activities, N. of website accesses, N. companies interested in ASTROTECH results	Delay in projects outcomes, poor involvement of industries, no opening to the public

2.2 Contribution to structuring doctoral/early-stage research training at the European level and to strengthening European innovation capacity, including the potential for:

ASTROTECH will adhere to the **European Principles for Innovative Doctoral Training**, offering advanced training, maximizing the career perspective of ESR in multiples disciplines. ASTROTECH research and training programme has the intent of preparing ESR to the challenging and highly competitive working scenario of the next few years. To this purpose, ASTROTECH will insist on providing outstanding research topic and improving ESR personal skills, enhancing **stronger links between the European Research Area (ERA) and the European Higher Education Area (EHEA),** supporting the knowledge triangle between research, innovation and education.

- **Meaningful contribution of the non-academic sector to the doctoral / research training (as appropriate to the implementation mode and research field).**

The private sector, which includes two beneficiaries and three partners, represents another essential pillar of ASTROTECH, removing barriers between university and industry, to train the next generation of scientists to both scientific innovation and marketing.

ASTROTECH is designed to create such work conditions and offers chances of **strengthening Europe's human**

capital base in R&I with a new generation of more entrepreneurial and highly-skilled early career researchers.
In particular, non-academic partners will impact on the following aspects: i) Normative procedures to protect new materials, devices, prototypes, (AVANZARE, OPTOCEUTICS). MEDTRONIC will support ASTROTECH participants to evaluate a proper path for each possible medical device arising from the research activities of the project, helping in defying the steps and the studies to be pursued to obtain an international certification (through EMEA or FDA); ii) Open-source software for customized biomedical products (CODEMART); iii)Funding development and technology transfer issues (NCURA);; iv) Development of clinical studies and providing operational and analytical support (MEDTRONIC);

2.3 Quality of the proposed measures to exploit and disseminate the results

All ASTROTECH relevant results will be either disseminated and/or exploited, as widely and effectively as possible, with the involvement of all the Organizations concerned and in full compliance with the objectives underpinning the MSCA 2018-2020 Work Programme. In this respect, CNR will coordinate dissemination and communication actions and exploitation of results, through the actions of the **Dissemination** and **Exploitation Supervisory Board**. These committees will follow the initiatives of each participant according both to the Dissemination and Communication Plan and to the Exploitation Plan, that will be drafted at the beginning of the project (M4). Non-academic beneficiaries and partners will be crucial in these communication and exploitation campaign and they will support participants in measuring results in terms of number of publications on high-impact journals, provisional applications, patents, further agreements with private companies interested in project outcomes, additional funds obtained with collateral projects.

- **Dissemination of the research results**

In order to maximize the impact of ASTROTECH, we will identify Key Results as well as the Target Audiences that may make use of results (dissemination actions) and groups and entities that are currently making use (Potential End Users) of these results (exploitation actions). We will also develop the strategy to use/protect/share these results. This will constitute the starting point to create an innovative management of the results.
According to the last report about the emerging technologies and their hype cycle (Gartner Research, 2018), brain computer interfaces are now entering in the peak of inflated expectations, while the proposed supradisciplinary field of **Glial Engineering** doesn't exist yet. We anticipate a surge of publications in this field in the near future. ASTROTECH will be a main driver of this novel approach to brain function and dysfunction, not only in the academic world but also to stakeholders involved in smart brain implants and companies devoted to bio-devices implementation and certification. ASTROTECH will disseminate intermediate and final outcomes to a large audience, with the intent of creating a new community of scientists and industrial partners. All participants will be involved in the dissemination activities according to their inclinations and expertise as envisaged in the provisions of the Consortium Agreement. In particular, dissemination actions will include: **1) Presentations at international meeting and conferences.** ESR will to the main European events (e.g. E-MRS, materials.it, FENS Forum). Moreover, due to the strong ties with several partners in USA, the participation of ESR to trans-European meetings (MRS, SPIE, SfN, IBRO) will be strongly encouraged either with poster or oral presentations. **2) Organization of a final open conference on Glial Engineering** to which appropriate advertising will be devoted, so as to involve as many stakeholders as possible. **3) Publication in international, peer reviewed high-impact journals of each** ESR with the target of 3-5 papers in journals specialized in nanotechnology (Nature Nanotech., Nanoletters, Nanoscale, Nanotechnology), advanced materials (Adv. Mater., Nature Mater., Chem. Mater., J. Mater. Chem.,) and advanced devices (Org. Electr., IEEE Transactions, Scientific Reports), in chemistry (JACS, Angew. Chem.), biology (PloS one, J. Biol. Chem.) and computational biology/neuroscience (PloSComput. Biol., Scientific Reports, Nature Neuroscience). **4) Publication of Open Research Data** – direct result of the activities carried out within the Project – according to the ASTROTECH Data Management Plan (see session 3.2). **5) Creating advertisement material for spreading news and results on social media**. ESRs should prepare video, vlog and multimedia contents for attracting stakeholders on the most popular social networks (Linkedin, Research-Gate, Twitter, Instagram, Youtube, Facebook). ESR will be awarded for their achievements also in dissemination and public engagement. **6) Organization and management of ASTROTECH website and national online content**. CNR, as coordinator, will be in charge for publishing and managing ASTROTECH website, as head of SB that control DSB.

- **Exploitation of results and intellectual property**

The research outcomes of ASTROTECH will be screened (Section 3.1), according to the exploitation plan envisaged in the Consortium Agreement and in its Attachments (n. 9 Specific Software provisions and n. X, Exploitation Plan), also evaluating IPR opportunities. Indeed, results coming from ASTROTECH could have a disruptive impact in many different fields. In particular, participants may assess the exploitation of new materials and synthesis methods (AVA, CNR), the fabrication of innovative devices for in vitro fast diagnostics (e.g. smart petri for astrocytes growth or disease diagnosis) (UCAM, IIT, OPTO, CNR, IEM), the implementation of techniques for discriminating glial cells functions (e.g. glioma vs healthy cells) (CNR, INEB, CSIC), the design and manufacturing of glial or brain flexible implants (CNR, UCAM), the fabrication of innovative tools for gliophotonics (IIT, UNIBA, OPTO), the

implementation of advanced imaging techniques (UNIBA, CSIC, IEM), the standardisation of software methods for acquiring and analysing data (AMU, BCAM, CODEMART). MEDTRONIC will support ASTROTECH participants to evaluate a proper path for each possible medical device arising from the research activities of the project, helping in defining the steps and the studies to be pursued to obtain an international certification (through EMEA or FDA). The Exploitation Plan will be designed to optimize and spread commercial applications of ASTROTECH results, also for the purpose of obtaining further agreements with private companies interested in project outcomes, and additional funds thanks to collateral projects. In this respect, project goals will be exploited by Beneficiaries, Partners and by the network of the ESRs – even after the end of the project activities – with the aim of maximising impact both of the research performed and of training programme provided. These will include measures to improve public awareness of ASTROTECH issues, which will reshape the underlying market, to transfer related technologies and to commercially exploit research results. Notably, as a part of the training process, ESRs will be involved in linking academic and private institutions within ASTROTECH network, driving the valorisation process and generating knowledge for the development of new research activities in the field. In this respect, intensive specific training on exploitation, open science, open innovation models and IPR strategies, will be provided to the ESRs through local courses and in network-wide schools and workshops.

Potential IPRs emerging from ASTROTECH include provisional applications, patents on materials, devices and software licenses. In this respect, CNR owns a good expertise in patent analysis and adaptation using a well-known methodology called TRIZ. This technique exploits lateral thinking, creative approach and legal competences to maximize the results from an innovation idea into a valuable product. TRIZ is a method used by all the leading companies in the world; it will be disseminated within ASTROTECH. To this end, part of this expertise will be delivered to ESRs via a specific training session. Moreover, each participant will be supported by the local IPR team both for highlighting the suitable claims and for creating a joint documentation (where needed) according to the policies described in the Consortium Agreement. In order to fully exploit the IPR potential underlying ASTROTECH, all Beneficiaries and Partners will be required to provide advance communication to the dissemination network (publications, presentations, etc.) of project results. As for the details on IPR management matters, are discussed in the Section 3.2 of the action focuses on **Intellectual Property Right and Knowledge Issues.**

2.4 Quality of the proposed measures to communicate the activities to different target audience

- **Communication and public engagement strategy**

The communication strategy of ASTROTECH will be coordinated by the DSB, with the purpose of spreading scientific knowledge and creating wider networks with other scientists and companies. ASTROTECH will pursue a specific communication towards students and the public. According to the European Charter for Researchers guidelines all the participants in ASTROTECH will be invited to successfully support project communication and public engagement activities. To this purpose, the training session devoted to the development of specific soft skills such as communication, leadership, creativity will be provided in the first year of the project. Communication activities will involve different audience such as general public, external scientists and professionals, patients and clinicians, and industrial stakeholders. **DSB** will define a Communication guideline that will be delivered at month 6 (D8.2, M8), with rules and suggestions for the messages such as: banned use of aggressive language, avoidance any terminology that could result offensive for any reason including gender, religion, race, sexual orientation, etc.; storytelling stile of the communication form. Initiatives for the general public are:

Gadgets (stickers, banners, posters), Press releases, Easy-to-use visual contents in project and local websites, ASTROTECH Website, Brochure/flyers/posters including all project infos, Media: Tv, radio, press, EU tools e.g. Cordis Wire, Internet-based professional networks (LinkedIn, ResearchGate), Internet-based social media (Facebook, Twitter, Instagram), ASTROMed, Open Days/MSC Project Open Doors/European Research night, EC campaigns/Marie Curie Alumni Association, Video channels (ASTROTECH Youtube, Vimeo, University channels), Meetup on potential industrial technologies , Communication at B2B events and meeting with venture capitalists

The goal of the communication strategy will be: Create a visual identity of the project, Awareness and deliver overall information on ASTROTECH objectives, progress and results and main impacts. Improving the public understanding of science. Networking with professionals and communitiesDirect engagement of researchers with the public.

Favoring a critical thinking of General public and students towards the topic of brain and its function/dysfunction, creating a critical mass of young researcher of ASTROTECH topics; Creating favorable conditions for the flourish of ASTROTECH foreseen industrial activities; Improving the ripeness of the technologies and tools developed in ASTROTECH to evaluate potential market of interest

3. Quality and Efficiency of the Implementation

3.1 Coherence and effectiveness of the work plan

Table 3.1 d Individual Research Projects M=month date m=month time

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
1:ESR-CNR-ISOF	CNR	Y	M9	36	D2.3, D3.1, D4.2, D7.2

Project Title and Work Packages to which it is related: Glial interface impact on astrocytes physiology and validation of Glioelectronic devices for stimulation and read-out of astrocytes in vitro **(WP2-WP4) Supervisors**: **Valentina Benfenati (Neuroscience)**, **Lorenzo Tommasi (Mathemathics), Marco Caprini (UNIBO)** (Molecular neuroscience), **Emanuele Treossi** (Chemistry Material Science)

Objectives: A) To identify the impact of biomaterials and bioelectronic interface on viability and the expression and function of ion channels by viability assay, time-lapse confocal imaging, immunofluorescence, patch clamp and calcium imaging **B)** Validation of AuSi/Nws, organic biolectronic devices for electrical stimulation and read-out in vitro on astrocytes and co-cultures. C) Identification of unprecedented astrocytes electrical signatures. **D)** Analyses of electrophysiological signal by means of new computational tools.

Expected Results: A) Identification the impact of glial interface and devices on the functional properties of astrocytes in primary cultures and co-culture (**D 2.2**) B) Validation of glioelectronic devices for electrical stimulation and read-out in vitro. C)Identification of unprecedented astrocytes electrical signatures (**D2.3**). D) Validation of optoceutic Device for photostimulation of astrocytes **D3.1**. E) Characterization of biological properties of gliomaterials interface (**D4. 2**) F) Analyses of electrophysiological signal by means of new computational tools **D7.1** G) Dissemination of results through publications (3) in international journals, participation to one international conference/workshop per year, participation in ASTROTECH workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on neurobiology, glial biology and physiology; preparation and manipulation of primary astrocytes and neuron co-cultures; ethical aspects; cell growth, viability and cell apoptotic assays; optical spectroscopy and confocal microscopy; time lapse microscopy, immunocytochemistry and immunofluorescence; calcium imaging, patch-clamp, device fabrication and characterization; comprehensive training on transferable skills. Data analyses and computation.

Planned secondments: UNIBO- M. Caprini, preparation and maintainance of primay cells (M10, 1m), IIT– M. R. Antognazza (M18, 1 month): Interfacing organic optoelectronic device with astroglial cells. UMD (M24, 2 month): defining actin dynamics in astrocytes. IEM (M36, 3 months, electrophysiology ex vivo, pathological mice models. CODEMA (M40,0,5month computational analyses and software development. MEDTRO (M42, 0,5 month).

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Cellular and Molecular Biology, Dept. of Pharmacy and Biotechnologies, University of Bologna, Italy, Nanoscience and Nanotechnology University of Bologna.

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
2: ESR-CNR-IMM	**CNR**	**Y**	**M7**	**36**	**D 2.2, D5.1, D6.2, D6.3**

Project Title and Work Packages to which it is related: Design, fabrication and characterization of Glioelectronic devices for stimulation and read-out of astrocytes *in vitro* and *in vivo* (**WP2-WP5). Supervisors**: **Luca Maiolo**, **Annalisa Convertino** (Advanced materials for neural interfaces)**,** Davide Polese (ad hoc electronics for bio-interfaces, data analysis), M. Usino (PhD supervision)

Objectives: A) To identify the best electromechanical properties of smart materials like silicon nanowires disordered forest to efficiently interface astrocytes **B)** To integrate smart materials in astrocytes interface together with flexible electronics circuitry for measurements in vivo and in pathological models **C)** Validation of AuSi/Nws, devices for electrical stimulation and read-out in vitro on astrocytes and co-cultures.

Expected Results: Identification of the best nanostructured material for inducing the natural differentiation in cultured astrocytes. (**D2.2).** Fabrication of astrocytes interfaces and smart devices for electrical stimulation and read-out in vitro and in vivo (**D2.2, D5.1, D6.2, D6.3**).Dissemination of results through publications (3) in international journals, participation to one international conference/workshop per year, participation in ASTROTECH workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis**. Skills acquired:** Fundamental knowledge on physical properties of disordered inorganic nanostructures grown by large area techniques (PECVD, Hydrothermal growth, etc.); integration of advanced materials in neural interfaces and fabrication of flexible devices for astrocytes recording; clean room process integration (EBL/optical lithography, etching/RIE, PECVD, ECR-PECVD, sputtering deposition); electrical, electrochemical and electromechanical characterization of smart devices for astrocytes recording; comprehensive training on transferable skills.

Planned secondments: AVA: (M22, 3 m) Training on advanced printable materials for reducing electrode impedance. UCAM: Training on organic transistor fabrication (M30, 1 m); BCAM M. d Pittà (M38, 1 m) In silico models of neuron astrocytes interaction. MEDTRO (M40 0,5 m): Training on the norms and procedures for implants certification.

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Biomedical, Electrical and Systems Engineering, Dept. of Electric, Electronic and Information Engineering (DEI), UNIBO.

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
3: ESR-CNR-IPCB	**CNR**	1	M7	36	**D4.1, D4.2, D6.1**

Project Title and Work Packages to which it is related: Design and fabrication of micro/nano structured platforms as organic polymer interfaces to study *in vitro* neural cells response (**WP4-WP5**). **Supervisor**: **Vincenzo Guarino (IPCB) (**Materials Science)

Objectives: A) to identify the optimal process conditions to fabricate 3D organic interface by electrospinning; **B)** to investigate the main chemical/physical properties of the electrospun fibres in order to validate their use for in vitro studies in healthy and gliotic astrocytes

Expected Results: Optimization of the morphology at the level of single fibre (i.e., defects occurrence, surface roughness) and fibre assembly (i.e., size distribution, fibre orientation) (**D4.1**). Characterization of chemical/physical properties of fibres (i.e., wettability, surface porosity, etc) to validate their use for cell interaction (**D4.2, D6.1**).Dissemination of results through publications (2) in international journals, participation to one international conference per year, participation in ASTROTECH workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on biomaterial science, processing of biodegradable polymers/biopolymers in solution, Safety and manipulation rules for chemicals and electric field assisted equipment, Optical microscopy, Transmission and Scanning electronic microscopy; Morphological analyses, Image analysis; Comprehensive training on transferable skills.

Planned secondments: UNIBA –P.Nicchia (M18, 2 m): Training on high resolution imaging methodologies to investigate astrocytes biomaterials interactions. INEB- A.P. Pego (M24, 2 month): Synergies on materials properties for in vitro models for gliosis. AVA (M36, 1 m): Training on device processing and fabrication from industrial perspective.

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Products and Industrial Processes engineering, Dept. of Chemicals, Materials, and Production Engineering, University of Naples Federico II, Naples, Italy.

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
4: ESR-UCAM	**UCAM**	Y	M7	36	**D2.1, D5.1, D6.2, D6.3**

Project Title and Work Packages to which it is related: Development of electrophysiology devices for the *in vitro* and *in vivo* detection of electrical activity of astrocytes. (WP2, WP5 WP6) **Supervisors**: **George Malliaras (UCAM) (**Bioelectronics)**, V Benfenati (glial physiology)**

Objectives: A) To understand how electrode area and impedance affect the recording of activities from astrocytes and neurons B) To develop soft electrophysiology devices that record selectively from astrocytes. C) To validate these devices in a rodent model.

Expected Results: Identify impact of electrode geometry on recording of electrophysiological activity (**D 2.1**). Demonstrate in vivo recordings from astrocytes (**D5.1**). Demonstrate in vivo recordings from astrocytes in healthy and pathological model (**D5.1, D6.2, 6.3**). Dissemination of results through publications (3) in international journals, participation to one international conference/workshop per year, participation in ASTROTECH workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on electronic materials and electrophysiology, microfabrication expertise, materials characterisation with different microscopies, impedance spectroscopy. Acquisition of animal licence from Home Office, training in in vivo electrophysiology. comprehensive training on transferable skills.

Planned secondments AMU: (M22, 3 months) Training on in vivo electrophysiology. AVA (M30, 1 month): Training on industrial research methods, applied research constraints. BCAM (M36, 1 m) In silico models of neuron astrocytes interaction. MEDTRO (M30, 0,5 month): Training on addressing emerging markets.

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Engineering, University of Cambridge.

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
5: ESR-IEM	**IEM**	Y	**M12**	36	**D2.3, D2.4, D6.2**

Project Title and Work Packages to which it is related: Electrophysiological recordings on astrocytes/glial cells by glioelectronic device and identification of astrocytes functions *ex vivo* (**WP 2-4-6**) **Supervisors**: **Miroslava Anderova, (A. P. Pego, biomaterial science)**

Objectives: A) Validation of glioelectronic device by means of electrophysiological recordings ex vivo in astrocytes, brain slices preparation, calcium imaging ex vivo, immunohistochemical identification of astrocytes **B)** Validation of glioelectronic device brain slices preparation from **ischemia mice model** and uncovering astroglial electrical signaling.

Expected Results: Validation of biolectronic devices for electrical stimulation and read-out in brain slice preparations **from rodents** (**D2.3**). Identification of contribution astrocytes ion channels in cell volume regulation in brain slice (**D2.3, D2.4**).Preparation of GFAP/GFP+ astrocytes for integration in the scaffold (**D4.3**).Validation of biolectronic devices for electrical stimulation and read-out in brain slice preparations **from ischemia model** (**D2.3, D2.4**). Identification of contribution astrocytes ion channels to alteration in bioelectrical activity in ischemia model (**D6.3**). Dissemination of findings through publications (2) in international journals and social media (twitter), data presentation to international conference/workshop (one per year), participation in workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on astrocytes and NG2 cells at the gene, protein, and functional levels. Definition of the properties of glial cells in the intact brain as well as following injury of the CNS. Electrophysiological recordings ex vivo in astrocytes, brain slices preparation, calcium imaging ex vivo by confocal microscopy, immunohistochemical identification of astrocytes, gene expression profiling of glial cells, various models of CNS focal cerebral ischemia disease.

Planned secondments: ISOF: In vitro cell culture BCAM (M36, 1 m) In silico models of neuron astrocytes interaction. ZUH (M30, 0,5 month): Training on Scientific Study OPTO: (M36, 2 months) Photostimulation in humans.

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Neuroscience, Charles University, Prague, Czeck Rep,

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
6:ESR-AMU	**AMU**	Y	M10	36	**D2.4, D 5.1, D6.2**

Project Title and Work Packages to which it is related: Disruption of K^+ clearance and metabolic processes in astrocytes at seizure onset (**WP 5, WP6**) **Supervisors**: **Christophe Bernard (AMU) (**Cellular and network neuroscience)

Objectives: A) To measure astrocytic function in experimental epilepsy, combining Ca^{2+} imaging, electrophysiological, metabolic (glucose and lactate) and ionic (K^+) recordings, and establish whether changes occur before seizure onset (biomarker identification) and are causally related to seizure genesis (mechanism) **B)** Validation of biolectronic devices for assessing astrocyte function *in vivo*. C) Testing predictions from ESR-7.

Expected Results: Validation of biolectronic devices for *in vivo* recordings (**D5.1**). Identification of a predictive biomarker of seizures (**D6.2**). Identification of the mechanism of seizure onset for a type of focal seizures (**D6.2**). Dissemination of results through publications (3) in international journals, participation to one international conference/workshop per year, participation in workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on neurobiology, glial biology and physiology; ethical aspects; animal models of epilepsy; *in vivo* electrophysiology and imaging; telemetry; functional morphology; patch-clamp; device fabrication and characterization; signal processing; comprehensive training on transferable skills.

Planned secondments: CNR-ISOF Valentina Benfenati (M18, 1 months): Ca^{2+} imaging in astrocytes. UCAM – G. Malliaras (M24, 1 month): Organic electronic devices. CODEMART (M36, 0,5m) data integration in TVB, MEDTRON, D.Carmina (M40, 0,5 month). Regultions for clinical trials

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD in Neuroscience – Neuroschool, AMU Marseille Université, France.

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
7:ESR-AMU	**AMU**	Y	M12	36	D7.3, 7.4

Project Title and Work Packages to which it is related: Integration of astrocytes function in computational model for the Neuron-Glial-Vascular Unit (**WP 7**). **Supervisors**: **Christophe Bernard (AMU) (**Cellular and network neuroscience)

Objectives: A) Incorporating neuron-glia-blood vessel coupling in the generative models used in The Virtual Brain. B) Constant interplay with partners to improve the model. C) Generating testable predictions for ESR-6.

Expected Results: Generative model for TVMB and validation using a dataset of 19 mice (**D7.3**). The experimental model used by ESR-6 can easily modeled in TVMB by changing the connectome and the glial-neuron interactions identified by ESR-6. ESR-7 will thus generate testable predictions for ESR-6. Transfer of knowledge to TVB platform, with CODEMART (**D7.4**), and possible tests on clinical data. Dissemination of results through publications (3) in international journals, participation to one international conference/workshop per year, participation in workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on neurobiology, glial biology and physiology; ethical aspects; animal models of epilepsy; *in vivo* electrophysiology and imaging; telemetry; functional morphology; patch-clamp; device fabrication and characterization; signal processing; comprehensive training on transferable skills.

Planned secondments: CNR – L. Tommasi (M24, 1 months): deciphing electrophysiological signalling in astrocytes. UCAM – G. Malliaras (M28, 1 month): Decoding sensing molecules BCAM (M 35, 4 m). CODEMART, L. Domide (M40, 3m).

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD in Neuroscience – Neuroschool, AMU Marseille Université, France.

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
8:ESR-BCAM	**BCAM**	Y	M12	36	**D7.1-D7.4**

Project Title and Work Packages to which it is related: Computational glioscience approach of volume signaling transmission in the in the Neuron-Glial-Vascular Unit (**WP7**). **Supervisors**: Maurizio De Pittà **(BCAM) (Computational Neuroscience and Glioscience**), C. Bernard (Neuropathology)

Objectives: (A) Build biophysical models of cortical activity in the healthy and diseased brain, leveraging on biophysical dissection of mechanisms of volume regulation by neuron-glial interactions and/or in association with the vasculature ; (**B**) Develop electrically-equivalent models of the neuron-glial parenchyma; (**C**) Implement prototypes in silico to guide design principles of implantable probes for neurological disorders such as epilepsy, spreading depression, and age-related dementia.

Expected Results: Build models of neuron-glial-vascular interactions, at multiple cortical scales: synaptic, cellular and network levels, all including mechanisms of extracellular volume regulation informed by experiments by partners. Accordingly, emphasis will be in particular, on aquoporines and swelling-activated chloride channels studied by the partners of the Consortium. (**D7.1**). Develop an electrically-equivalent formalism to describe neuron-glial interactions to bridge biophysical modeling to neuromorphic engineering, tailored to the design of implantable nano-devices for diagnostics and possible therapy of epilepsy, depression and, potentially applicable to other neurological disorders (**D7.2**) Dissemination of results through publications in peer-reviewed open-source international journals, and social media platforms and institutional repositories; Patenting of any prototype ensuing from the project, Participation to 1+ international conference/workshop per year; Attendance of one international summer tailored to computational Neuroscience and the Annual School on Glial research in Bertinoro; Engagement with regional and international industrial partners to promote commercialization. **Skills acquired:** Fundamental biophysics and biology of neuron-glial interactions, cutting-edge knowledge multi-scale neuron-glial modeling; expertise in physics of diffusion, PDEs formalisms, circuital analysis, theory of signals and neuromorphic engineering design; development of top-notch programming skills for

HPC and GPU-based simulations; emphasis on a strongly multi-disciplinary professional profile at the interface of biology, engineering, physics and computer science.

Planned secondments: CNR-ISOF- L. Tomasi (M18, 1 m) Collection of data on astrocytic bioelectricity and familiarization with glioelectronic devices. UNIBA: G. P. Nicchia (M24 2 m). Experiments in vitro and ex vivo on astrocytic aquoporin-4 expression and KO and volume regulation in mouse models. AMU- C Bernard (M30, 3 m) development and integration of models in the TVB with emphasis on glial-vascular coupling. CODEMART- L. Domide (M36, 3 m) software development tailored to clinical and translational technology.

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD course in **Neuroscience**, University of Basque Country (UPV/EHU).

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
9:ESR- INEB	**INEB**	Y	M9	36	**4.1, 4.2, 4.3, 6.1**

Project Title and Work Packages to which it is related: Astrocytic Tissue Engineered Models – Dissecting the role of the extracellular matrix mechanical properties towards the astrocytes' phenotype (WP4-WP6). **Supervisors**: A. Pêgo and S. Santos (INEB) and V. Benfenati (CNR-ISOF)

Objectives: A) to identify the optimal process conditions to fabricate 3D organic interface. **B)** Study the impact the extracellular matrix mechanical properties on astrocyte behavior in the context of homeostasis and disease. C) Study of mechanotransduction mechanisms involved in astrocyte behavior modulation.

Expected Results: Establishment of the material processing conditions that can mimic in vitro and in 3D different astroglial activation stages (homeostasis and disease) (Del n°). Identification of the astrocytic phenotype changes as a function of the extracellular matrix mechanical properties. (**D4.1**) Identify the alterations on the activation levels of mechanotransduction signaling pathways in healthy arocytes, in organoids models and astrogliotic cells. (**4.2, 4.3**, **6.1**). Dissemination of results through publications (3) in international journals, participation to one international conference and one workshop per year, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on neurobiology, glial biology and physiology, tissue engineering and biomaterials synthesis and characterization; preparation and manipulation of primary cells; ethical aspects; Cell biology; bioimaging; comprehensive training on transferable skills.

Planned secondments: CNR-IPCB (V.Guarino) synergies for biomaterial synthesis and characterization (M18, 1m). UNIBA (P.Nicchia, M24, 1m): Training on high resolution imaging methodologies to investigate astrocytes biomaterials interactions. CNR-ISOF (V.Benfenati, M36, 1m): electrophysiological recording of cells on ASTROTECH scaffold. AVA (J. Gomez, M40, 1m): Training on nanomaterial processing and fabrication from industrial perspective.

Institution where the ESR will be enrolled to obtain a doctoral degree: Doctoral Programme in Molecular and Cellular Biotechnology Applied to Health Sciences, Instituto de Ciências Biomédicas Abel Salazar (ICBAS), University of Porto (UPORTO).

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
10:ESR UNIBA	**University of Bari**	Y	M12	36	**3.1,4.2, 4.3, 6.1, 6.2, 7.1**

Project Title and Work Packages to which it is related: Monitoring of astroglial water channel proteins structure and function **(WP3-4-6-7)**
Supervisors: Grazia Paola Nicchia (UNIBA) (Neurophysiology), V. Guarino (Biomateials)

Objectives: A) To study the role of water channel proteins in astrocyte physiology in vitro in healthy and diseased astrocytes by performing functional and dynamics assays using superesolution microscopy, TIRF microscopy and fluorimetric assays on primary cultures and transfected cells. B) to investigate the role of cell actin dynamics in cell/material interaction; **C)** To define the role of AQP4 in astrocytes differentiation and neural development
D) To analyse how astrocytes mechanisms and functions are affected by altering physical, chemical and molecular parameters E) To analyse how astrocytes mechanisms and functions are affected in glioma cells.

Expected Results: Identifications of the effect of photostimulation on water transport (**D3.1**). Validation of glial interface in vitro model at molecular and cellular levels and identification of the role of astrocytes water channels and permeability in cell material interaction **(Dl 4.2.)** Identification of mechanisms underlying gliotic cell migration and gliotic scar formation in ASTROTECH scaffold, role of water channels and cell volume in organoids and gliotic astrocytes and relative model (**D4.3, D7.1**). Identification of mechanisms beyond glioma cells proliferation role of water channels and cell volume in 3D ASTROTECH model (**Del 6.1)**. Definition of the role of AQP4 assembly in Ischemia (**D6.3**). Dissemination of results through publications (3) in international journals, participation to one international conference/workshop per year, participation in ASTROTECH workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on neurobiology, glial biology and physiology; preparation and manipulation of primary astrocytes and neuron co-cultures; organotypic cultures and animal research, transgenic, knock-in mouse models, ethical aspects; cell growth, viability and cell apoptotic assays; cell migration and proliferation assays, optical spectroscopy and confocal microscopy, superesolution and TIRF microscopy; time lapse microscopy, immunocytochemistry and immunofluorescence; calcium imaging, patch-clamp, water transport and cell volume changes assays; behavioral assays; device fabrication and characterization; comprehensive training on transferable skills. Glioma and pathological models.

Planned secondments: INEB (A.P. Pego, M15, 2 month): training on biomaterials preparation and scaffold fabrication synergies for validation of ASTROTECH in vitro model for glioma. OPTO (M24, 1 month): training on Photonic device for photostimulation of astrocytes. UMD (W. Losert, M30, 2 month): Study the role of aquaporins in actin dynamics. CNR-IPCB validation of ASTROTECH in vitro model for glioma (M40, 1 month).

Institution where the ESR will be enrolled to obtain a doctoral degree: University of Bari, PhD in Neuroscience

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
11:ESR-IIT	**IIT**	Y	M8	36	**D3.2, D5.2**

Project Title and Work Packages to which it is related: Optoelectronic devices for gene-less, spatially and temporally selective excitation of astrocytes (**WP 3-5**); **Supervisors**: **Maria Rosa Antognazza (**Physics/device technology), Guglielmo Lanzani (POLIMI), G.P Nicchia (UNIBA)

Objectives: A) To develop and optimize light-sensitive, nanostructured actuators for efficient photomodulation of astrocytes activity; B) Characterization of phototransduction mechanisms in dependence on photoexcitation protocols parameters and device architecture; C) Identification of photo-activated biological pathways and assessment of temporal and spatial resolution of astrocytes optical modulation, at the supra-, sub- and cellular level.

Expected Results: Acquisition of solid background in organic and hybrid devices technology; characterization techniques of bio-interfaces (**5.2**).
Validation of the proposed gene-less approach for photomodulation of astrocytes physiology, as an innovative tool to gain the required temporal and spatial resolution (**D5.2**) Dissemination of results through publications (3) in international journals, participation to one international conference/workshop per year, participation to ASTROTECH workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis.
Skills acquired: In depth knowledge on organic electronics technology and biotechnology applications; materials development and device fabrication; characterization with optical, electronic, electrochemical and microscopy techniques; fundamental knowledge of cell physiology; fluorescence microscopy, confocal ion imaging, electrophysiology; comprehensive training on transferable skills.

Planned secondments: CNR–ISOF-UNIBO (M. Caprini, M12, 1 m): Interfacing organic optoelectronic device with astroglial cells. UCAM (G Malliaras, M18, 2): Integrating light sensitive organic actuators and electrochemical sensing devices. AVA (J. Gomez, M15, 1 m): Training on device processing and fabrication from industrial perspective, device patterning by Ink-jet. CSIC (G. Perea, M24, 2 m): Electrophysiological recording in situ of astrocytes upon photomodulation by hybrid devices. OPTO (M36, 1 m): Photonic Device in industrial Environment

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Physics or Biotechnology, Politecnico di Milano

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
12:ESR-CSIC	**CSIC**	Y	M8	36	D3.1-3.3, D5.2, 6.3

Project Title and Work Packages to which it is related: Modulation of astrocyte-neuron signalling properties by optogenetic and photonic devices in control and a depression mouse model **(WP3-5-6**) **Supervisors**: **Gertrudis Perea (I. CSIC) (**Functional and Systems Neurobiology. I. CSIC**), Christophe Bernard (AMU**)

Objectives: A) Identification of astrocyte-neuron communication signaling by optogenetic manipulation of astrocytes. **B)** Validation of AuSi/Nws organic biolectronic devices for optogenetic stimulation and electronic read-out in vitro on astrocytes and co-cultures of astrocytes and neurons. **C)** Validation of label free optical stimulation of astrocytes *ex vivo* in healthy and disease model of depression.

Expected Results: Identification of astrocyte-neuron communication signaling by optogenetic manipulation of astrocytes in brain slices **(D3.1-D3.3)** with defined optical fiber (**D5.2**). Definition of glioelectronic devices potential for optogenetic stimulation and electronic read-out in ex vivo preparations control animals and a mouse model of depression (**D6.3**). Dissemination of findings through publications (2) in international journals and social media (twitter), data presentation to international conference/workshop (one per year), participation in workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on glial biology and synaptic physiology; preparation and manipulation of primary astrocytes and neuron co-cultures; obtaining acute brain slices. **Optogenetics, electrophysiology, behavioral studies.** Particular attention to the ethical aspects of animal experimentation; whole-cell patch-clamp, calcium imaging, confocal microscopy; time lapse microscopy, immunocytochemistry and immunofluorescence; comprehensive training on transferable skills.

Planned secondments IIT (M.R.Antognazza, M15, 1 m): Interfacing organic optoelectronic device with astroglial cells. OPTO (M20, 2 m): Interfacing photonic device with astroglial cells ex vivo and in pathological models. CNR-ISOF (V. Benfenati M24, 1 m): electrophysiological recording of cells on ASTROTECH scaffold.

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD in Neuroscience, Dept. of Anatomy, Histology and Neuroscience, University Autonoma of Madrid (UAM), Spain.

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
13:ESR-AVA	**AVA**	Y	M7	36	D2.1, D5.1

Project Title and Work Packages to which it is related: Advanced nanomaterials for developing glioelectronic device (**WP2-5**)
Supervisors: **Julio Gomez, (AVA), Jesús Berenguer (UR)**

Objectives: A) To create new nanostructures in order to design devices for in-vitro astrocytes **B)** Optimize the performance of the electronic conductors to reduce impedance and improve ratio signal/noise.

Expected Results: Expected Results: Identification of the needed electronic properties for developing the biosensors **(D2.1)** Development of nanocomposites for creating new technologies for electrophysiology. (**D2.4).** Characterization of the properties of the nanomaterials using different technologies such as RAMAN, XRD, EIS. (D2.1, D5.1) Materials production for exchanging with other partners to prepare the devices. **(D2.1)** The results will be disseminated in workshops and publications in international journals. **Skills acquired:** Fundamental knowledge on material science, graphene and nanomaterials. Biosensors manufacturing and basic knowledge about neuroscience based on the participation in the project.

Planned secondments: CNR-IMM (L. Maiolo, M22, 1 m). Manufacturing of neural interface UCAM (G. Malliaras, M25, 1month). Characterization and fabrications of biosensors. IPCB (V. Guarino, M29, 1 m). 3D electrodeposition techniques.

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Chemistry, Dept. of Chemistry. Universidad de la Rioja

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
14:ESR-OPTO	**UPCH - OPTO**	Y	M12	36	D3.1-3.3, D5.2

Project Title and Work Packages to which it is related: Neurostimulation with non-invasive light source (WP 3-5)
Supervisors: Jakob Andersen (Medical Science) Troels W. Kjær (Neurophysiology and Neuropathology)

Objective: A) understanding of the effect non-invasive gene-less photonic stimuli has on the brain B) Evaluation of safety and efficacy of non-invasive, gene-less photonic stimulation in humans. C) To understand the role of astrocytes in light induced impact on pathology

Expected Results: Validation of safety of non-invasive gene-less photoic stimulation in vitro and in vivo (through secondments to patner and beneficiaries) and in humans as a future tool for potential modulation of cellular process in vivo and in humans (D3.1-3.3, 5.2). Dissemination af results through publication (3-4) in international peer-reviewed journals. One international scientific conference/workshop per year participation to ASTROTECH workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** In depth knowledge in clinical research and fundamental knowledge of cell physiology and animal models. Photonics device development and plli cation for testing in humans, Regulatory practice for human testings.

Planned secondments: UNIBA (P. Nicchia, M18, 2 m,): photostimulation by of astrocytes by optical fibre device and understanding of molecular mechanisms in vitro. ZUH (M30, 7 m): protocols for photnic device test in humans, CSIC (G. Perea, M40, 1 m): Electrophysiological recording ex vivo of astrocytes upon photomodulation in optogenetic and geneless mode.

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Neuroscience, Dept. Clinical Research, Copenhagen University

Fellow n° and name	Host institution	PhD enrolment	Start date	Duration	Deliverables
15:ESR-OPTO	**DTU - OPTO**	Y	M12	36	D5.2, D6.3

Project Title and Work Packages to which it is related: Light induced neurostimulation with measurements of the modulation of neural activity and astrocytes physiology (WP5-WP6) **Supervisors**: Paul Michael Petersen

Objectives: A) To investigate the impact of gliophotonics using invisible spectral flicker, by measuring the SSVEP and fMRI response during exposure and by analysing the long-term changes. **B)** To develop and optimize the optical fiber for optogenetic and light therapy by Optoceutics. **C)** To develop a paradigm for testing the potential and effects of light induce neurostimulation that aims at maximizing comfort and inducement.

Expected Results: Gain knowledge about and validate of the proposed gene-less approach for photomodulation of astrocytes physiology, as an innovative tool to gain the required temporal and spatial resolution (**D3.1**). Dissemination of results through publications (3) in international journals, participation to one international conference/workshop per year, participation to ASTROTECH workshop and schools, direct involvement in the organization of events and outreach activities, PhD thesis. **Skills acquired:** Fundamental knowledge on neurobiology, glial biology and physiology; in depth knowledge on photonic technology, optical spectroscopy, EEG and fMRI methodologies; comprehensive training on transferable skills. Regulatory practice for human testing.

Planned secondments: ZUH (M15, 7m) Preparation of clinical paradigm. Fundamentals on EEG and fMRI techniques CNR-ISOF (M24, 1m – V. Benfenati (M30, 1 m): photostimulation by of astrocytes by optical fibre device and understanding of molecular mechanisms in vitro. CSIC (G. Perea, M30, 1 m): Electrophysiological recording ex vivo of astrocytes upon photomodulation in optogenetic and geneless mode. AMU photostimulation in epileptic mice models (M 40, 1m).

Institution where the ESR will be enrolled to obtain a doctoral degree: PhD Course in Photonics Engineering, Dept. Photonics Engineering, Technical University of Denmark

3.2 Appropriateness of the management structures and procedures

- **Network Organization and management structure**

ASTROTECH is a project with a large number of participants, therefore a robust management structure is needed to organize research and training activities as well as to communicate and disseminate project results. Additionally, project management must provide a transparent administrative support to the appointed ESRs to create a proactive

working environment. To this end, the management structure will be composed of a **Supervisory Board (SB),** a **Training and Tutoring Board (TTB), an Exploitation Supervisory Board (ESB), a Dissemination Supervisory Board and Companion Committee.**

- **Supervisory Board (SB)**

The Supervisory Board is the most important tool to manage the project. SB will be composed of a representative of each beneficiary and will be chaired by the ASTROTECH coordinator and co-coordinator. At least a female representative of ½ will be encouraged. All decisions will be taken by consensus or by following simple majority of present participants. In case of draw, the Coordinator will express the final preference. SB will be elected at **kick-off** and will meet every year and will have a web meeting every six month with **TTB**. In any case, additional meetings will be scheduled based on special needs. The main tasks of SB oversee: i) coordination of network-wide training events and research plan; **b**) Management of the quality and completeness of the proposed training (e.g. scientific/technological, soft skills, industrial oriented); **c**) control of any scientific misconduct, (e.g. plagiarism) according to the guidelines provided by the European Code of Conduct for Research Integrity; **d**) supervision of the **PCDP**s of each ESR; **e**) Supervision the overall activity of the network, ensuring the achievement of ASTROTECH goals and recommending actions in case of issues; **f**) Ensuring that personalised and network wide training is in line with inter- and intra-sectoral needs as to ensure wide employability of the fellows; **g**) Ensuring the realization of a fair communication and exchange of knowledge among participants. The SB will also be responsible for delivering annual reports and will have overall responsibility for the recruitment of ESR positions. The **project Coordinator and the Coordinator Unit (CU)** will supervise the research and training activities as well as the management, the financial support, the legal and exploitation aspects by active and continuous participation, supervision and decisions making procedures along with the SB and TTB board. Due the high level of interdisciplinariety and intersectoriality aspects present in ASTROTECH, the **CU** is formed by a Coordinator (Dr V. Benfenati) and Co-coordinator (Dr L. Maiolo) that will propose the best strategies to reach ASTROTECH scientific and training objectives and control project timeline (checking milestones and deliverables status). In case of issues, correction mechanisms will be assessed according to the risk management strategy (**Table n°3.2a**). Moreover, the **CU** will include **experts** in **project financial managing** and Intellectual Properties rights (**Dr Roberta Chiodini, Dr Ignazio La Rosa**) that will comply with the financial and administrative management timeline of the planned activities and react proactively to contingencies. The experts will also ensure **accordance of rules** for the hiring of ESRs at beneficiary sites.

- **Other Boards and Management structures**

The Training and Tutoring Board (TTB) will be formed by the coordinator that acts as chair, and other 5 members of the SB elected during the Kick-off meeting, maximizing representation of all expertise and partner typology (at least two partners belonging to private sector). The role of TTB will be i) **controlling the scheduled timing of training and secondments for each ESR**; ii) promoting training and tutoring actions permitting the exploitation of high quality results; iii) ***overview*** implementation of the training actions with a coherent day-by-day training strategy; iv) **help** in organizing *and* maximizing content cross-fertilization ***of all training actions***; v) **adapt** training implementation to cutting-edge trends developed, with **assessment** as well as **suggestions** from the ESR by considering the output of the ***Companion Committee; vi) monitoring*** **of the** ***personal career development plan*** of the ESRs. Each ESR will discuss with the **TTB** the specific training actions that she/he would like to adopt/add (e.g., tutorials on special technical or soft skills knowledge); vii) manage student issues in case of serious misbehaviour or training failures; viii) TTB will **report** on a regular quarterly basis to the SB. **The Dissemination Supervisory Board (DBS)** will be formed at Kick-off and will care about: i) support ESR for the dissemination of the results with particular emphasis on potential business awareness (e.g. organizing selected meeting with companies, investigating market ripeness, studying potential technology transfer) ii) supervise outreaching activities to spread project general contents to the public both to academic and industrial stakeholders (e.g specific brochure, website content update, social exploitation, etc.). **The Exploitation Supervisory Board (ESB)** will take care about rights and obligations as set out in Consortium Agreement including Intellectual Property Rights: i) draw up guidelines for handling sensitive information produced according to the NDA document ii) define the provisions of the Annex I in terms of achieving the project deliverables, reporting, dissemination, financial administration. **Companions Committee (CC)** an informal board **formed by ASTROTECH ERSs** with the following purposes: (i) strengthen the cohesion both among the recruited researchers themselves and between the ESR and the other members of the projects regardless their position and role; (ii) promote innovative ideas and training desires related to ASTROTECH topic towards the TTB (iii) facilitate the spreading of information about training sessions and secondments experiences. The first meeting of the CA will take place at **M15**. Further meetings will take place during common network events or remotely through online meetings.

Financial management. The **CU** will carry out transfer of funds transparently, and the distributed amounts will depend on the number of recruited ESRs in each beneficiary institution. Proper Management is ensured by the long lasting expertise of the CU in managing large consortium initiatives such as Graphene Flagship and Kick Raw Materials. After the kick-off meeting, **CU** will consider asking a fraction of the research, training and networking

funds to cover the unfunded partner costs in attending appointed events and meetings and for network-wide events. In any case, this statement will be ratified in the Grant Agreement. Each beneficiary will take care of paying the recruited researchers on a monthly basis and will provide financial statements to the CU. During this stage, the CU will verify the full payment of ESR and their allowance as well as secondment in terms of person month expenses.

- **Recruitment Strategy and Selection Process.**

The SB will draw the guidelines for a non-discriminatory, impartial and equitable recruitment strategy according to the European Code of Conduct for the Recruitment of Researchers. The selection procedure will envisage the following items: 1) **Definition of ESR profile**: for each project within the scientific program, beneficiaries will draw a profile of the desired research and training activities. According to the multidisciplinary nature of ITN, the required competences of ESR will be not too specialized with the intent of not discouraging possible suitable candidates with attitude to long-term vision project such as ASTROTECH. The presence of private companies will guarantee also the recruitment of ESR interested on more entrepreneurial aspects of R&D in this field. The profile will include clear information about working conditions in terms of salary, family allowance, benefits in respect of accidents at work and occupational diseases, pension rights and other social security coverage; the SB will also highlight the rules for application (e.g. European CV, letters of references, publications, etc.) and direct contacts for requesting additional information. 2) **Advertisement campaign for recruitment**: ASTROTECH ESR available positions will be published using a large variety of dedicated online portals to reach the maximum number of candidates. In particular, EUROAXESS, EuroScience Jobs, TipTopJobs, EuroJobs Studyportals, will be utilized together with social networks (e.g. Linkedin) as well as dedicated pages of the project website and national sites of universities and research centres and partner sites. 3) **Selection Process**: Each ESR could apply for a maximum of two positions submitting their CV through an online procedure. All the ESR CVs and additional documentation will be evaluated in two steps, starting with a pre-selection led by a specific board of experts and with a final interview at Beneficiary sites, according to recruitment rules of the Beneficiary Country and Institution. To select high-quality ESRs, the interview will concern on scientific background as well as English fluency and soft skills (e.g. attitude to teamwork, creativity, personality, ethics, candidate plan over short and long term, etc.). In case of similar evaluation, ESR based by gender and younger age will be preferred. Official acceptance letter will be sent to the selected candidates by each beneficiary supervisor, while for all ineligible or not selected applicants a rejection letter will be personally sent with the reasons for the exclusion. Selected ESRs will obtained a full-time employment contract and will be informed about their rights, duties and working conditions. All ERSs will have access to all legal documents (GA, ECC) and will be supported in finding accommodation, VISA procedures, and social integration in the hosting country. **All the recruitment procedures will be completed within the first 9 months** from the kick-off meeting. To reasonably allow a large participation of candidates in the recruitment process beneficiaries will set a period of at least 2 months between the position advertisements and the submission deadline. The selection process will cover a timeline from the deadline of the application submission of about 1 months.

- **Progress Monitoring and evaluation of individual Projects**

The Training and Tutoring Board (TTB) (see above page24), will check progress and evaluation of **individual ESR Projects by** i) **controlling the respect of scheduled timing of training and secondments for each ESR**; ii) ***overview*** implementation of the training actions with a coherent day-by-day training strategy; iv) **help** in organizing *and* maximizing content cross-fertilization ***of all training actions***; v) **adapt** training implementation to cutting-edge trends developed, with **assessment** as well as **suggestions** from the ESR by considering the output of the ***Companion Committee;*** *vi)* ***monitoring*** **of the** ***personal career development plan*** of the ESRs. Each ESR will discuss with the **TTB** the specific training actions that she/he would like to adopt/add (e.g., tutorials on special technical or soft skills knowledge); vii) manage student issues in case of serious misbehaviour or training failures; viii) TTB will **report** on a regular quarterly basis to the SB. The (ESR-specific) PhD committees at each Partner or Beneficiary site are mainly responsible for progress monitoring of the ESRs during the PhD Programme. PhD committee at each Beneficiaries or Partner site evaluates the progress every year, by means of a reporting evaluation session, where the ESR should present progress on research program and training skills. The PhD committees will report to the ASTROTECH Supervisor whenever a major delay or problem arises in one of the projects. Projects progress will be also discussed by ESRs and supervisors and evaluated at ASTROTECH network meetings, at least every six months, and during with annual reviews. Adjustments on the level of the individual research projects and in the PCDP. Supervisors will dedicate adequate time to provide appropriate support to the training of ESRs and for the necessary progress and feedback mechanisms after review procedures by meeting on regular basis. The supervisor will inform the TTB every **six months** about the progress of ESR activities.

- **Intellectual Property Right and Knowledge Issues**

As regards the former, considering that innovative materials, devices, techniques and tools may arise during the project – generating shared know-how, capable of being further developed – fair and transparent IPRs policies will be managed and ratify, according to the relevant national/European/international rules, commonly laid down in this matter. As for the latter, it should be pointed out that knowledge management within ASTROTECH, consequently,

entails the management of project outcomes and related subsidiary technologies, including patents, rights of ownership and exploitation of results. In that sense, and without prejudice to the protection usually assured to the Background and the Sideground held by the Beneficiaries and the Partners, both the Foreground and the Postground will remain in the property of those who carry out the work that leads to such knowledge, as better detailed in the ASTROTECH Consortium Agreement.

Furthermore, the Project Coordinator will make available its solid experience in this field benefiting, if necessary, from the support that can be provided by a structure present at central level, dedicated solely to the exploitation of research results and to the Technology Transfer issues aspects.

The aforementioned Consortium Agreement will include, among others: 1) Provisions to prevent and settle disputes concerning IPRs issues which may arise among Beneficiaries and/or Partners, also in compliance with rules set out in the Grant Agreement; 2) Rules for publication, with due regard to open access objectives and guiding principles drawn up by the EU; 3) Confidentiality handling, in order both to safeguard the Parties' know-how and to pursue the H2020 scientific knowledge dissemination objectives, thus stimulating a fair cooperation between researchers and Institutions involved.

As for Dispute Resolution: the general principle to be applied is that measures to settle any conflict should be taken at the most appropriate level of government, closest to the matter at stake. If the issues raised cannot be satisfactorily dealt, they will be referred to the TTB or ESB and finally to the SB. All disputes which cannot be settled amicably, shall be subject to international arbitration, according to the Rules of the International Chamber of Commerce, and shall comprise at least one arbitrator of legal education.

Data Management Plan (DMP) will be drafted at the beginning of the project and updated during its course. DMP will include information on experimental procedures aiming at standardized experimental designs, or standardized reporting of experimental design, that prevents lack of comparisons of results across data sets and that decreases reproducibility. DMP will be updated on ASTROTECH website and Protocols generated within ASTROTECH will be collected in DMP through internal sharing platform, managed by a private cloud system in an Online Data Base and Repository following rules regarding Open Access and Open Data under Horizon 2020.

Gender aspects ASTROTECH guarantee a work environment in which ESRs have equal access to programs, facilities, services, and employment. ASTROTECH will prohibit any kind of discrimination against any person for any reason (e.g. gender, age, color, national origin, religion, sexual or affectional orientation, etc.). ASTROTECH personnel will encourage reporting every misbehavior at any level. Once ascertained, the issue will be immediately communicated to the SB in order to respond with adequate actions according to the seriousness of the situation. These aftermaths will include verbal warnings, pecuniary fines up to the exclusion from the positions held in the project or the removal of the person from the working team of a specific partner. ASTROTECH consortium is composed by beneficiary teams with a majority of female leaders (above 60%) and it is coordinated by a woman. This gender proportion will be guaranteed also in the other positions and committees of the project (e.g. *Scientist in Charge,* WP leaders, *SB, TTB*, etc.). Likewise, the recruitment criteria will envisage a gender target of at least 50%. This goal will be achieved considering gender-smart work policies including family-friendly policies concerning flexible working time and parental leave as well as robust anti-harassment mechanisms. ASTROTECH personnel will work to guarantee gender equality at all the phases of the project, according to the different needs that may arise, maintaining an environment free of discrimination, including harassment, bullying, and retaliation.

3.3 Appropriateness of the infrastructure of the participating organizations

ESRs will have a complete access to all the facilities described in Sec.5. and summarised below in the Table 3.3 and with respect to specific local rules and safety policies of the participants.

Table 3.3 infrastructure of the participating organizations

Activity	Infrastructure	Remote access	Beneficiary/partner
Material Synthesis and deposition and advanced characterization (Gliomaterials)	Plasma Enhanced CVD; Hydrothermal bath deposition, Confocal spectroscopy and time-resolved photoluminescence; a 3D two photon (Femtonics) system; Scanning-probe microscopy (AFM, STM); Electron microscopy (TEM, SEM) and spectroscopy (XPS, UPS); NMR, Raman, UV Spectroscopy; Rheometer; Probe stations.		CNR, UCAM, AVA, IIT,
Device fabrication (Glioelectronics and Gliophotonics)	Clean rooms fully equipped with high vacuum evaporators, sputtering; Materials etching systems (RIE, DRIE); Printing technologies (Inkjet, Gravure and Screen Printing); Spin coating; Optical and Electron Lithography; Soft lithography; etc.		CNR, UCAM, IIT, OPTO
In vitro, *ex vivo* and *in vivo* Validation of ASTROTECHnologies	Animal facility; Cell culture lab; Patch-clamp; MEA; Molecular biology lab; HTS Varioskan spectrometer and microplate reader; ELISA reader; Western blot; qRT-PCR; Calcium imaging; Patch-clamp and MEA systems.		CNR, IEM, INEB, UNIBA, CSIC
Computational Glioscience	HPC cluster is composed of 6 new computational nodes. The current specifications are: 18 computational nodes (1 with Nvidia Tesla K40 GPU), 624 cores, 4TB of RAM memory and Infiniband network. The Virtual Mouse Brain platform for whole brain dynamics in silicon from virtualised mice.	X	AMU, BCAM, CODEMA,

3.4 Competences, experience and complementarity of the participating organizations and their commitment to the programme

- **Consortium composition and exploitation of partners' complementarities**

ASTROTECH implementation has been conceived to fully exploit the experience and know-how of Beneficiaries and partner covering both academic and private peculiarities. As detailed above, participants competences cover Engineering (UCAM, CNR-IMM), Material science (CNR-IPCB, CNR-IMM, INEB, AVA), Chemistry (AVA, CNR-ISOF, CNR-IPCB), Physics (UCAM, CNR-IMM), Photonics (IIT-CNST, OPTO), Mathematics and Computational science (AMU, BICAM) Neuroscience and Neuropathology (IEM, UNIBA, CNR-ISOF, AMU, CSIC) together with expertise in professional development and clinical practise (MEDTR, CODEMA).

- **Commitment of beneficiaries and partner organizations to the programme**

Experience of beneficiaries and partner institutions are fully committed to the proposed research and training programme. Most of involved institutions have already collaborated successfully on projects targeting objectives related to ASTROTECH and all beneficiaries and partners will be committed to provide ESRs with adequate support for training and research, including full access to facilities and infrastructures and time for supervision of mentoring. Private beneficiaries (OPTO, AVA) provide intersectoral aspect offering commercial techniques and tools to further improve the impact of the devices proposed in the project, as outlined above.

Partner organizations: Partner organizations will be strongly committed in the research and training activities of ASTROTECH by cooperating in the collaborative research plan, hosting secondments and research visits, contributing to the organization of network-wide events and delivering Doctoral degrees. Non-academic partner will offer further opportunities for ESR to know complementary working scenario. The role of each partner is detailed in the description of WPs and in network wide event Table and their commitment was proved by signed statement in the Letters of Commitments enclosed in B2.

4. Ethics Issues

The present session is updated to comply with **Ethics Summary Report Associated with document Ref. Ares(2020)2175081 - 22/04/2020**. All the copies of the document requested were asked to Beneficiaries and Partners. All the documents will be kept as file on a folder called ASTROTECH Ethics shared with all the Beneficiaries and Partners Responsible involved and The Project Officer and available at the link:
https://drive.google.com/drive/folders/1BSQBi09cIFc9aNSjMJuA0q0LEIJTK1co?usp=sharing

The folder will be updated with copies of all the **original forms documents and permissions requested to comply** with the Ethical Summary Report and all the translated documents will be available in the folder and the specific requested (indicated below) will be submitted as Deliverable on due date. **The information included to comply with The Ethics Summary Report are reported below**

4.1 RESEARCH OBJECTIVE:

The present training program aims at forming scientists on a novel emerging supradisciplinary field that is Glial Engineering and Glial Interfacing and Gliophotonics. It deals with combination of Neuroscience and Bioelectronics and Biophotonics and Biomaterials with the ultimate goal of generating unique know-how on engineering new tools that will be essential to approach the study of the role of astrocytes in the brain and therapy of the brain neuropathologies such Epilepsy, Alzheimer disease and glioma and Depression. **The potential impact that ASTROTECH will have on diagnostics, regenerative medicine, and targeted delivery raises the question, which ethical, legal, and social aspects have to be addressed to create an environment for the socially acceptable and economically successful development of organic-optoelectronic-neural interfaced applications.** Among potential foreseen implementation of the field we recognize the potential to produce bioelectronics devices or materials interface to address behavioural disturbances or psychiatric disorders, such as depression or schizophrenia, or prosthesis for electrostimulation of injured arts. Moreover, ethical questions can arise, such as "when and how to manipulate the brain cells?" "Which is the border line definition of "therapy" and "social behaviour control?" As this action is mainly focus on training of future scientists, these critical ethical aspects should be considered in their education program. Thus, we sought to give our contribution to ethical issues rising from the project by inserting specific sessions of the training devoted to "Bio-ethical" as well as "Socio-Ethical" issues generated by the development of neuro-inspired Organic bioelectronics and opto-electronic technologies. Thus, we included an Ethical issue thematic workshop with the following topic - Animal use in Neuroscience:3Rs - Bioethics in therapeutic application: protection of individuals from fundamental investigation to clinical research (see **Table1.2b –part B**).

4.2 USE OF HUMAN SUBJECTS IN RESEARCH

ASTROTECH will also include a human study in Denmark, performed by ZUH and OPTO. The purpose is to test safety and efficacy of non-invasive light stimuli in humans.

OPTO and ZUH have significant experience in the preparation and execution of clinical studies that comply with the appropriate ethical rules. The Danish Scientific Ethics Committee have already conditionally approved the following:

- Safety test on 4 healthy and 10 Alzheimer's Disease patients (approval SJ-806)
- Exposing 40 humans for MR scans under light and sound stimulus (SJ-781)
- Exposing 40 humans for electroencephalogram (EEG) with notification number 60078

- The Beneficiary or any Third parties responsible for a specific task will be in charge of anticipating and highlighting any potential ethical issues that may arise during the project in order to implement an appropriate solution. **No person unable to give informed consent, vulnerable persons or children (minors age <18 years) will be asked to join the study. The Beneficiary is clarifying that no vulnerable individuals/groups will be involved. The measures to protect them and minimise the risk of their stigmatisation is provided and described in the "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" section 14 "Study Ethics",** that will be translated by Beneficiary (in language and terms intelligible to the participants) within the date requested (m12 of the project).
- The procedures and criteria that will be used to identify/recruit research participants are described in the document called the "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" in section 8 and section 9 and will be submitted as a deliverable.
- The informed consent procedures that will be implemented for the participation of humans are described in the "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" in section 14.1 and appendix 1 "Informed Consewnt and Patient Information" as well as Appendix 5 "Guidelines for verbal information on the investigation" and will be submitted as a deliverable.
- Templates of the informed consent/assent forms and information sheets, that was provided by the Beneficiary, will be kept on the online ASTROTECH-Ethics folder as file called "Informed concent for named "S1 Samtykke, V1.1, 2019-11-17" (National standard), that will be translated by Beneficiary (in language and terms intelligible to the participants) within the date requested (m12 of the project).

There will be **no** experimental activity that modifies or is intended to modify the genetic heritage of human beings by alteration of germ cells or by acting at any other stage in embryonic development and which can make such alteration hereditary.

Similarly, there will be **no** research activity on human embryos or foetal tissues, human embryonic stem cells (hESCs) or that can be understood in the sense of the term "cloning", with the aim of replacing a germ or embryo cell nucleus with that of the cell of any patient, a cell from an embryo or a cell coming from a later stage of development to the human embryo.

Therefore, **OPTO and ZUH deals with three aspects where ethical issues apply, namely:**

- **Clinical trials (with healthy volunteers and with patients)**
- **Use of human cells (from blood samples)**
- **Privacy and data protection**

Legal and ethical requirements associated to the development of the 40 Hz ISF light are similar to those required by any other clinical trial of this nature. There is a requirement to submit a request to the regulatory agency prior to conducting a clinical trial, as part of the authorization procedure to conduct the study. The clinical trials within ASTROTECH will be **handled by** OPTO and ZUH. Ethical approval for this study and any subsequent amendments will be sought from the relevant local ethics committee in Denmark.

Copies of opinions/approvals by ethics committees and/or competent authorities for the research with humans will be submitted as a deliverable.

The document of approval from national medical agency called: "DMA approval AZLIGHT Pilot". Approval from ethics committee "Conditional approval Ethics SJ-806" and "Email on final approval" are provided by the Beneficiary and will be translated and submitted as a deliverable at the due date **(month 12)**

In addition to the authorization for conducting the study, prior to participating in a clinical trial, participants must be fully informed about the scope and potential risks of participation in the project and they must sign an informed consent form in order to participate in the clinical trial.

The study will be submitted to ethics and competent authorities at each of the test sites where it will be conducted, as well as registration under ClinicalTrials.gov or European Clinical Trials Database (EudraCT). We will collect personal (for example age, height, weight) and health information (for example co-morbidities) from consenting patients. Consent will be sought for the data to be used to report the results of the study and will not be used for any other purpose.

No specific ethics challenges are anticipated with patient screening and recruitment, data storage during and after the completion of the study or in the use of 40 Hz light. Regular assessments of any adverse events will be sufficient to rapidly identify any adverse local or systemic effects of the product. Any serious adverse event should be immediately reported.

4.2.1 Study Description

The pilot study on humans is conducted to see if mice research can be translated to humans with mild to moderate Alzheimer's using a novel 40 Hz light stimulating device. The device masks the flickering rendering it invisible to the patient, whilst still entraining 40 Hz brain waves. It is a two-stage protocol. In the first stage, four elderly subjects with only age-related abnormalities in the brain. Once the first group of subjects has finalized the protocol and the data have been reviewed, the second stage will be initiated to recruit 10 subjects with mild to moderate Alzheimer's Disease. It is hypothesized that exposure to the 40 Hz masked light will clear disease related proteins from the brain, show changes in cognitive behaviour; induce gamma oscillations at 40 Hz; change resting state EEG metrics and show changes in magnetic resonance parameters such as functional connectivity, perfusion, metabolism and cerebral atrophy.

Details on incidental findings policy is provided and described in the document called "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" section 14.13 "Incidental Findings"

- For each clinical study, the following documents/information will be submitted as a deliverable (in one package) prior to enrolment of first study subject: (i) Final version of study protocol as submitted to regulators/ethics committee(s), (ii) Registration number of clinical study in a WHO-or ICMJE- approved registry (with the possibility to post results), (iii) Approvals (ethics committees and national competent authority if applicable) required for invitation/enrolment of first subject in at least one clinical centre.
- All the document requested have been provided by OPTO and are kept in the folder ASTROTECH-Ethics as file in National language. They will be translated and submitted as a Deliverable on the due date (m12)
- For each clinical study, a report on the status of posting results in the study registry(s) will be submitted as a deliverable on due date (m12), including timelines if/when final posting of results is scheduled after end of funding period.
- **Before the beginning of activities involving human cells, namely blood samples c**opies of relevant documents for using, producing or collecting human cells or tissues (e.g., ethics approval, import licence, accreditation/designation will be kept on file **in ASTROTECH Ethics file.**

4.3 PROTECTION OF PERSONAL DATA (POPD)

- **The following action will be performed before the beginning of activities involving personal data:** The beneficiary OPTO will check if special derogations pertaining to the rights of data subjects or the processing of genetic, biometric and/or health data have been established under the national legislation of the country where the research takes place and submit a declaration of compliance with respective national legal framework(s).
- The entire project will be performed according to the national Data Protection Agency and in accordance with GDPR
- The host institution confirmed (OPTO and ZHU) that it has been appointed Professor Troels Wesenberg Kjær as Data Protection Officer (DPO) and the contact details of the DPO are made available to all data subjects involved in the research.
- The beneficiary explain how all of the data they intend to process is relevant and limited to the purposes of the research project (in accordance with the 'data minimisation 'principle) as described in the document called "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" section 12 "Data handling and analysis" that is available in the ASTROTECH ETHICS folder and will be Translated and submitted as a deliverable on due date **(m12)**
- A description of the technical and organisational measures that will be implemented to safeguard the rights and freedoms of the data subjects/research participants is provided in the document called "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" section 12 "Data handling and analysis" that is available in the ASTROTECH ETHICS folder and will be Translated and submitted as a deliverable on due date **(m12)**
- A description of the security measures that will be implemented to prevent unauthorised access to personal data or the equipment used for processing is provided in the document called "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" section 12 "Data handling and analysis" that is available in the ASTROTECH ETHICS folder and will be Translated and submitted as a deliverable on due date **(m12)**
- Description of the anonymysation/pseudonymisation techniques that will be implemented is provided in the document called "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" section 12 "Data handling and analysis" that is available in the **ASTROTECH ETHICS folder and will be Translated and submitted as a deliverable on due date (m12)**
- Detailed information on the informed consent procedures in regard to data processing is provided in the document called "Protocol ALZLIGHT Pilot 2019-12-17, v1.0" in section 14.1 and appendix 1 "Informed Consent and Patient Information" as well as Appendix 5 "Guidelines for verbal information on the investigation", that is available in the **ASTROTECH ETHICS folder and will be Translated and submitted as a deliverable on due date (m12)**

- Templates of the informed consent forms and information sheets (in language and terms intelligible to the participants) are kept on file named " Informed concent for named "S1 Samtykke, V1.1, 2019-11-17" (National standard) in **ASTROTECH ETHICS folder.**

4.4 ANIMAL USE IN THE PROJECT

The development of the ASTROTECH research project rises important ethical issue related to small animal (rodents: mice and rat) use in research. Actions to exploit this issue are indicated in specific paragraphs for each partner and associated partner that will have to use small animals for implementation of the research project, **namely CNR-UNIBO, UCAM, IEM, CSIC, AMU, UNIBA, INEB, OPTO**. The detailed **methodology** involving animal use (primary cultures, in situ and ex vivo experiments) is defined in separate chapters by each Partner. As a general rule, experiments involving animals will be performed complying with the principles of the 3 Rs: reduction, refinement and replacement. Every authority is identified by each partner and specified in the paragraph.

Each partner has contributed to development of the present part of the proposal testifying that the network had maximal care to this issue. With respect of this, a specific part of the training will be devoted to the present ethical aspect (see Part B).

To comply with **Ethics Summary Report Associated with document Ref. Ares(2020)2175081 - 22/04/2020** b**efore the beginning of animal experiments the following actions will be implemented:**

- Copies of relevant authorisations for animal experiments (covering also the work with genetically modified animals, if applicable) **will be kept on file on ASTROTECH ETHICS folder** at the link above
- Where applicable, copies of training certificates/personal licenses of the staff involved in animal experiments **will be kept on file on ASTROTECH ETHICS folder** at the link above
- In case activities undertaken in non-EU countries raise ethics issues, the applicants **will** ensure that if any secondment will occur on US partners by ESRs the research conducted outside the EU is legal in an EU Member State and approved by US IUAAC Committee for Animal Welfare.

4.4.1 METHODOLOGIES:

The present proposal **is not concerned with human stem cells** neither from embryonic preparations or adult materials. ESR projects based on experiments on rodents (mice and rats) will be animal species used for biological testing both *in vitro* (WP2, WP3, WP4), *ex vivo* (WP 3) and *in vivo* (WP5; WP6). All animal experiments are designed with a commitment to refinement, reduction, and replacement (3 Rs), minimizing the numbers of animal used and their suffering via emphasis on humane end points, while using biostatistical advice for optimization of vertebrate's numbers. The project seriously observes these principles: Reducing the number of animals used to a minimum; Refining the way experiments are carried out, to make sure animals suffer as little as possible, and Replacing animal experiments with non- animal techniques such as in vitro cultures wherever possible. The experiments described use the absolute minimum of animals possible, and none of the scientific goals requires large numbers of replicates.

4.4.1.1 CNR-ISOF- UNIBO *Cell culture preparation UNIBO*

All studies involving the use of animals performed at the University of Bologna must be previously evaluated by the Scientific Ethics Committee for animal experimentation of the University of Bologna. The service monitors the welfare and health of animals, in order to avoid lasting harm, pain, unnecessary suffering or distress.

The service also checks the proper execution of the experiment procedures and at the end decide whether the animal shall be kept alive or deleted; however, proceeds to its suppression in animals persist when conditions of suffering or distress, or when it is impossible to keep the animal in welfare conditions.

The service provides advice and veterinary care, as well as advice on animal welfare.

The Committee is composed by members of Central Veterinary Service for the Protection of animals used for experimental purposes

- Responsible: Prof. Angelo Peli (Clinical Veterinarian and Medical Clinic Legal)
- Dott.ssa Alessandra Buonacucina (Attending Veterinarian)
- Dott. Giuseppe Cascio (Attending Veterinarian)

Ethics Application that encompass the experiments described are running and valid as a supporting document together with the official Authorization by the Ministry of Health (n. 1138/2020-PR, valid for 5 years).

The experiments will be performed at UNIBO were performed according to the Italian law on protection of laboratory animals, after the approval of a local bioethical committee and under the supervision of a veterinary commission for animal care and comfort of the University of Bologna. Every effort will be made to minimize the number of animals used and their sufferings.

Since the use of primary cultures of neural cells is mandatory in light of the project goal, the use of small animals (rodent) cannot be avoided. The number of animals that will be sacrificed has been estimated but will be reduced to a minimum, in accordance with rules mentioned above. In order to Reduce the number of animals cells preparation from the same animals will be plated on different device substructure (i.e different materials). Cell cultures obtained

from rodent are suitable for experiments for 3-5 weeks. Sprague-Dawley rats (4-12 weeks old) are available from standard commercial sources, such as Charles River Laboratories in Calco. Animal breeding at UNIBO will be performed and pups will be scarified at PO-P3 to prepare cell culture according to approved Protocols.
The first two weeks of culturing are necessary to reach standard conditions to perform the experiments. This means that in order to have continuity in the experimental schedule in a month, culture preparations must once per month for astrocytes and one per week for co-culture with neuron. Each culture preparation experiment will sacrifice at 3 newborn animals for astrocytes as well as for co-culture. However, from 1 flask preparation $14X10^5$ could be obtained. Considering single-cell patch-clamp experiment for defining in vitro biocompatibility, from each animal several number of cells can be tested. For each material tested, electrophysiological analyses from a number of 20 cells will be considered significant. On calcium imaging experiments from 3 independent culture preparation will be considered significant, since we could test around 200 cells per experiment. The patch-clamp and electrophysiology experiments will be run simultaneously so cell will derive from the same flask preparation and in turn from the same animal we will collect a large number of results. For in vitro biocompatibility assays results obtained from interfacing each kind of substrate with cultured cells from 4 different pups will be considered significant and the same culture will be plated on different materials. In this way we shouldn't overcome a number of forty pups for task 2.2 and 2.3 and 20 for task 4.2 and 4.3. The procedure to prepare neuronal and glial cells primary cultures are well standardized in order to attempt to Refinement rule. Cadavers of pups and neonatal rats are collected and temporarily stored in -20 °C freezer before being transported in a -80 °C specifically used for this purpose. Every month a specialized company collect the animals for incineration.
Astrocytes primary culture. Primary cultures of cortical astrocytes will be prepared once monthly for the entire duration of the whole project. The housing facility of the Department of Pharmacy and Biotechnology of UNIBO has also been authorized to carry out in-house breeding. All the procedures to prepare the cultures as well as those necessary to handle the animals before (housing, breeding, etc.) and after the cell culture preparations (disposal of dead animals) have been approved by the Ethical Committee for Animal Experimentation of the University of Bologna. For each preparation a number ranging from 6 to 10 1-2 days old pups are used. Following anesthetization with halothane animals are decapitated. From this point all the procedures are performed under sterile condition in a vertical laminar flow hood. From each head cerebral cortices devoid of meninges are extracted. Following trituration and passage through a sterile nylon mesh cortical material is collected in cell culture flasks containing grown medium composed of DME-glutamax medium supplemented with 15% fetal bovine serum (FBS) and penicillin/streptomycin (100 U/ml and 100 µg/ml, respectively). Culture flasks are maintained in a humidified incubator with 5% CO2 for 3-5 weeks. During this period culture medium is changed every 3 days. Non-astrocytic cells which are seeded on top of the astrocyte monolayer are detached by shaking procedures before each change of medium for the first 2 weeks. Three days before electrophysiological or microfluorimetric analyses confluent astrocytes contained in 2-3 culture flasks are detached by trypsinization and replated in Petri dishes of 33-mm diameter at a density of 30-50 x 10^3 per dish for electrophysiology or glass coverslip at a density of 10-20 x10^3 per cover for microfluorimetry. Purity of the astrocytic culture is assessed by immunostaining for the specific astroglial antigene Glial Fibrillary Acidic Protein (GFAP).
Preparation of co-cultures.
For the preparation of co-cultures the previously published protocol will be used [1]. For co-cultures the remaining part of the bark will be used, so that the same animal can be used both for pure astrocyte cultures and for co-cultures, which will be prepared as described above. The use of the same post-natal animal for the preparation of co-cultures avoids the practice of extracting neurons from embryos, which on the other hand would instead require the sacrifice of much higher numbers of animals. For this purpose the remaining bark, deprived of the rostral explant of 3 mm x 3 mm per hemisphere, used for the preparation of pure astrocyte cultures will be cut into small pieces (1 mm cubes) as with sterile knives and transferred the tissues in a 50 ml tube. The tissues are trypsinized in 10 ml of trypsin solution (0.25% of trypsin, 100 µg / ml of DNase in PBS) and incubated at 37 ° C for 15 minutes. Subsequently, an equal amount of 10% FBS-DMEM and pipettes up and down a few times will be added to encourage dissociation of the tissues. The preparation will be centrifuged at 300 x g for 3 minutes at room temperature, discard the supernatant and resuspend the pellet in fresh DMEM without serum. The cells will be filtered through a 70 µm nylon cell filter to obtain the single cell suspension, which will then be re-centrifuged at 300 x g for 3 minutes at room temperature. the cell precipitate will be resuspended in fresh serum-free DMEM and the cells will be counted and re-plated with a density of 5 x 10^4 cells / well and kept in an incubator at 37 ° C with 5% CO2 until the analysis date. To achieve co-cultures, neurons will be plated in the wells where astrocytes had been plated in the previous preparation.
4.4.1.2 UNIBA Animal research at UNIBA will be performed according to our local Ethical Review Boards. In order to get the official approval for performing a scientific project involving animal experimentation, a two-step evaluation process is undertaken according to the Italian legislation, whereby a research proposal is evaluated first by the Animal Welfare/Ethic Committee (Organismo Preposto al Benessere Animale, OPBA) of the animal facility where the animals are to be kept and maintained, which includes: the animal facility managers and responsible for animal

welfare at UNIBA (Prof. Grazia Paola Nicchia is responsible for animal welfare at the animal facility of the Dept of Bioscience, Biotechnologies and Biopharmaceutics), the appointed veterinary Prof Angelo Quaranta, few expert scientists and an expert in ethics. Secondly, the research proposal is evaluated by a panel of experts appointed by the Italian Ministry of Health. Once the Ministry has positively evaluated the project, a formal approval letter is prepared and the research is allowed to start.

The experiments involving animal experimentation will be conducted in the following institution: Animal Facility F2AEC Dipartimento di Bioscienze, Biotecnologie e Biofarmaceutica, Palazzo degli Istituti Biologici, Università degli Studi di Bari Aldo Moro. Via Orabona 4 - 70125 Bari. Authorization number: DM n. 23/98A - April 7, 1998. (Contact person: Prof Grazia Paola Nicchia email: graziapaola.nicchia@uniba.it; phone: +39-080-5443335).

The application includes (i) a first part in which the background, rationale and state-of-the-art of the proposed approach are outlined, supported by the relevant literature; (ii) a part concerning the experimental procedures, where all the experimental protocols to be performed are described in detail, specifying the severity of each procedure according to the EU and Italian legislation. This part contains also a specific section on statistical analysis and on how the "3R" principle is taken into account when calculating the number of animals to be employed in each procedure. In addition, the application includes (iii) a list of the persons involved in the project, with their qualifications, and (iv) the description of all the health and safety procedures in place to ensure maximum security for both the animals and the experimenters. Our institution and laboratories adhere to the following national law: Italian Decreto Legislativo 4 Marzo 2014, n. 26, legislative transposition of Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. One ethics application that encompasses the experiments described is currently running and valid as a supporting document together with the official Authorization by the Ministry of Health (Protocol no. 710/2017-PR).

The present proposal **is not concerned with human stem cells** neither from embryonic preparations or adult materials. Since the use of primary cultures of neural cells is mandatory in light of the project goal, the use of small animals (rodent) cannot be avoided. Mice will be animal species used for biological testing both *in vitro* and *ex vivo*. All animal experiments are designed with a commitment to refinement, reduction, and replacement (3 Rs), minimizing the numbers of animal used and their suffering via emphasis on humane end points, while using biostatistical advice for optimization of vertebrates numbers. The project seriously observes these principles: Reducing the number of animals used to a minimum; Refining the way experiments are carried out, to make sure animals suffer as little as possible, and Replacing animal experiments with non- animal techniques such as *in vitro* cultures wherever possible. The experiments described use the absolute minimum of animals possible, and none of the scientific goals requires large numbers of replicates. In order to reduce the number of animals, cells preparation from the same animals will be tested on different device substrates. For *in vitro* biocompatibility assays, results obtained from interfacing the materials under study with cultured cells from 3 independent dissections will be considered significant. Of note the same culture preparation could be used for all the assays to be performed.

AQP4 knockout (CD1) and knockin (C57BL/6) mice and relative WTs are available at UNIBA. All animal usage and care adheres to the strict ethical guidelines and review committees of the participating Institutions that implement the highest international standards of laboratory animal care, as well as strict national legislation. The project seriously observes these principles: *Reducing* the number of animals used to a minimum; *Refining* the way experiments are carried out, to make sure animals suffer as little as possible, and *Replacing* animal experiments with non-animal techniques wherever possible. Animals are sacrificed humanely before *in vitro* and *ex vivo* experiments. The estimated number of animals will be reduced to a minimum, in compliance with the above-mentioned rules. In order to reduce the number of animals, cells preparation from the same animals will be plated on different device substructure (i.e different materials).

We foresee to employ the following number of mice to cover the need for astrocyte primary cultures and neurosphere (neuronal stem cell) preparations for all the planned experiments. Considering that for mouse females the average litter comprises of 5 embryos (or pups) and that cell cultures are suitable for 5 weeks, we foresee to plan 6 preparations per year. We will sacrifice the pregnant mother to isolate neurospheres from embryos (6 mothers with 30 embrios/year), while astrocytes will be cultured from newborn mice (P0). 5 pups per preparation with 6 preparation/year is 30 pups/ year. The total number of animals to be used throughout the project can therefore be estimated as follows: [(6 mothers / year) + (30 embryos / year) + (30 pups / year)] * 3 years *4 strains = **792 animals**

The number of animals to be used - detailed above – was calculated so as to allow a statistical significance ($p<0.05$) on the expected results, based on the sample sizes of similar studies previously published in international, indexed journals. Of note, the same culture preparation could be used for all the assays. According to the reducing principle, the estimated number of animals will be reduced to a minimum by plating cells prepared from the same animals on different substrates/devices. Thanks to our long-term experience in culturing procedures the planned number of animals in three years is motivated by the need of daily accessing a few cell culture dishes of similar "age" (i.e. days-in-vitro). In fact, this will guarantee statistical significance and reproducibility of experimental results. After the

experimental procedures, cadavers will be temporarily stored in -20 °C freezer specifically used for this purpose. Routinely, a specialized company collect the animals for incineration.

Preparation of astrocyte primary cultures. Primary cultures of mouse astrocytes will be prepared from P0 brains of pups sacrificed by cervical dislocation. Brains from the entire littermate will be pulled for each preparation. Cells will be cultured in DMEM with stable L-glutamine supplemented with 10% fetal bovine serum (FBS), 100 U/mL penicillin and 100 mg/mL streptomycin, and maintained in a humidified incubator with 5% CO_2 for 3 weeks, as described in Mola et al. (2016). Microglial and progenitor cells will be detached by shaking before each change of medium for the first 2 weeks. The astrocytic marker GFAP will be used to assess astrocyte purity in the culture.

Rat and mice Neural Stem cell preparation. Neurospheres will be prepared as described by Duval et al. (2002). Brain embryos from mice will be mechanically dissociated in ice-cold HBSS (Ca^{2+}-and Mg^{2+}-free), and cells transferred to tissue culture dishes containing DMEM-F12 Ham's medium supplemented with 5% B27, 1% antibiotics, and 20 ng/ml EGF. Neuronal stem cells will grow as floating neurospheres. Cell differentiation will be induced by removing EGF from culture medium and plating the neurospheres on polylysine (10 μg/ml) and fibronectin-coated (10 μg/ml) glass-bottom microwells.

4.4.1.3 CSIC C57BL/6J mice and IP3/R2 null mice are available in the animal facility of Cajal Institute, and they will be used for in vitro, ex vivo and in vivo studies.

Spanish regulations: RD 53/2013, Experimentación Animal. Spanish Government; PROEX032_17, valid for 5 years.

Responsible of Animal facility at I. Cajal: Laudelina Garmendia (laude@cajal.csic.es).

Researcher in charge: Gertrudis Perea, PhD (gperea@cajal.csic.es)

The members of the Comité de Bioseguridad y Bioética of the Instituto Cajal (CSIC) have reviewed these protocols and certified that (1) they comply with current deontological codes and Spanish (RD 53/2013, Experimentación Animal. Spanish Goverment) and European legislation on bioethics and animal research (2010/63/UE); (2) the Instituto Cajal is fully equipped to guarantee the execution of the proposed research plan (WP2-6). The laboratories, common installations and animal house have the adequate safety level required by the national and European laws; (3) the methodology of the proposal is in accordance to the requirements of replacement, reduction and refinement; (4) the procedures have been designed to minimize suffering, pain and distress of the animals; (5) the methods of killing are designed according the Spanish and European laws; (6) anaesthesia and analgesia are contemplated and correctly proposed; and (7) all associate researchers conducting experiments with animals, including ESRs, will have the necessary training that will be supported by the corresponding training certificates. Furthermore, the electrophysiological, optogenetic/pharmacogenetic and behavioural procedures included in this ITN application, have been already approved by the Comunidad de Madrid, Spain (PROEX032_17, valid for 5 years). The three Rs have been incorporated into the application. Reduction: We have sought professional statistical and Ethical advice before submitting this grant application and the number of animals has been given to reduction. Furthermore, we have designed experiments so that more than one question is confronted in each animal, and implemented in a longitudinal design (several observations per animal) when possible. Replacement: We have explored non-animal alternatives for this project. However, the main aim of our work is to uncover the principles underlying information coding by neuron-glia networks and this will depend on experimentation involving animals. Neither computers nor tissue samples can fully imitate the complex interactions found in living organisms. Therefore, the use of animals in this project is absolutely necessary. Refinement: A particular emphasis will be paid to minimize the suffering of the animals. We will apply methods that will alleviate or minimize potential pain, suffering or distress to the animals, with specific attention to the behavioural testing, where animal welfare is a fundamental prerequisite to obtain valid results. WP3, 5 and 6 will be carry out following the Bioethical Committee of the CSIC and the Instituto Cajal, in complete accordance with Spanish Animal Regulations (RD 53/2013, Experimentación Animal).

Protocols and experimental approaches:

C57BL/6J mice. We foresee to employ adult mice (2-4 months) and new born mice to cover the need of primary neuronal cells and brain slices for all the planned experiments. For each dissection we will sacrifice the pregnant mother to isolate neurons from embryos, while brain slices will be dissected form adult mice. Considering that for C57Bl6/J females the average litter comprises of 5 embryos, the total number of animals to be used throughout the project can be estimated as follows: [(12 mothers / year) + (12*5= 60 embryos / year) + (24 adult / year)] * 3 years = 288, which involves both wildtype and transgenic mice.

Preparation of primary neuronal cultures. Cultured primary neurons are prepared from mouse embryos (embryonic stage E18) as previously described (Limongi, T. et al, Small 9, 402-412 (2013). Briefly, a dish containing HBSS. When all of the hippocampi have been removed, they are placed 15-ml conical centrifuge tube reaching the volume of 4.5 ml HBSS. Addition of 0.5 ml of 2.5% trypsin and incubation for 15 min in a water bath at 37 °C allow the dissociation of the tissues. Then, trypsin solution is gently removed, leaving the hippocampi at the bottom of the tube. Hippocampi are washed out twice using HBSS bringing the final volume to 2-3 ml. Mechanical dissociation is performed by repeatedly pipetting hippocampi up and down in a Pasteur pipette. After determination of cell density with a hemo-cytometer, neurons are plated on various substrates. According to the reducing principle, the estimated

number of animals will be reduced to a minimum by plating cells prepared from the same animals on different substrates/devices. Thanks to our long-term experience in culturing procedures the planned number of animals in three years is motivated by the need of daily accessing a few cell culture dishes of similar "age" (i.e. days-in-vitro). In fact, this will guarantee statistical significance and reproducibility of experimental results.

Preparation of acute brain slices. Animals will be anesthetized by halothane or CO2 and sacrificed by decapitation. The brains will be extracted and kept in artificial cerebrospinal fluid (ACSF) before cutting acute slices (350-400 mm thick), which will be incubated during 1 h in (ACSF) and then transferred to a recording chamber where they will be continuously perfused with this fluid and used for electrophysiological recordings.

Such slices are characterized by intact neuronal connections, which is a fundamental requisite for studying the physiological mechanisms of neuronal excitability and synaptic plasticity. Particular regions such as hippocampus and prefrontal cortex will be evaluated. G. Perea have previous experience with these experimental approaches, which will guarantee the unnecessary pain or distress of animals during procedures.

- Stress protocol. The unpredictable chronic mild stress (UCMS) protocol is one of the most realistic and well validated models of depression for the major depressive disorder (MDD) core symptom, called anhedonia (in humans) or anhedonia-like behaviour (in animals) [2]. UCMS consists by exposing mice to a relatively continuous variety of mild stressors, such as periods of food and water deprivation, changes of cage mates, tilted cages and other similarly innocuous manipulations during 3-4 hr daily for 8 weeks that induce long-lasting changes in behavioural, neurochemical and neuroendocrinology parameters [3]. Control groups will be manipulated with similar frequency without any additional stressor (UCMS).

- Behavioural tasks. Animals will perform several behavioural tasks to evaluate mood state and cognitive capabilities. i) Forced swimming test (FST): measurement of despair. ii) Sucrose preference test (SPT): considered as an index of anhedonia. SPT will be performed before (baseline) and after UCMS exposure, and FST will be performed after UCMS exposure to evaluate the depressive-like phenotype. iii) Open field tests: fewer entries to the centre area are indicative of more anxiety-like phenotype. iv) Social choice test: evaluate sociability and social novelty preference (novel vs familiar mouse). v) Alternation maze Test (Tmaze): based on the on the willingness of rodents to explore a new environment. This task is used to test reference and working memory in rodents. vi) Object-in-place test: recognition memory test in which mice discriminate between familiar objects at particular locations.

- Surgeries. For in vivo experiments mice will be anesthetized with isoflurane 1.5-2% in O_2 as necessary and placed in a stereotaxic apparatus. Body temperature will be maintained at 37.5ºC with a heating blanket. A craniotomy will be made over the prefrontal cortex or hippocampus and optical fiber will be implanted bilaterally, which will be cemented avoiding significant movement of the fiber during recovery and recordings. Antibiotics and painkiller will be administrated i.p during 3 days after surgery. Similar approach will be follow for viral injection: viral vectors will stereotaxically placed into regions of interest with a borosilicate glass micropipette, and a volume of 0.4-0.5 μl per hemisphere will be injected at 30 nl/min. After injection the skin will be sutured and we will allow mice to recover from anaesthesia before return to home cage.

- ***Viral constructs.*** For specific manipulation of astrocyte population activity, we will use viral transfection of melanopsin gene [4] into an adeno-associated virus (AAV) in both hemispheres in C57BL/6J and IP3/R2 null mice, and control mice and mice exposure to UCMS. 3 weeks after surgery, animals will be ready for *ex vivo* experiments and behavioural testing.

4.4.1.4 IEM CAS

All procedures involving the use of laboratory animals will be performed in accordance with the Council Directive 2010/63EU of the European Parliament and the Council of 22 September 2010 on the protection of animals used for scientific purposes and with animal care guidelines approved by the Institute of Experimental Medicine, Academy of Sciences of the Czech Republic (Animal Care Committee on April 7, 2011; approval number 74/2018, 40/2019, 49/2019, 84/2019). All efforts will be made to minimize both the suffering and the number of animals used. In order to minimize the number of experimental animals, the experiments will be planed so as to collect sufficient data for statistical analysis, taking into account the sample sizes of similar studies previously published in international, indexed journals. Individual experiments are designed after verification in medical databases (www.pubmed.com, EBSCO, www.webofknowledge.com) to avoid unjustified repetition of animal experiments.

Animal models : ***Constitutive Aquaporin-4 knockout mice*** (RBRC04399**;** RikenBRC, Tsukuba, Japan), in which Aqp4 gene is interrupted by neomycin insert [5]. These mice are now routinely bred in the Department of Cellular Neurophysiology, IEM AS CR. ***Constitutive Trpv4 knockout mice - trpv4$^{-/-}$ mice*** – these mice were kindly provided from dr. Liedtke (Duke University, Durham, USA) and are now routinely bred and used in our department [6]. ***Conditional, inducible trpv4 knockout mice – trpv4$^{lox/lox}$ mice*** – these mice will be generated in Biocev, in the Czech Centre of Phenogenomics. When crossed with tamoxifen-dependent, cell-specific Cre-driver mice, the littermates will, after tamoxifen administration, show recombination in Cre-expressing cells leading to *trpv4* gene deletion followed by cessation of TRPV4 channels expression in specific cell types. ***Cspg4-creER^{TM} mice*** – B6.Cg-Tg(Cspg4-

cre/Esr1*)BAkik/J (Jackson Laboratory, Bar Harbor, Maine, USA) mice in which Cre recombinase is expressed under the chondroitin sulfate proteoglycan (Cspg4) promotor. After breeding with reporter mice (B6/12956-Gt(ROSA)26Sortm14(CAG-td-Tomato)Hze/J), NG2-positive cells express Tom after tamoxifen administration and remain Tom+ (further identified as Cspg4/Tom). Moreover, they will be used to create conditional *Trpv4* deletion in oligodendrocyte precursors (NG2 cells). These mice are now routinely bred and used in our department. ***Pdgfra-creER^{TM} mice*** – B6N.Cg-Tg(Pdgfra-cre/ERT)467Dbe/J (Jackson Laboratory, Bar Harbor, Maine, USA) will be used to create conditional *Trpv4* deletion in oligodendrocyte precursors (NG2 cells). They are now routinely bred and used in our department. ***GFAP-creER^{TM} mice*** – B6.Cg-Tg(GFAP-cre/ERT2)505Fmv/J (Jackson Laboratory, Bar Harbor, Maine, USA) mice express tamoxifen-inducible Cre recombinase under the control of human glial fibrillary acidic protein promoter sequence. These mice will be used to create conditional *Trpv4* deletion in astrocytes. They will be purchased from Jackson Laboratory. ***Camk2a-CreERT2 transgenic mice*** - B6;129S6-Tg(Camk2a-cre/ERT2)1Aibs/J (Jackson Laboratory, Bar Harbor, Maine, USA) mice express tamoxifen-inducible Cre recombinase under the control of the mouse Camk2a (calcium/calmodulin-dependent protein kinase II alpha) promoter region, and may be useful for generating conditional mutations for studying gain or loss of function and/or fate mapping in subgroups of Camk2a-expressing neural tissues (including cortex, hippocampus, striatum, and other structures). They will be purchased from Jackson Laboratory. ***Tomato (Tom) mice*** - B6;129S6-Gt(ROSA)26Sortm14 (CAG-tdTomato)Hze/J (Jackson Laboratory). These Cre reporter mice harbor a loxP-flanked STOP cassette preventing transcription of a CAG promoter-driven red fluorescent protein variant (tdTomato). TdTomato is expressed when bred to mice that express Cre recombinase. These mice thus allow the visualization of Cre expressing cells after tamoxifen administration. These mice are routinely bred in Department of Cellular Neurophysiology, IEM AS CR.

Number of animals planned to be employed: ~150 mice per year

Tamoxifen administration To activate tamoxifen-dependent Cre-recombinase, two 200 μl doses of tamoxifen will be administered intraperitoneally (20 mg / kg corn oil), the second dose 24 hours after the first one.

Models of cerebral ischemia ***Middle cerebral artery occlusion (MCAO):*** Mice (40–70 days old) will be anaesthetized with 2% Isoflurane using a vaporizer. A skin incision between the orbit and the external auditory meatus will be made. A 1–2 mm hole will be drilled through the frontal bone 1 mm rostral to the fusion of the zygoma and the squamosal bone and about 3.5 mm ventral to the dorsal surface of the brain. The middle cerebral artery (MCA) will be exposed after the dura is opened and removed. The MCA will be occluded by short coagulation with bipolar tweezers at a proximal location, followed by transection of the vessel to ensure permanent disruption. Sham operated animals (controls) will be subjected to same surgery procedure, without vessel occlusion. ***Transient global cerebral ischemia:*** In the first part, mice (40–70 days old) will be anaesthetized with 2% Isoflurane using a vaporizer. A skin incision on ventral part of neck will be made and basilar artery will be occluded by short coagulation with bipolar tweezers. After one week, a bilateral common carotid occlusion will be performed for 10 minutes. Sham operated animals (controls) will be subjected to same surgery procedure, without vessel occlusion.

Preparation of brain slices for 3D morphometry, electrophysiology and Ca^{2+} imaging *in situ* Brain slices will be prepared from post-ischemic as well as sham-operated transgenic mice at different times after ischemia. Animals will be transcardially perfused with ice-cold artificial cerebrospinal fluid (aCSF) under the deep pentobarbital anesthesia (100 mg/kg) and then decapitated. The brain will be quickly removed from the skull and washed with ice-cold aCSF solution. Then the tissue will be cut into 200-300 μm thick slices on a vibratome. Immediately after cutting, the slices will be incubated in oxygenated aCSF (34ºC) for one hour and then kept in oxygenated aCSF solution at room temperature.

Morphological and immunohistochemical analysis Non-ischemic and ischemic brains will be isolated after the transcardial perfusion under the deep pentobarbital anesthesia (100 mg/kg) with 4% paraformaldehyde. The brain will be removed from the skull and postfixed with 4% paraformaldehyde over night. Then the tissue will be cut into 30 μm thick slices.

Cranial window Mouse will be anaesthetized with 2% Isoflurane and placed on a stereotaxic apparatus during surgery. A small oval piece of skin together with underlying muscles will be cut out to expose the skull over the target area for the window. A thin layer of cyanoacrylate glue over the entire surface of the skull will be applied, except over a circular region where the window will be placed. Using a dental drill a round portion (2 mm in diameter) of the skull will be carefully carved out. The skull overlying the cortex will be removed with the utmost care so as not to damage the underlying dura. A round cover glass (3 mm in diameter) will be placed over the exposed dura. Fresh cyanoacrylate glue will be applied to the edges of the window to seal it in place. Dental cement will be applied around the glass and to the edges of the skin.

4.4.1.5 AMU National agreement: C 14 118 001, 16.12.2005. (general agreement, a common approval for all animal studies performed at cyceron) Décret n° 87-848 du 19 octobre 1987 pris pour l'application de l'article 454 du code pénal et du troisième alinéa de l'article 276 du code rural et relatif aux expériences pratiquées sur les animaux.

Décret n° 2001-464 du 29 mai 2001 modifiant le décret n° 87-848 pris pour l'application de l'article 454 du code

pénal et du troisième alinéa 276 du code rural et relatif aux expériences pratiquées sur les animaux. Décret n° 2001-131 du 6 février 2001 portant publication de la Convention européenne sur la protection des animaux vertébrés utilisés à des fins expérimentales ou à d'autres fins scientifiques adoptée à Strasbourg le 18 mars 1986 et signée par la France le 2 septembre 1987. In France, legislation requires an institutional and project license before testing on vertebrates is carried out. An institution must submit details of their facilities and the reason for the experiments, after which a five- year license may be granted following an inspection of the premises. The project licensee must be trained and educated to an appropriate level. Personal licenses are not required for individuals working under the supervision of a project license holder. These regulations do not apply to research using invertebrates.

Dr. Pascale Quilichini, a senior permanent researcher of the Bernard group involved in this project is legally authorized by French Authorities to conceive and perform experimental protocols involving animals. Antoine Ghestem and Anton Ivanov, engineers with permanent positions in charge of the *in vivo* and *in vitro* platforms in the Bernard group, respectively, have a similar authorization. The principles of Reduction, Refinement and Replacement (the 'three Rs') will be applied to animal experiments. The AMU laboratory is inspected and certified for accordance with the OECD principles of good laboratory practice. Power analyses will be carried out by qualified biostatisticians to ensure that the minimal, but meaningful, number of animals is used in a given experiment. Specifically, for each experiment, the number of animals to be used will be calculated to avoid type I errors with an alpha level <0.05 and type II errors, at a statistical power of 0.8. We anticipate a total number of 50 animals for *in vivo* experiments. The *in vivo* experiments are similar to those already approved for the ongoing ITN m-Gate, in which AMU mentors two ESRs.

4.4.1.6 INEB In the context of the proposed work, animals – Wistar rats - will be use as a source of primary cells to conduct the experiments proposed in the work program of ESR 9 - INEB. This will work will be conducted in the premises of INEB/i3S. All procedures involving animals and their care will be conducted in conformity with institutional guidelines in compliance with national (Decreto-Lei 113/2013, which is the national transposition of the European Directive 2010/63/EU) laws and policies. The Animal Facility of the i3S is licensed by the Portuguese official veterinary department (*Direccão Geral de Alimentação e Veterinaria* - DGAV), complies with the Portuguese law (*Portaria 1005/02* and *Portaria 1131/97*), the European Directive 2010/63/EU, and follows the FELASA (Federation of European Laboratory Animal Science Associations) guidelines and recommendations concerning laboratory animal welfare. In the present project, Wistar Rats will be used as a source of primary astrocytes and no other procedures will be conducted. Consequently, the Research projects need to be solely evaluated by the Institute ethical committee. All experimental protocols, including anaesthesia and euthanasia will be carried out with the prior written approval and supervision of the constituted Institutional Animal Care and Use (Ethics) Committee.

These procedures ensure that, in accordance with the ***Russel and Burch 3R's principle*****,** alternatives to animals are used whenever possible (replacement), that the number of animals is minimized (reduction), and that any suffering or other harmful effects experienced by the animals are minimized (refinement) and have been weighed against the potential benefits to humans or animals. ***Replacement and Reduction*** The biocompatibility of the developed alginate hydrogels will be initially evaluated with astrocyte cell lines (A7 cell line – rat astrocyte). Only the most promising materials will be tested with primary astrocyte cultures (obtained from rat pups). In this manner one will reduce to the minimum the use of animals in the current project. ***Refinement*** Astrocyte primary cultures, will be obtained from post-natal day 2 (P2) Wistar rat pups, according to a previously described process [7]. Animals will be kept under experimental conditions a maximum of 2 days. In brief, Wistar Han rat pups in P2 will be sacrificed by decapitation and brain removed to further dissociate the cortex and the meningeal tissue. Approximately 8-16 pups will be sacrificed every two weeks (for a period of 2 years). Removal of brain will be performed using straight micro-scissors and fine forceps. The procedure will be conducted under a magnifying glass in a Petri dish containing Hank's Balanced Salt Solution (HBSS, Gibbco) without calcium and magnesium supplemented with 2% (v/v) penicillin/streptomycin. Firstly, the skin of the head will be cut until the nose with a sharper scissor with the other hand holding the head (from the ear) with big forceps. The skin will be opened to the corners in order to let the skull bones be visible. Then, with a straight microscissor, the skull bone will be cut until the nose and to the sides. The bones will be removed with thinner forceps and a special care will be taken to not damage the cortex. With the same forceps, the cortex will be carefully removed (from the olfactive bulbs) and cut by the cerebellum. Subsequently, using thinner forceps, the two hemispheres will be separated and the meningeal tissue detached from the cortex. Isolated cortices will be digested in HBSS without calcium or magnesium, supplemented with papain(0.2U/ml), for 30min.Dissociated cortices will be cultured in 75cm2 flasks and maintained in DMEM supplemented with 10% (v/v) FBS and 1 % (v/v) PS. When confluence will be reached (~12days) the flasks will be shaken overnight on an orbital shaker (240rpm) at 37◦C to remove loosely attached microglia, oligodendrocytes and neurons. The remaining cells, mainly astrocytes, adhered to the 75cm2 flasks will be then trypsinized and cultured in new flasks. Further, tripsinizations will be performed in order to increase culture purity.

All rats will be bred and/or maintained in accordance with the European and institutional guidelines. All persons handling them are specially trained for the appropriate procedures. Animal housing and experimentation are under

constant monitoring from the veterinary in charge, to ensure that all handling and interventions are performed according to suitable and humane techniques.
Furthermore, animal experimentation will be performed only by trained researchers with the FELASA B or C Laboratory Animal Science accredited course. Our ESR will obtain the necessary certification to conduct the proposed experiments in year 1 of his/her contract. All the certificates of involved researchers will be kept on file and will be provided upon request.
Prior the start of the experiments involving animal use all the necessary ethical approvals will be obtained and kept on file. These will be provided to REA upon request.
4.4.1.6 UCAM We will minimize the total number of animals needed by optimizing the implant designs using computer modeling and in vitro tissue engineering whenever applicable. *We will engage to respect the 3Rs principles to the full.* All animal experiments will be carried out in accordance with EU (2010/63/UE) and UK (Animals Scientific Procedure Act of 1986) guidelines on animal research. Approval from the Home Office is currently pending for the UCAM partner for possible in vivo experiments (led by Prof. G. Malliaras). For experiments on animal tissue ex vivo, tissue will be removed from previously committed rodents post mortem. Mice/Rats will be killed using a schedule 1 method, brain tissue removed (after death) and taken back to the lab where it will remain perfused for 48 hours. This is considered a non-regulated use of an animal. Before commencing animal experiments at a particular partner site, the partner will provide all required documents, including:

- Copies of project authorizations obtained from Home Office and ethical committees to conduct animal experiments
- Copies of the agreements and establishment authorisation of the facilities housing the animal experiments.
- Copies of training certificates/personal licenses of the staff involved in animal experiments.

4.5 ENVIRONMENTAL PROTECTION AND SAFETY
Animal experimentations may involve the use of genetically modified animals (rats, mice), viral vectors and other methods to genetically and molecularly manipulate animal tissue.
All these procedures take place according to national regulations, upon the authorization of the relevant regulatory bodies. When required, activities are carried out in safety-certified facilities (Cf CSIC documents available in ASTROTECH ETHICS folder). All authorizations and certifications for procedures and facilities are on file and available upon request.
The project has some ethic issues related to health and safety of workers.
The possible harm to humans is related to the tasks proposed by the partner AVA, due to the use of nanomaterials. Before the beginning of activities potentially involving health and safety for staff involved, in compliance with the advice of the EU Commission Ethics Review Summary t, AVA proposes the following measures:

- AVA will follow the health and safety legislation stablished by the Spanish Government regarding the use of hazard substances. These measures are already implemented in their facilities.
- AVA will work in ASTROTECH project following the recommendations of European Commission Recommendation of 07/02/2008 on a Code of Conduct for a Responsible Nanosciences and Nanotechnologies Research and Second Regulatory Review on Nanomaterials. Moreover, AVA is involved in different Committees regarding the use of nanomaterials (ISO/TC 229, CEN/TC 352 and AEN/GET 15), and it is a partner in the EU project NANOUPTAKE.

AVA confirm that recommendations of EU-OSHA on safety in the workplace while using nanomaterials will be ensured (https://osha.europa.eu/en/tools-and-publications/publications/e-facts/e-fact-72-toolsfor-themanagement-of-nanomaterials-in-the-workplace-and-prevention-measures).

References [1] A. Gustavsson et al., Eur Neuro Psychopharmacol., 22, 2012. [2] A. Verkhratsky et al., Brain Pathol., 5, 2017. [3] V. Benfenati et al., Neurosci., 2010. [4] A. Chvátal et al., Physiol. Res. 2008. [5] A. Verkhratsky, ASN Neuro., 4, 2012. [6] World Health Org., 2016. [7] A. L. G. Mestre et al., Sci Rep., 7, 2017. [8] M. David-Pur et al., Biomed. Microdev., 16, 2014. [9] T. Cohen- Karni et al., Nano. Lett., 12, 2012. [10] F. Patolsky et al., Science, 313, 2006. [11] J. T. Robinson et al., Nat. Nanotech.,7, 2012. [12] M. Kwak et al., Small, 11, 2015. [13] G. Hong et al., Nat. Rev. Neurosci., 20, 2019. [14] J. Rivnay et al., Sci. Adv., 3, 2017. [15] D. Khodagholy et al., Nature Neurosci.18, 2015. [16] D. Khodagholy et al., Nature Comm., 4, 2013. 15b] D. Khodagholyet al., Nature Neurosci. 18, 310 (2015). [16b] V. Benfenati et al., Nat. Mat., 7, 2013. [17] D., Khodagholy et al., Adv Mater., 36, 2011. [18] J. Rivnay et al., Nature Rev. Mater, 3, 2018. [19] J. Rivnay et al., Sci, Adv., 4, 2015. [20] A. Borrachero-Conejo et al., Adv. Healthc. Mater., 8, 2019. [21] A.Williamson et al., Adv Mater. 30, 2015. [22] A. Jonsson et al., Proc. Natl. Acad Sci U S A, 34, 2016. [23] M. J. Donahue et al., Neuro., 5, 2018. [24] L. Kergoat et al., Eng. Med. BiolSoc., 2018. [25] C.M. Proctor et al., Sci Adv., 8, 2018. [26] J.J. Pas et al., Neural Eng., 6, 2018. [27] I. Uguz et al., Adv. Healthc. Mater., 24, 2016. [28] H. Kumar et al., Mol. Neurobiol. 55, 2018. [30] A. Moghaddam et al., Nat. Rev. Neurosci. 4, 2003. [31] A.O. Jo et al., J. Neurosci. 35, 2015. [32] C. Rakers et al., Glia , 65, 2017. [33] O. Butenko et al., PLoS One, 7, 2012. [34] M. Chmelova, et al., Eur. J. Neurosci, 2019. [35] V. Benfenati et al., Proc. Natl. Acad. Sci. USA, 108, 2011. [36] V. Benfenati et al., Adv. Health. Mater., 3, 2014. [37] A.C. Thompson et al., Curr. Mol. Imaging 3, 2014. [38] D. Ghezzi et al., Nat. Commun. 2, 2011. [39] S. Mederos et al., Meth. Mol Biol., 2019. [40] T. Posati et al., Sci. Rep., 6, 2016. [41] D.N. Rocha et al., Front. Cell. Neurosci. 9, 2015. [42] V. K. Jirsa et al., Brain 137, 2014. [43] T. Proix et al., J Neurosci 34, 2014. [44] J.C. Frisbee et. al., J Vis Exp. 106, 2015. [45] V. Guarino et al. Nanotech., 28, 2017. [46] F. Melozzi et al., Proc. Natl. Acad. Sci. USA, 2019. [47] V. Benfenati, AFOSR-ASTROMAT-FA9550-16-1-0502, V. Benfenati, AFOSR ASTRONIR-FA9550-17-1-0052, V. Guarino, AFOSR-3D NEUROGLIA- FA9550-18-1-0255. [48] Muramatsu et al., 2013, Neurons. Bio-protocol 3(8): e496. DOI: 10.21769/BioProtoc.496. [49] Frisbee, J. C., Brooks, S. D., Stanley, S. C. & d'Audiffret, A. C. An Unpredictable Chronic Mild Stress Protocol for Instigating Depressive Symptoms, Behavioral Changes and Negative Health Outcomes in Rodents. J Vis Exp, doi:10.3791/53109 (2015). [50] Willner, P. Chronic mild stress (CMS) revisited: consistency and behavioural-neurobiological concordance in the effects of CMS. Neuropsychobiology 52, 90-110, doi:10.1159/000087097 (2005). [51] Mederos, S. et al. Melanopsin for precise optogenetic activation of astrocyte-neuron networks. Glia 67, 915-934, doi:10.1002/glia.23580 (2019). [52] Ikeshima-Kataoka, H., Abe, Y., Abe, T., & Yasui, M. (2013). Immunological function of aquaporin-4 in stab-wounded mouse brain in concert with a pro-inflammatory cytokine inducer, osteopontin. Mol Cell Neurosci, 56, 65-75. doi: S1044-7431(13)00020-1 [pii]10.1016/j.mcn.2013.02.002 [53] O'Conor, C. J., Ramalingam, S., Zelenski, N. A., Benefield, H. C., Rigo, I., Little, D., et al. (2016). Cartilage-Specific Knockout of the Mechanosensory Ion Channel TRPV4 Decreases Age-Related Osteoarthritis. Sci Rep, 6, 29053. doi: 10.1038/srep29053. [54] Rocha DN, Ferraz-Nogueira JP, Barrias CC, Relvas JB, Pêgo AP. Extracellular environment contribution to astrogliosis-lessons learned from a tissue engineered 3D model of the glial scar. Front Cell Neurosci. 2015; 9. [55] Gustavsson et al., 2012 "Cost of disorders of Brain in Europe", Eur Neuropsychopharmacol. 2012 Mar;22(3):237-8

ESTIMATED BUDGET FOR THE ACTION

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			Estimated eligible[1] costs (per budget category)											EU contribution		
			A. Costs for recruited researchers						B. Institutional costs				Total costs	Reimburse-ment rate %	Maximum EU contribution[2]	Maximum grant amount[3]
			A.1 Living allowance		A.2 Mobility allowance		A.3 Family allowance		B.1 Research, training and networking costs		B.2 Management and indirect[4] costs					
	Number of units (person-months)	Form of costs[5]	Unit		Unit		Unit		Unit		Unit					
			Costs per unit[6]	Total a[7]	Costs per unit[6]	Total b[7]	Costs per unit[6,8]	Total c[7]	Costs per unit[6]	Total d[7]	Costs per unit[6]	Total e[7]	f = a+b +c+d+e	g	h	i
1. CNR	108.00		3 413.88	368 699.04	600.00	64 800.00	250.00	27 000.00	1 800.00	194 400.00	1 200.00	129 600.00	784 499.04	100.00	784 499.04	n/a
2. UCAM	36.00		4 571.46	164 572.56	600.00	21 600.00	250.00	9 000.00	1 800.00	64 800.00	1 200.00	43 200.00	303 172.56	100.00	303 172.56	n/a
3. UEM AVCR	36.00		2 674.21	96 271.56	600.00	21 600.00	250.00	9 000.00	1 800.00	64 800.00	1 200.00	43 200.00	234 871.56	100.00	234 871.56	n/a
4. AMU	72.00		3 783.39	272 404.08	600.00	43 200.00	250.00	18 000.00	1 800.00	129 600.00	1 200.00	86 400.00	549 604.08	100.00	549 604.08	n/a
5. BCAM	36.00		3 119.58	112 304.88	600.00	21 600.00	250.00	9 000.00	1 800.00	64 800.00	1 200.00	43 200.00	250 904.88	100.00	250 904.88	n/a
6. INEB	36.00		2 753.34	99 120.24	600.00	21 600.00	250.00	9 000.00	1 800.00	64 800.00	1 200.00	43 200.00	237 720.24	100.00	237 720.24	n/a
7. UNIBA	36.00		3 413.88	122 899.68	600.00	21 600.00	250.00	9 000.00	1 800.00	64 800.00	1 200.00	43 200.00	261 499.68	100.00	261 499.68	n/a
8. IIT	36.00		3 413.88	122 899.68	600.00	21 600.00	250.00	9 000.00	1 800.00	64 800.00	1 200.00	43 200.00	261 499.68	100.00	261 499.68	n/a
9. CSIC	36.00		3 119.58	112 304.88	600.00	21 600.00	250.00	9 000.00	1 800.00	64 800.00	1 200.00	43 200.00	250 904.88	100.00	250 904.88	n/a
10. AVA	36.00		3 119.58	112 304.88	600.00	21 600.00	250.00	9 000.00	1 800.00	64 800.00	1 200.00	43 200.00	250 904.88	100.00	250 904.88	n/a
11. OPTOCEUTICS	72.00		4 414.50	317 844.00	600.00	43 200.00	250.00	18 000.00	1 800.00	129 600.00	1 200.00	86 400.00	595 044.00	100.00	595 044.00	n/a
Total consortium	540.00		n/a	1 901 625.48	n/a	324 000.00	n/a	135 000.00	n/a	972 000.00	n/a	648 000.00	3 980 625.48	100.00	3 980 625.48	3 980 625.48

[1] See Article 6 for the eligibility conditions.
[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), unless it can demonstrate that the operating grant does not cover any costs of the action.
[5] See Article 5 for the forms of costs.

ESTIMATED BUDGET FOR THE ACTION

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[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).
[8] The amount for the family allowance inserted by the system represents an average (with/without family). For the financial statements (Annex 4), this amount will be adjusted according to the actual family status of the recruited researchers (as specified in the 'researcher declaration').

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

MSCA-ITN unit costs

Costs for the recruited researcher(s) — Living allowance

Units: months spent by the researcher(s) on the research training activities ('person-months')

Amount per unit *: see Annex 2

* Amount calculated as follows:
{the monthly living allowance for researchers in MSCA-ITN actions
multiplied by
country-specific correction coefficient of the country in which the researcher is recruited}

The monthly living allowance and the country-specific correction coefficients are set out in the Work Programme (section 3 MSCA) in force at the time of the call:

- for calls *before* Work Programme 2018-2020:
  - for the monthly living allowance:
    - ITN: **EUR 3 110**
  - for the country-specific correction coefficients: see Work Programme 2014-2015 and Work Programme 2016-2017 (available on the Participant Portal Reference Documents page)
- for calls *under* Work Programme 2018-2020:
  - for the monthly living allowance:
    - ITN: **EUR 3 270**
  - for the country-specific correction coefficients: see Work Programme 2018-2020 (available on the Participant Portal Reference Documents page).

Estimated number of units: see Annex 2

Costs for the recruited researcher(s) — Mobility allowance

Units: months spent by the researcher(s) on the research training activities ('person-months')

Amount per unit[1]: see Annex 2

Estimated number of units: see Annex 2

[1] Same amount for all beneficiaries.
Amount for the mobility allowance set out in the Main Work Programme — MSCA in force at the time of the call.

Costs for the recruited researcher(s) — Family allowance

Units: months spent by the researcher(s) on the research training activities ('person-months')

Amount per unit[2]: see Annex 2

Estimated number of units: see Annex 2

Institutional costs — Research, training and networking costs

Units: months spent by the researcher(s) on the research training activities ('person-months')

Amount per unit[3]: see Annex 2

Estimated number of units: see Annex 2

Institutional costs — Management and indirect costs

Units: months spent by the researcher(s) on the research training activities ('person-months')

Amount per unit[4]: see Annex 2

Estimated number of units: see Annex 2

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2 Same amount for all beneficiaries.
Average based on the amount for the family allowance set out in the Main Work Programme — MSCA in force at the time of the call (half of the number of units with family, half without).

3 Same amount for all beneficiaries.
Amount for research, training and networking costs set out in the Main Work Programme — MSCA in force at the time of the call.

4 Same amount for all beneficiaries.
Amount for management and indirect costs set out in the Main Work Programme — MSCA in force at the time of the call.

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

THE CHANCELLOR MASTERS AND SCHOLARSOF THE UNIVERSITY OF CAMBRIDGE (UCAM), established in TRINITY LANE THE OLD SCHOOLS, CAMBRIDGE CB2 1TN, United Kingdom, VAT number: GB823847609, ('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 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

USTAV EXPERIMENTALNI MEDICINY AKADEMIE VED CESKE REPUBLIKY VEREJNA VYZKUMNA INSTITUCE (UEM AVCR), established in VIDENSKA 1083, PRAHA 4 14220, Czech Republic, VAT number: CZ68378041, ('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 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITE D'AIX MARSEILLE (AMU), established in Boulevard Charles Livon 58, Marseille 13284, France, VAT number: FR84130015332, ('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 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BCAM - BASQUE CENTER FOR APPLIED MATHEMATICS (BCAM), established in AL MAZARREDO 14, BILBAO 48009, Spain, VAT number: ESG95543526, ('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 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INEB-INSTITUTO NACIONAL DE ENGENHARIA BIOMEDICA (INEB), established in RUA ALFREDO ALLEN 208, PORTO 4200 135, Portugal, VAT number: PT502312220, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('6')

in Grant Agreement No 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITA DEGLI STUDI DI BARI ALDO MORO (UNIBA), established in PIAZZA UMBERTO I 1, BARI 70121, Italy, VAT number: IT01086760723, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('7')

in Grant Agreement No 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FONDAZIONE ISTITUTO ITALIANO DI TECNOLOGIA (IIT), established in VIA MOREGO 30, GENOVA 16163, Italy, VAT number: IT09198791007, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('8')

in Grant Agreement No 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

AGENCIA ESTATAL CONSEJO SUPERIOR DEINVESTIGACIONES CIENTIFICAS (CSIC), established in CALLE SERRANO 117, MADRID 28006, Spain, VAT number: ESQ2818002D, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('9')

in Grant Agreement No 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

AVANZARE INNOVACION TECNOLOGICA SL (AVA), established in AVENIDA LENTISCARES 4 6, NAVARRETE 26370, Spain, VAT number: ESB26370908, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('10')

in Grant Agreement No 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

OPTOCEUTICS APS (OPTOCEUTICS), established in DIPLOMVEJ 381, KONGENS LYNGBY 2800, Denmark, VAT number: DK39769689, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('11')

in Grant Agreement No 956325 ('the Agreement')

between CONSIGLIO NAZIONALE DELLE RICERCHE **and** the Research Executive Agency (REA) ('the Agency'), under the powers delegated by the European Commission ('the Commission'),

for the action entitled 'Disruptive materials, technologies & approaches to unravel the role of Astrocytes in brain function and dysfunction: towards to Glial interfaces (ASTROTECH)'.

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

ⓘ print format A4

MODEL ANNEX 4 FOR H2020 MGA MSCA-ITN — MULTI

FINANCIAL STATEMENT FOR BENEFICIARY [name] FOR REPORTING PERIOD [reporting period]

Name of the fellows [6]	Number of units (person-months)
Total beneficiary	

	Eligible [1] costs (per budget category)											EU contribution		
	A. Costs for recruited researchers						B. Institutional costs				Total costs	Reimbursement rate %	Maximum EU contribution	Requested EU contribution
	A.1 Living allowance		A.2 Mobility allowance		A.3 Family allowance		B.1. Research, training and networking costs		B2. Management and indirect [2] costs					
Form of costs [3]	Unit		Unit		Unit		Unit		Unit					
	Costs per unit [4]	Total a [5]	Costs per unit [4]	Total b5	Costs per unit [4]	Total c [5]	Costs per unit [4]	Total d [5]	Costs per unit [4]	Total e [5]	f = a+b+c+d+e	g	h	i
Total beneficiary														

Checkbox 1:	I confirm that the total amount of the allowances used (including compulsory deductions) for the researcher is equal to or higher than the living allowance, the mobility allowance and the family allowance as set out in Annex 2 of the Agreement or that any underpayments in reporting period 1 will be corrected by the end of the action.

Checkbox 2:	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?		Number of person-months	
	If yes, can you confirm all of the following: - the operating grant is a partial operating grant (i.e. does not cover your entire annual budget) - you have used analytical accounting which allows for a cost accounting management with cost allocation keys and cost accounting codes - you have recorded: - all costs incurred for the operating grant (i.e. personnel, general running costs and other operating costs linked to the work programme) and - all costs incurred for the action grants (including the indirect costs linked to the action)~~ion)~~ - you have used allocation keys and cost accounting codes to identify and separate the recorded costs (i.e. to allocate them to either the action grant or the operating grant) - you have done the allocation in a way that leads to a fair, objective, realistic result.		❍ YES ❍ NO	

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 person-months, even if you exceed the estimated budget (see Annex 2). Only person-months that were declared in your individual financial statements can be taken into account lateron, in order to replace other costs that are found to be ineligible.

[1] See Article 6 for the eligibility conditions

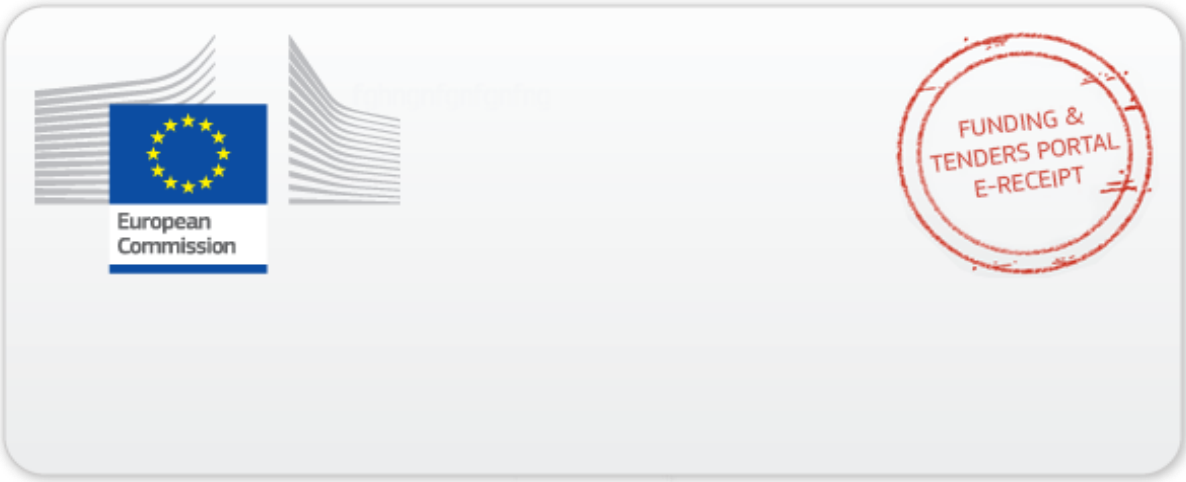
[2] The indirect costs claimed must be free of any amounts covered by an operating grant (received under any EU or Euratom funding programme; see Article 6.3(b)). If you have received an operating grant during this reporting period, indirect costs will not be reimbursed for the person-months incurred during the period covered by the operating grant, unless you can demonstrate that the operating grant does not cover any costs of the action.

[3] See Article 5 for the forms 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)

[6] Name of the researcher and related units for living (A.1) and family (A.3) allowances will be prefilled on the basis of the information provided by the beneficiary in the 'researcher declaration'



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