IMI2 821513 – NEURONET

Efficiently Networking European Neurodegeneration Research

WP2 – Programme Integration

D2.3 Report #2 on activity of SCB, WGs and TFs.

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Contents

Document history

Version	Date	Description
V1	20/01/2021	Outline
V1.1	28/01/2021	First draft for discussion
V1.2	15/03/2021	Comments and updates on the Task Forces.
V1.3	30/04/2021	Additional information to capture the summary of last SCB meeting (22/03/2021)
V1.4	27/05/2021	Additional information to capture the summary of last sustainability WG (20/05/2021)
V1.5	04/06/2021	Final version

Definitions

Partners of the NEURONET Consortium are referred to herein according to the following codes:

1. SYNAPSE: Synapse Research Management Partners SL
2. NICE: National Institute for Health and Care Excellence
3. AE: Alzheimer Europe
4. JANSSEN: Janssen Pharmaceutica NV
5. LILLY: Eli Lilly and Company Limited
6. ROCHE: F. Hoffman – La Roche AG
7. SARD: Sanofi-Aventis Recherche & Développement
8. PUK: Parkinson's Disease Society of the United Kingdom LBG
10. TAKEDA AG: Takeda Pharmaceuticals International AG

Consortium: The NEURONET Consortium, comprising the above-mentioned legal entities.

Consortium Agreement: Agreement concluded amongst NEURONET participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

CSA: Coordination and Support Action.

Grant Agreement: The agreement signed between the beneficiaries and the IMI JU for the undertaking of the NEURONET project.

IMI: Innovative Medicines Initiative.

ND: Neurodegenerative Disorders.

Project: The sum of all activities carried out in the framework of the Grant Agreement.

SCB: Scientific Coordination Board.

SGG: Strategic Governing Group.

TF: Task Force.

WG: Working Group.

WP: Work Package.

Work plan: Schedule of tasks, deliverables, efforts, dates and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.

Abstract

The NEURONET Coordination and Support Action has the main objective of setting up an efficient platform to boost synergy and collaboration across the IMI projects of the Neurodegenerative Disorders portfolio, assisting in identifying its gaps, multiplying its impact, enhancing its visibility and facilitating dovetailing with related initiatives in Europe and worldwide.

Deliverable D2.3 *Report #2 on activity of SCB, WGs and TFs* constitutes a report on the activities of the Scientific Coordination Board, the four Working Groups, and two new Task Forces from March 2020 until the end of April 2021.

1. Introduction

NEURONET is the Innovative Medicines Initiative (IMI) Coordination and Support Action (CSA) aiming to support and better integrate projects in the IMI Neurodegenerative Disorders (ND) portfolio. The primary objective of the NEURONET CSA is to establish an efficient platform to drive synergy and collaboration across IMI ND projects, multiplying their impact, enhancing their visibility and facilitating dovetailing with related initiatives both in Europe and the rest of the world.

NEURONET is built around 5 Work Packages (WP) as shown in Figure 1.

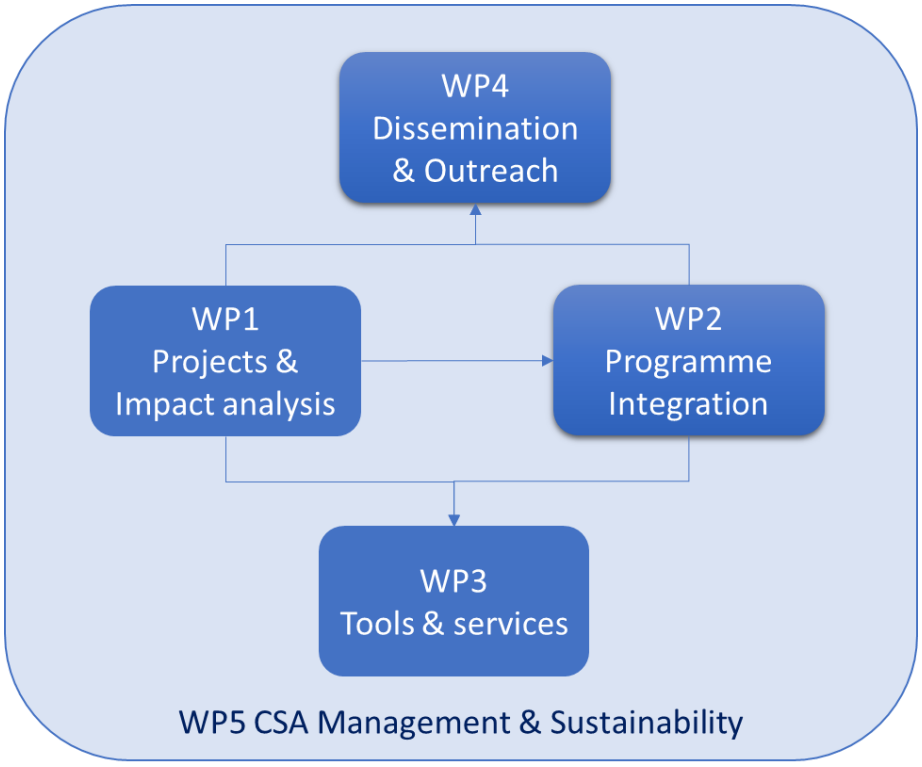

Figure 1. NEURONET WPs

WP2 Programme Integration is responsible for creating and implementing the governance and organisational structures of NEURONET, including the definition of associated workflows and procedures.

The first task in this WP (*Task 2.1: Set up and maintenance of NEURONET structures, procedures and workflows for programme management*), entailed defining the terms and procedures for the creation of the Scientific Coordination Board (SCB) Working Groups (WGs) and Task Forces (TFs) that complement NEURONET's own governance structure, as reported in deliverable D2.1 *Report on establishment and procedures of SCB and foundational WGs*.

Figure 2 below provides a graphical view of the conceptual project design, with NEURONET providing the core connections between projects through the SCB, WGs and Task Forces (TFs), and acting as a link to external initiatives beyond IMI. All three bodies are conceived as open structures, therefore catering for new projects in the IMI pipeline and potentially including representatives from external initiatives or other stakeholders with whom NEURONET may want to collaborate.

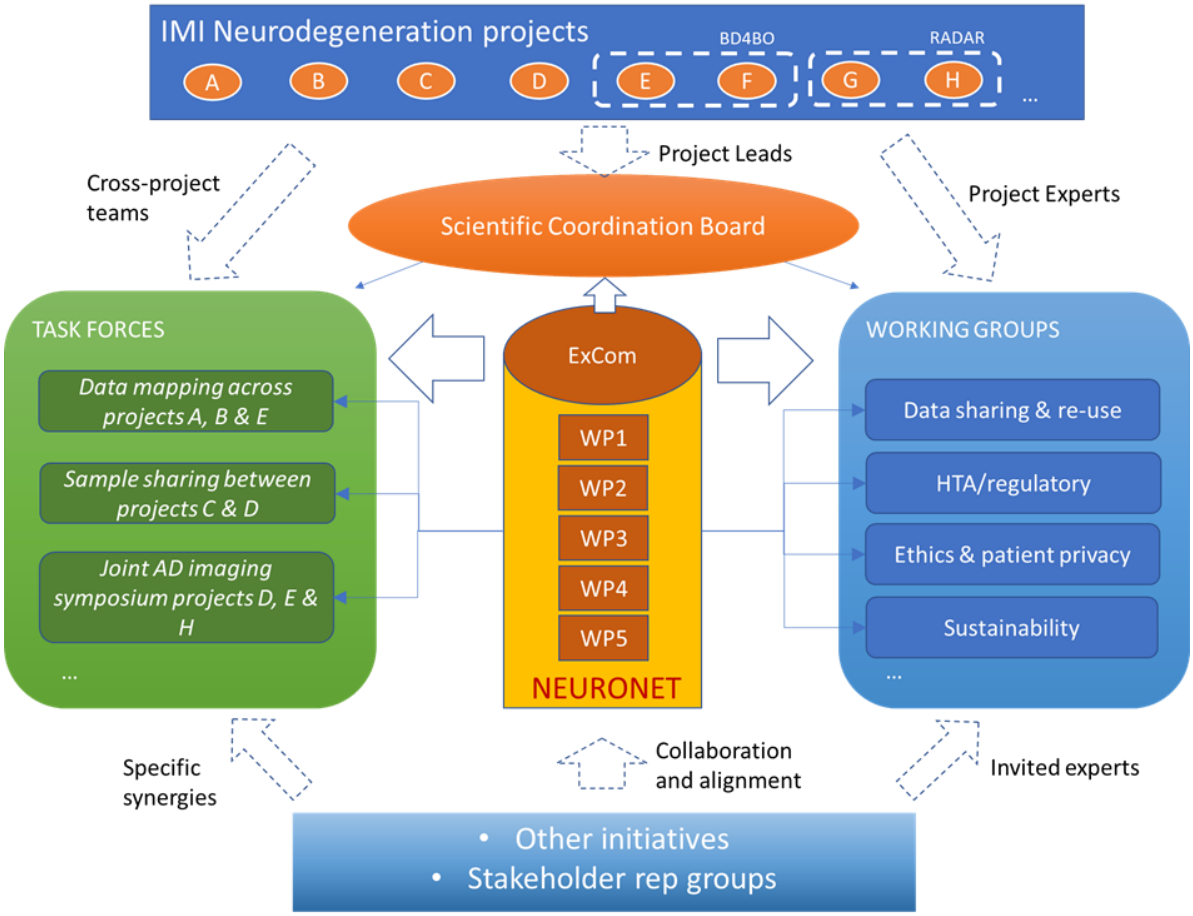

Figure 2. NEURONET operational framework

2. The Scientific Coordination Board

2.1 Scope and membership

The Scientific Coordination Board (SCB) is a pivotal body in NEURONET's governance structure, because it plays a crucial role in the definition of the strategic agenda for the CSA. The SCB objective is to provide expert advice, recommendations and guidance in terms of scientific and strategic evaluation of synergies, priority areas and opportunities for collaboration within NEURONET, while also pointing at gaps in the portfolio or specific areas that require concerted action.

Each IMI ND project nominates one representative for the NEURONET SCB. Normally it should be either the academic lead or the EFPIA lead, but the project may choose to nominate another person that the project leadership decides to delegate to.

As shown in the table below, there are currently 17 project leads sitting in the SCB, gathering a total of 18 IMI ND projects (Dag Aarsland is the project lead for two projects: RADAR-AD and PD-MIND), which represents the virtual totality of the IMI ND portfolio. Two new project leads have joined the SCB this year: Walter Maetzler and Lynn Rochester of IDEA-FAST and MOBILISE-D, respectively. There was also a change of lead for AMYPAD, with Gill Farrar taking over from José Luis Molinuevo.

Name	Project	Background	Organization
Margot Bakker	ADAPTED	EFPIA	Abbvie
Martin Hofmann-Apitius	AETIONOMY	Academia	Fraunhofer Gesellschaft
Gill Farrar	AMYPAD	Academia	GE Healthcare
Pieter Jelle Visser	EMIF	Academia	Maastricht University and VU University Medical Center
Craig Richie	EPAD	Academia	The University of Edinburgh
Malcolm Macleod	EQIPD	Academia	The University of Edinburgh
Walter Maetzler	IDEA-FAST	Academia	University Medical Center Schleswig-Holstein
Dominique Lesuisse	IM2PACT	EFPIA	Sanofi
George Tofaris	IMPRIND	Academia	University of Oxford
Lynn Rochester	MOBILISE-D	Academia	Newcastle University
Mercè Boada	MOPEAD	Academia	Fundació ACE
Dag Aarsland	PD-MIND & RADAR-AD	Academia	King's College London
Jochen Prehn	PD-MITOQUANT	Academia	Royal College of Surgeons in Ireland
Andreas Ebneth	PHAGO	EFPIA	Janssen
Hugh Marston	PRISM	EFPIA	Eli Lilly
Matthew Hotopf	RADAR-CNS	Academia	King's College London
John Gallacher	ROADMAP	Academia	University of Oxford

2.2 SCB meetings

In the second year of the project, the SCB has met online on three occasions, representing their 4th,5th and 6th meetings for the whole project so far:

4th meeting	05/06/2020
5th meeting	01/10/2020
6th meeting	22/03/2021

In the following sections we will provide a summary of discussions and decisions made at the SCB meetings.

4th SCB meeting (June 2020)

The first SCB meeting of this period gathered eleven project leaders. The meeting agenda can be found in the Annexes.

NEURONET leaders began the meeting with a brief introduction and update of the project. This included:

- A description of the tools and platforms produced within the first project year (asset map, Knowledge Base, and NEURONET forum).
- The overall progress of the project, including the submission of five project deliverables to IMI.
- An update on the communication work package led by Alzheimer Europe.
- The role of SCB members and feedback for the IMI interim review meeting (25th June).

Attendees discussed the sustainability of NEURONET, which in turn would be relevant for the IMI interim meeting. Overall, given the fact that IMI2 is ending, and with the Strategic Governing Group (SGG) having an uncertain future, the SCB was minded to consider other funding initiatives for the project. Similarly, NEURONET could be maintained and developed by other non-IMI projects and initiatives, such as DPUK, EBRA and JPND. The topic of sustainability was also affected by the fact that EC/IMI JU new calls are currently more focussed on COVID-19 than other disease areas.

The SCB reviewed the impact of COVID-19 on current research projects. The range of members reported on differing types and degrees of delays and setbacks, from closed laboratories preventing sample processing to a complete halt to recruitment and study visits. A commonly-cited issue was the cost of staff who are unable to work and produce project outputs and deliverables. To this end, the group confirmed that no-cost extensions were not adequate solutions for projects experiencing COVID-related delays. The SCB reflected on a survey of Scottish Dementia Research Consortium (SDRC) ECRs who reported insecurity about careers in dementia research and a need to move to other disease areas with more funding, such as respiratory research. The SCB committed to also relaying this message to IMI directly. The SDRC has prepared a ECR Resource Suite to address these concerns, which would be shared with IMI ND projects through NEURONET.

The SCB considered future priorities for NEURONET. It discussed the potential role of NEURONET in IMI Call 23, the creation of a federated access to biobanks across Europe. Overall, it was agreed that NEURONET would have more of a role at the second stage of application, acting in support of the selected proposal.

The SCB discussed the possibility of a neurodegeneration cohort in response to the end of EPAD and to sustain the potential of the Longitudinal Cohort Study. Overall, this proposal was to harmonise EPAD-related site cohorts to act as a pan-European cohort for neurodegenerative research. This proposal was supported by the SCB and would be presented to the EPAD national leads to understand exactly what resources would be available to support or progress it. This in turn would lead to the formation of the NEURO Cohort Task Force (see Section 4.1).

NEURONET underlined the importance of the collaboration and synergies that it had identified across the IMI ND portfolio, and encouraged SCB members to consider similar, potential future opportunities.

The SCB concluded by raising the possibility of a NEURONET Academy, modelled on the work and structure of the EPAD Academy. Essentially, this would provide a network and structure to support researchers across IMI ND projects, to help foster a sense of community and provide an important asset for sustainability.

5th SCB meeting (October 2020)

Nine SCB members attended the 5th SCB online meeting. The agenda for the meeting is included in the Annexes.

This meeting began with a general update from NEURONET. This confirmed the status and development of the asset map, Knowledge Base and NEURONET forum. Specifically, it was discussed whether the asset map should include non-ND IMI projects, and which sections of the Knowledge Base should be made publicly available (following recommendations from the IMI mid-term review). This update also included other, general feedback from the IMI review, relaying that the external reviewers of NEURONET had provided positive feedback with few specific recommendations, including the need for a sustainability plan and to update guidance on patient privacy and data sharing. The SCB also received feedback that EFPIA will reach out to the SGG to explore sustainability options for NEURONET.

The SCB then reviewed actions from the previous meeting. First, attendees discussed the role of COVID-19 and its impact on research projects. Overall, the group confirmed the extent and nature of the difficulties that the pandemic introduced but underlined that there was also a need to focus on positive messaging. Specifically, it was important to communicate to funders that it can be possible to overcome these difficulties and sustain a viable research portfolio post-pandemic. To this end, a NEURONET white paper detailing an approach and solutions to COVID-related challenges was floated as a welcome idea.

The SCB reviewed potential collaborations between IMI projects. Two were discussed explicitly: (1) EPAD and PHAGO and (2) IDEA-FAST and MOBILISE-D. In the case of the first, the SCB were supportive of furthering the collaboration, where Roche Diagnostics would analyse EPAD biological samples that are of interest to PHAGO. This led to the formation of the EPAD – PHAGO Task Force (see Section 4.2). In the case of the second, successful collaboration hinged on the effective and efficient sharing of digital datasets, which in turn could be informed by lessons learned and practical experience of data sharing (e.g., standardised data curation, metadata curation and pre-processing pipelines). Finally, it was noted that RADAR-AD may join as a third collaborator on (2) once the initial collaboration´s intention had been processed.

The group then reviewed Deliverable 1.4 *First report on impact of IMI neurodegeneration portfolio*. This included both a network and in-depth analysis of publications by projects. Most discussion concerned the latter, as publications are a useful index for impact, but are not necessarily the most sensitive indicator of collaborations between academic and industry/EFPIA partners, due in part to the nature of contributions of the latter, and whether this satisfies authorship, in addition to the legal and administrative hurdles that joint publications may also introduce. Overall, it was recommended that NICE, as lead on this deliverable, consider other forms of impact beyond publications for the second version of the impact analysis due towards the end of the project.

The SCB discussed its representation at the Alzheimer Europe conference in October 2020. NEURONET would have dedicated sessions and resources during this conference, including posters, quick oral presentations and roundtable discussions from the WGs, SCB members and related ECRs.

As in the previous SCB meeting, there was a discussion about the maintenance of the EPAD resources, cohort and network under the aegis of NEURONET. The advantages of maintaining the EPAD infrastructure were understood and supported by the SCB, but the role of funding was a significant necessity, leading the group to discuss possible options, including contacting EFPIA. Before this idea could be progressed, the EPAD centres would need to be contacted for their interest in such a proposal.

Finally, the SCB discussed the 'Neurodegeneration Summit' for 2021, which would act as a meeting for high-level experts to provide views on topics of interest and a vision for research direction and priorities over the next five to ten years. In discussions, it was confirmed that the first key objective of the summit was to focus on the clinical and translational aspects of research. This summit and discussion would benefit from the insights that have come from EQIPD, and on the recommendation from PHAGO, concern neurodegenerative conditions outside of (but including) Alzheimer´s and Parkinson´s disease. The summit was suggested for Q1 2021.

6th SCB meeting (March 2021)

Twelve SCB members attended the 6th SCB online meeting. The agenda for the meeting is included in the Annexes.

The meeting began with a general update on NEURONET. Specifically, the SCB heard of the publication of the NEURONET Knowledge Base and Asset Map, the recent submission of Deliverables D1.4 First report on impact of IMI neurodegeneration portfolio and D5.3 Interim NEURONET sustainability report, and the formation of two task forces: EPAD – PHAGO and NEURO Cohort. The SCB discussed the utility of the Asset Map as a form of conceptualising project outputs, and agreed that NEURONET's proposed asset definition was key. Moreover, the group considered NEURONET's potential role as an asset broker. From here, WP1 discussed its proposed work to map relevant initiatives and gap analysis. Specifically, the group would be requesting IMI ND project partners, through surveys and workshops, to provide their personal perspective on which initiatives they consider to be of relative/strategic importance, and also any gaps in the research landscape they have identified. In discussion, the group identified the need to help accommodate as many different stakeholder voices and perspectives as possible. To this end, more than one online workshop may be necessary.

The SCB reviewed two ongoing collaborations within the IMI ND portfolio: EPAD – PHAGO which is also reported in this Deliverable (see Section 4.2) and IDEA-FAST – MOBILISE-D that had culminated in the production of the Digital Health Catalyst.

Further to this point, the SCB discussed the formation of a digital endpoints workshop, which would consider how to obtain regulatory approval for said endpoints, given that there is no clear path to do so, at present, and how to align digital outcomes with disease progression models. This workshop idea was considered to be of great interest, and NEURONET agreed to organise this for Q3 of 2021.

The SCB heard of progress that had been made on the NEURO Cohort (see Section 4.1) and EPND which was progressing to Stage 2 and it was projected to started in autumn/Q4 of 2021. Given that both projects consider the identification and sharing of cohort data, it was agreed that there would be some alignment between NEURO Cohort and EPND.

Finally, the SCB discussed a proposed EFPIA impact survey and the sustainability of NEURONET. In both cases, the SCB considered the services the NEURONET provides, the extent to which these services have positively impacted the stakeholder groups, and how they can be maintained as a new IMI/IHI project or other public or private initiatives.

3. The Working Groups

NEURONET has successfully established the four thematic Working Groups (WGs) as per the DoA description. These groups are cross-project spaces for experts to discuss on common issues, priorities and opportunities for synergy and collaboration, providing NEURONET with expert advice on the four identified areas of interest:

WG1. Data sharing and re-use

WG2. HTA/regulatory interaction

WG3. Ethics and patient privacy

WG4. Sustainability

Details about the process for defining the areas of interest covered by the WGs were given in the first WP2 deliverable, D2.1 Report on establishment and procedures of SCB and foundational WGs.

The expected WG results are, among others:

- More consistent and informed decision-making.
- Improved awareness and re-use of project results and outputs.
- Enhanced networking across projects and more exposure of expert knowledge.
- Creation and homogeneous application of standards.

Ultimately, the aim of NEURONET is to leverage and compile the knowledge that is presently scattered across the different projects in these key areas.

3.1 WG1. Data sharing and re-use

The WG Data sharing and re-use focuses on developing specific guidance to aid projects on data sharing policies and tools, incentives, value propositions, infrastructural solutions, etc. With the support of the Data sharing and re-use working group, Task 3.2 is developing guidelines aimed at facilitating the sharing of and access to data, biological tools and other materials amongst IMI projects, as well as with other interested researchers at a European and global level.

Membership

The WG Data sharing and re-use, led by partner Janssen, consists of subject matter experts in data sharing and NEURONET members. The current membership is:

Name	Organization	IMI project
Andrew Owens	King's College London	RADAR-AD
Andrew Peter McCarthy	Eli Lilly	n/a
Angela Bradshaw	Alzheimer Europe	NEURONET
Anthony Brookes	University of Leicester	EMIF / EPAD
Carlos Díaz	SYNAPSE	NEURONET
Clint Hansen	Kiel University	Mobilise-D
Cindy Birck	Alzheimer Europe	NEURONET
Emma Dodd *(until Sep 2020)*	Roche	NEURONET
Francoise Le Vacon	Biofortis Mérieux NutriSciences	n/a
Judi Syson	University of Edinburgh	EPAD
Lennert Steukers	Janssen	NEURONET
Lewis Killin	SYNAPSE	NEURONET
Loes Rutten-Jacobs (*from May 2021*)	Roche	NEURONET
Manuela Rinaldi	Janssen	NEURONET
Martin Hofmann-Apitius	Fraunhofer	AETIONOMY

Name	Organization	IMI project
Mikkel Misfledt *(from Sep 2020 to May 2021)*	Roche	NEURONET
Niamh Connolly	Royal College of Surgeons in Ireland	PD-MITOQUANT
Nigel Hughes	Janssen	EMIF-AD
Nikolay Manyakov	Janssen	RADAR-CNS/RADAR-AD
Pieter Jelle Visser	VUmc & Maastricht University	EMIF-AD
Rodrigo Barnes	Aridhia	EPAD
Sandra Pla	SYNAPSE	NEURONET
Serge Van der Geyten	Janssen	EPAD
Walter Maetzler	University Medical Center Schleswig-Holstein	IDEA-FAST

Meetings

The WG met four times this reporting period; one F2F and three teleconferences.

The first meeting on the 26th of February 2020 was a F2F meeting held in Diegem, Belgium. The meeting began with an introduction to the NEURONET concept and the NEURONET governance structure, delineating it from other IMI projects like the European Health Data & Evidence Network (EHDEN) or FAIRplus. This then made the scope and expectations of the WG clearer. From here, the WG discussed the range of tools and solutions that can be utilised against the challenges of data sharing, such as participant rights, retention, etc. Data harmonization, dataset life cycles and use case scenarios for data sharing were also discussed. In discussions, the WG underlined important data sharing problems that were relevant to IMI projects. Critically, the maintenance of data was identified as a key issue that was related to sustainability. In essence, tools that allow data sharing must be promoted as important assets. EPAD acted as a case study for producing a successful data sharing platform (PREPAD).

The second meeting on the 29th of September 2020 was by teleconference. This meeting began with a general update from NEURONET and confirmed that the WG would have a presence at the upcoming Alzheimer Europe conference through several presentations. From here, it confirmed that the WG deliverable D3.2 First version on guidance tools on data/sample sharing and use had been submitted in June 2020 and was published on the NEURONET website. The WG discussed the need to produce further guidelines and recommendations in future deliverables (i.e., D3.7 Final version on guidance tools on data/sample sharing and use) but also acknowledged the benefit of publishing white papers about the impact of the COVID-19 pandemic and other factors that impede best practice. The WG identified champions to lead on different topics contained as part of D3.7.

The remainder of this meeting was a discussion of relevant WG projects, including the ADDI AD Workbench Initiative, the European Health Data & Evidence Network (EHDEN) project and the EMIF COHORT 1000. There was also an additional discussion regarding the challenges of harmonising ND-specific real-world data (RWD) to a common data model.

The third meeting on the 17th of December was by teleconference. This meeting was composed of a general NEURONET update, a presentation from Bigdata@Heart, a review of three two-pagers and an outline of legal challenges. The presentation from Ghislaine van Thiel at Bigdata@Heart – an IMI2 project – covered the work this project had concluded on ethical and legal issues that could help establish sustainable governance for its data infrastructure.

The remainder of this meeting reviewed two-page documents regarding the sociotechnical barriers to real world data in ND, organisational hurdles associated with sharing health data and lessons learned from data harmonisation. The WG was tasked with reviewing these documents and in some case to consider the utility of combining documents to form a white paper. Similarly, the outline of legal challenges and recommendations was discussed, and from this, it was

recommended that the two-pagers would be expanded to contain documentation regarding data transfer, contribution and processing agreements.

The fourth meeting on the 5th of March 2020 was by teleconference with sixteen attendees. The meeting was composed of a general NEURONET update, a presentation from FAIRplus, and a review of pending two-pagers. The presentation from FAIRplus – and IMI2 funded project – relayed the work that the team has completed since 2019, which has been to produce templates and guidelines to help make project data compliant with the FAIR principles, and working with specific IMI projects to make their data more FAIR compliant. As part of the meeting discussions, the idea of a digital data sharing task force was proposed, which would represent work technically outside of the scope of the working group. Finally, the working group reviewed a report regarding data sharing in dementia research, which aims to map the Horizon 2020 portfolio, reflect on EU policy and research landscape, and to develop recommendations on how these policy context and research infrastructures can be strengthened.

3.2 WG2. HTA/Regulatory interaction

A HTA and Regulatory interaction WG has been established to generate insights into the regulatory and HTA challenges and opportunities that are unique to neurodegenerative diseases. Specifically, the WG will:

- Contribute, as applicable, to the development of tools to support effective engagement with regulators, HTA agencies and payers in the EU.
- Identify projects' needs and knowledge gaps in relation to specific procedures and processes for engagement with HTA and regulatory bodies where external expertise may be sought.
- Provide a forum for projects to share lessons learned from previous HTA and regulatory engagement.
- Support the projects in the development of their regulatory, HTA and payer strategy, as applicable.

Membership

The HTA and Regulatory interaction WG, led by partner NICE, brings together a selection of representatives of the individual IMI neurodegenerative projects with members of the NEURONET consortium. External experts may also be invited to attend meetings as and when required.

The WG members are listed in the table below. There is flexibility in the membership with the opportunity for new project members to join the WG or to attend specific meetings depending on the needs of their project.

Name	Organization	IMI project
Angela Bradshaw	Alzheimer Europe	NEURONET
Carlos Díaz	SYNAPSE	NEURONET
Christophe Bintener	Alzheimer Europe	NEURONET
Cristina Saugar *(until March 2021)*	SYNAPSE	NEURONET
Dalia Dawoud *(from Jan 2021)*	NICE	NEURONET
Diana O'Rourke	NICE	NEURONET
Emilse Roncancio	GE	NEURONET
Emma Dodd *(until Sept 2020)*	ROCHE	NEURONET
Jacoline Bouvy *(until Jan 2021)*	NICE	NEURONET
Jean Georges	Alzheimer Europe	NEURONET
Lewis Killin	SYNAPSE	NEURONET
Mikkel Misfeldt *(from Sept 2020)*	ROCHE	NEURONET
Nina Coll	SYNAPSE	NEURONET

Name	Organization	IMI project
Robin Thompson	Biogen	ROADMAP
Sandra Pla	SYNAPSE	NEURONET
Suzanne Foy	Janssen	EPAD

Meetings

The WG met two times in this reporting period, both by teleconference.

The first meeting on the 29th of April 2020 began with a review of the Decision Tool for HTA and Regulatory Engagement. The final report of this activity is due in August 2021 (M30). The group commented that the tool represented an original and useful way of representing the processes of approval and engagement and saw a clear utility for stakeholders. The WG considered room for improvement, discussing the possibility and benefit of adding:

- Examples of best practice from IMI projects that have undertaken relevant HTA or Regulatory procedures.
- Procedures and processes for engagement in other regulatory regions (e.g., North America).
- Signposts to published guidance (e.g., published qualification advice and opinions).

The meeting concluded with other points of future discussion, including how to understand the impact that regulatory processes could have on projects' outputs, and the role of patient engagement as part of these processes.

The second meeting was held on the 15th of February 2021 with a discussion focused on the considerations and issues for the use of digital endpoints in HTA submissions for new health technologies and in other guidance, and the best processes for engagement with HTA bodies. This topic was chosen following consultation with some of the projects in the portfolio who identified a knowledge gap in relation to the best ways to engage with HTA bodies, specifically in relation to the perspectives of HTA bodies on digital endpoints (for example digital mobility outcomes).

Three HTA experts (specifically Anja Schiel (NoMA), Niklas Hedberg (TLV/EUnetHTA) and Sheela Upadhyaya (NICE)) attended the meeting to answer questions from those projects that have a particular interest in this topic (IDEA-FAST, Mobilise-D and RADAR-AD). The questions for discussion centred around 4 broad areas:

1. **Experience**: Have digital endpoints been previously submitted as evidence of clinical benefit during an HTA assessment and, if so, what was the outcome? If not, do the HTA bodies have any other experiences with digital endpoints?
2. **Interest**: In which ways/areas of use do HTA bodies anticipate digital endpoints might be considered? For example, in cost effectiveness analysis, technology appraisal, clinical guideline development, real world evidence, primary endpoints etc.
3. **Expectation**: What are [or are likely to be] the requirements for a digital endpoint to be accepted by HTA bodies as evidence of clinical benefit?
4. **Engagement**: What is the best process for discussing the evidentiary requirements for digital endpoints with HTA bodies?

Whilst the experts explained that HTAs have limited experience when it comes to considering digital endpoints in HTA submissions, there was a great deal of discussion about the requirements and expectations that HTA bodies would have if these were included in the future. Discussions regarding processes for engagement highlighted that unlike the clear processes that available through the EMA, for HTAs the system is more fragmented and no formal engagement routes exist. Projects should instead consider work that has been undertaken through other H2020 and IMI projects and consider other informal routes for engagement, through for example, ISPOR or HTAi.

3.3 WG3. Patient privacy and ethics

Compliance with the ethical and data protection requirements that underly patient privacy is seen as pivotal to achieve real excellence in health research. However, patient privacy concerns have also been perceived as a barrier to primary health research and, in particular, research that involves secondary use of patient data. An initial survey performed by NEURONET identified "guidance/best practice on data privacy and related regulations" and "guidance/best practice on ethics approvals and Informed Consent Forms" as priority areas in which IMI ND projects would like more support. The WG on Patient Privacy and Ethics was formed in 2019 to meet this need.

The primary aim of this WG is to compile and share learnings on patient privacy, to ensure best practice, reduce duplication of effort and create resources that will be of value to existing and future IMI ND projects. Goals for 2019-2021 would include the following:

- Mapping and understanding the ethical and legal frameworks of IMI ND projects supported by NEURONET, focusing on:
    - Patient & data privacy
        - Data governance systems
        - Data protection: challenges and best practice
    - Informed consent
        - Patient information sheets and informed consent forms
        - Clauses for data sharing and re-use
        - Ethics: challenges and best practice

In addition, the WG on Patient Privacy and Ethics acts as a forum for discussion of key ethical and legal topics currently being addressed in the individual IMI ND projects. Where necessary, the WG also provides support to IMI ND projects on new ethical and legal challenges that may arise. Finally, the WG will provide input on two related WP3 deliverables:

- D3.4 *First version of guidance on standards and practices for protecting data privacy* (submitted)
- D3.9 *Final version of guidance on standards and practices for protecting data privacy* (due in August 2021, M30)

Membership

The WG on Patient Privacy and Ethics is led by partner Alzheimer Europe. WG members are listed in the table below:

Name	Organization	IMI project
Angela Bradshaw	Alzheimer Europe	NEURONET
Carlos Díaz	SYNAPSE	NEURONET
Christophe Bintener	Alzheimer Europe	NEURONET
Cristina Saugar *(until March 2021)*	SYNAPSE	NEURONET
Diana O'Rourke	NICE	NEURONET
Dianne Gove	Alzheimer Europe	NEURONET
Edo Richard	Radboud UMC	AMYPAD/EPAD
Federica Lucivero	University of Oxford	RADAR-AD
Jean Georges	Alzheimer Europe	NEURONET
Mercè Boada	Fundació ACE	MOPEAD
Nathan Lea	UCL	EMIF
Nikolaus Forgo	University of Vienna	AETIONOMY
Pilar Cañabate	Fundació ACE	MOPEAD

Rebecca Pinto	King's College London	PD-MIND
Richard Milne	University of Cambridge	EPAD

Meetings

The working group met two times this period, via teleconference on both occasions.

The first meeting on the 3rd of June 2020 took place by teleconference. The meeting began with a review of NEURONET to the WG members and a short introduction of all present members. From here, the group considered a short survey that had been distributed to members about their prioritised topics of interest. In discussion, these areas of interest were categorised into those that have a direct impact on participants (e.g., disclosure of risk, contact) and those that had an indirect impact (e.g., data governance). From here, it also made sense to consider the ethics of PPPs as meta to these two categories. These topics were collated after the meeting and identified for priority action. Finally, the WG considered the potential for a large, joint publication, which would draw in the ethics, patient privacy and PPI work conducted across the IMI ND portfolio. The WG was in support of this idea.

The second meeting on the 6th of October 2020 took place by teleconference. After introductions, the WG reviewed a proposal for developing a model of applied ethical, legal and social implications (ELSI) in collaborative research. Specifically, Richard Milne and Federica Lucivero reported on a collaboration where they had been developing a model for ELSI that would be directly applicable to IMI projects at a study-activity level (e.g., recruitment), but also for broader project considerations such as research direction. If successful, the proposed model would facilitate conversation and knowledge exchange between projects about best practice regarding ELSI and allow the WG to meet its aims and objectives. The WG were supportive of this proposal and, as part of the WG, NEURONET were tasked with helping its development. In the first instance this included facilitating conversations between the proposal authors and the SCB.

3.4 WG4. Sustainability

The Sustainability WG looks at exploitation activities and sustainability models (spanning business design, modelling, financial estimates, IP issues, organisational models, legal solutions, etc.) that can help projects with long-term sustainability. The idea is to compile sustainability and business models used in (or applicable to) IMI projects, focusing on common issues related to sustainability, namely IP, legal, financial, technical issues. WG members provide their expert feedback and perform a critical analysis of the models identified.

Membership

The WG on Sustainability is led by partner Synapse. The current members of the WG are:

Name	Organization	IMI project
Aneleen Stinckens	Janssen	NEURONET
Carlos Díaz	SYNAPSE	NEURONET
Caroline Schuster	ARTTIC	PHAGO
Christophe Bintener	Alzheimer Europe	NEURONET
Cristina Saugar *(until March 2021)*	SYNAPSE	NEURONET
Derya Ayaz	Janssen	PHAGO
Frank Tennigkeit	UCB	EPAD
Gill Farrar	GE	AMYPAD
Jean Georges	Alzheimer Europe	NEURONET
Jelle Praet	Janssen	PHAGO
John Gallacher	University of Oxford	ROADMAP
Kristy Draper *(until Oct 2020)*	University of Edinburgh	EPAD
Lennert Steukers	Janssen	NEURONET

Name	Organization	IMI project
Lewis Killin	SYNAPSE	NEURONET
Manuela Rinaldi	Janssen	NEURONET
Martin Hofmann-Apitius	Fraunhofer	AETIONOMY
Natalie Piton	Sanofi	NEURONET
Paul Peeters	Janssen	NEURONET
Philippe Rocolle (*until May 2021*)	Sanofi	IM2PACT
Pieter Jelle Visser	VUmc & Maastricht University	EMIF-AD
Saira Ramasastry	SYNAPSE	NEURONET
Thomas Steckler	Janssen	EQIPD

Meetings

The WG met five times this reporting period. The first four of these meetings were focussed on the sustainability plans and strategies of specific studies in the IMI ND portfolio, and the fifth focussed on a sustainability tool and framework, intended for use across IMI projects.

The first meeting on the 12th of March 2020 took place by teleconference and represented the formal establishment of the group. Here, project leads and other working group members introduced themselves and outlined the group's goals and priorities. Specifically, the group agreed to compile and review sustainability and business models from IMI projects and beyond, and to share lessons, ideas and best practice where possible.

The second meeting on the 16th of April 2020 took place by teleconference. The agenda was concerned with the sustainability plans of EMIF, DPUK and EPAD. From EMIF, Pieter Jelle Visser presented the data catalogue and TranSMART, a platform for data hosting and sharing, supported by EPAD and Janssen, and a set of two cohort studies, sustained by funding from the Netherlands.

The meeting continued with a presentation from John Gallacher regarding DPUK which sustains 42 cohorts on its data platform and had received a further five years of funding from MRC. It was described the four stages of the project's data curation process, which involved collaboration with Gates Ventures and EMIF at different stages. The current sustainability model is based on the production of desktops and operating systems that can be used for on-premises analysis for free. The future plan would move to federated analysis using a cloud infrastructure for a fee. Ultimately, the business model of DPUK is pay-to-access, where private partners pay a membership fee to gain access to the entire platform. DPUK do not claim any IP for subsequent IP that may come from analysis of its data. Cohorts that participate in DPUK benefit from increased visibility.

EPAD was the third project presented at this meeting. Kristy Draper relayed that the continuation of EPAD was based on maintaining five of its key assets: EPAD Site Network, Registers, Cohort, Trials and Academy. Regrettably, some assets were not able to be carried over. Kirsty relayed that there had been a significant amount of work dedicated to EPAD's sustainability, but a combination of factors made this a challenge. Specifically, the scope and size of the project, requiring feedback from multiple stakeholders within a limited timeframe, provided a difficult context to reach a confirmed sustainability plan.

This meeting concluded with a general discussion about sustainability and lessons learned, including whether a top-down or bottom-up approach should be taken, whether there is any benefit in formulating sustainability plans early on, and how to reach out to funders.

The third meeting on the 18th of May 2020 took place by teleconference. The agenda was concerned with the sustainability plans of EQIPD and AETIONOMY. Thomas Steckler relayed that EQIPD contained three main outputs: a database, e-learning platform and quality management system (QMS). A challenge for the project has been having to plan for this asset sustainability in

the absence of specific or dedicated guidance from IMI or EFPIA, requiring the project group to seek advice from other organisations and contacts.

Similarly, Martin Hofmann-Apitius outlined the utility of the AETIONOMY Knowledge Base, which has a 5-year sustainability plan funded by Fraunhofer and LCSB. Access to the Knowledge Base would still be governed by the Data Access Committee. Importantly, the Knowledge Base has been used to form two other incentives: the PHAGO Knowledge Base and the H2020 Virtual Brain Cloud. The quality of the AETIONOMY data remains a valuable asset for the project, and has the potential to be approached by companies that provide disease modelling services.

The fourth meeting on the 25th of January 2021 was a review of the sustainability plans for AMYPAD and PHAGO. Here, Gill Farrar commented on two main activities for AMYPAD, which has been working on an extension to take the project to October 2022. The first activity was a follow-up for patients, which was scheduled to take place in Q1/Q2 of this year. The second activity was a potential collaboration with Gates Ventures Alzheimer´s Disease Data Initiative (ADDI), that could derive on the use of ADDI Workbench. The AMYPAD project has been initiating internal discussion to move forward on their sustainability plans.

From here, Andreas Ebneth commented on the sustainability plans for PHAGO, which is due to end in a year and a half. He reviewed how the approach to sustainability was based on identifying and leveraging the project's assets. Here, work packages are based around assets, such as the identification of risk genes within microglia pathways (WP2); animal models of TREM2/CD33 and patient imaging (WP3); the identification of modulators of TREM2/CD33 (WP4) and the production of a Knowledge Platform (WP5). PHAGO contains a sustainability working group which is dedicated to working out how to make these assets available and to help prevent other research groups from repeating the same efforts.

In the general discussion, attendees considered the definition of sustainability in terms of assets rather than projects. Specifically, where projects seek to sustain themselves through second projects, it was discussed that it may be preferable to dedicate funding and effort towards identifying, maintaining and brokering assets. Furthermore, because the maintenance of assets tends to be a multifaceted problem, it can often burden sites or projects and hinder collaboration. The need for an asset manager and broker then became clear. Furthermore, defining what an asset was still not certain across IMI projects. To this end, NEURONET had provided a working definition for what an asset must be and shared it with the group.

The fifth sustainability WG meeting took place on the 20th of May 2021 and focussed on a proposed sustainability tool developed by Lisa Leenhouts-Martin from Edge Impact Consulting and funded by EFPIA. This tool was designed to help investigators overcome common challenges that come from making IMI project assets sustainable. Specifically, it is intended to provide a pragmatic framework that can help project teams develop sustainable assets by, for example, considering their targeted market and research landscape. Information about this tool is due to be published on IMI and EFPIA sites for investigators' reference. At the WG meeting, this tool was identified as an important potential resource and could help clarify what sustainability entails as part of IMI project management.

4 Task forces

As mentioned in previous sections, NEURONET aims to become a platform for cross-project collaboration and exploitation of potential synergies. To carry out this work, NEURONET relies on the SCB at the strategic level and the WGs at the technical level but, ultimately, the implementation of such synergies will usually involve the creation of Task Forces (TFs).

Two TFs were created in the second year of NEURONET:

1. The NEURO Cohort TF
2. The EPAD – PHAGO TF

4.1 NEURO Cohort

At present, the members of the NEURO Cohort Task Force are:

Name	Organization	IMI project
Angela Bradshaw	AE	NEURONET
Carlos Diaz	SYNAPSE	NEURONET
Cristina Saugar *(until March 2021)*	SYNAPSE	NEURONET
Isadora Lopes Alves	VUMC	AMYPAD
Lennert Steukers	Janssen	NEURONET
Lewis Killin	SYNAPSE	NEURONET
Nina Coll	SYNAPSE	NEURONET
Sandra Pla	SYNAPSE	NEURONET

In response to the dissolution of the EPAD Longitudinal Cohort Study, members of the EPAD team and NEURONET met on the 30th of October 2020 to review the state of the cohort as a potential asset that could be sustained as a Neurodegeneration Parent Cohort (hereafter "NEURO Cohort").

Specifically, the initial inspiration behind the NEURO Cohort was to devise a practical and cost-effective method to follow-up people who were recruited to the LCS and, in this way, keep a network of sites active and harmonious in data collection (i.e., maintain some or all of EPAD's Trial Delivery Centre Network). Importantly, the NEURO Cohort would be represented by a smaller protocol than the one associated with the LCS Cohort and would be concerned with collecting and maintaining a minimum dataset in order to keep overheads low.

The initial proposal was refined further with a TF meeting on the 20th of November 2020. Here, the NEURO Cohort study design, data management, governance, infrastructure, and finances were discussed in more detail. The prevailing thought for the proposal was that NEURONET would position itself as the central manager of the cohort/study, and in turn also act as an honest broker between cohort sites across Europe and studies that were interested in recruiting from the NEURO Cohort. From this position, however, there were multiple options as to how resource and responsibilities should be distributed, aiming ultimately to strike the right balance between network co-ordination and cohesion against site autonomy. Similarly, the role of funding was underlined given the relative expense of the EPAD LCS and the limited amount of remaining NEURONET budget. Finally, the TF reviewed the extent to which the NEURO Cohort could dovetail with the European Alzheimer's Disease Consortium, which has also attempted to create a minimum dataset across multiple sites.

These discussions led to a proposal, which was then taken to EPAD sites in a teleconference on the 4th of December 2020. Here, the spirit of the proposal was supported. Attendees at the meeting underlined the need for fast and pragmatic action in order to avoid follow-up attrition, to reduce or avoid any new burden on researchers, and to expand the scope of the NEURO Cohort beyond that of the original EPAD TDC network.

Following this, members of the TF met on the 21st of January 2021 to collate comments that had been made to the proposal and generate a drafted Expression of Interest (EoI) for sites.

The finalised EoI was sent to sites on the 29th of January 2021. A pre-kick off (KO) meeting was arranged on the 5th of March 2021 to communicate the proposal in more detail with the interested sites. These details included the proposed assessment plan, governance structures and sustainability models. At the time of the pre-KO meeting, 36 sites relayed their interest in the NEURO Cohort, and of these, 32 confirmed the interest with signed EoIs.

Following the pre-KO meeting, 36 of 37 interested sites had returned signed EoIs. Of these, seven sites opted to act as pilot sites for the NEURO Cohort, and a further three as back-up pilot sites. At present, the TF is working with these pilot sites to implement the technical, legal and governance infrastructure that would be necessary to establish NEURO Cohort. Completion of the successful pilot will lead to the wider establishment across all other sites.

4.2 EPAD – PHAGO

At present, the members of the EPAD – PHAGO Task Force are:

Name	Organization	IMI project
Andreas Ebneth	Janssen	PHAGO
Angela Hodges	King's College London	PHAGO
Carlos Diaz	SYNAPSE	NEURONET
Craig Ritchie	University of Edinburgh	EPAD
Cristina Saugar *(until March 2021)*	SYNAPSE	NEURONET
Harald Neumann	University of Bonn	PHAGO
Henrik Zetterberg	University of Gothenburg	PHAGO
Jean Manson	University of Edinburgh	EPAD
Lewis Killin	SYNAPSE	NEURONET
Nina Coll	SYNAPSE	NEURONET

The EPAD – PHAGO TF was first established in August 2020 and represented the first formal collaborative effort between two IMI ND projects for NEURONET. Here, both EPAD and PHAGO stand to benefit from the analysis of CSF samples collected by the former. Specifically, CSF samples collected from the EPAD cohort are to be identified, sent over to, and analysed by the PHAGO team using the Roche Diagnostics NeuroToolkit. Successfully completing this work would satisfy a clause in the EPAD LCS protocol to conduct TREM2 analysis and would enrich PHAGO's overall sample data.

Since August 2020, the TF has met eight times to clarify and confirm both the nature and subsequent logistical implications of this collaboration. In these conversations NEURONET has acted as a key facilitator in producing management and action plans.

Over these meetings it has become clear that the EPAD-PHAGO collaboration will act as a pilot study that may produce results and insights that can be leveraged as part of a larger analysis of the entire EPAD sample set. The pilot is projected to finish by the beginning of Q3 2021.

5 Conclusion

All of the key organisational structures described in NEURONET'S operational framework (Scientific Coordination Board, Working Groups and Task Forces) have been successfully set up, complementing the project's own governance structure built around 5 Work Packages and an Executive Committee.

A total of 18 IMI neurodegeneration projects have been approached by NEURONET so far, and all of them have a designated representative at the SCB. NEURONET has generally been very welcomed by IMI ND projects, and the interest and engagement of the project leaders has allowed the CSA to successfully bring them together. SCB members continue to actively discuss in a dynamic way and appreciate the opportunity for exchange of views with peers, which is a unique benefit of NEURONET.

Output from future SCB and WG meetings and discussions will be compiled and submitted to IMI as project deliverable: D2.4 *Report #3 on activity of SCB, WGs and TFs* (due at the end of the project).

6. Annexes

6.1 4th SCB meeting agenda

NEURONET 4th Scientific Coordination Board meeting

05/06/2020

No	Topic	Speakers	Time - CET
1	**Brief introduction and general updates from NEURONET** • Tools: Asset Map, Knowledge Base, Forum • Guidelines and recommendations • D1.2 Integrated Programme Analysis • Communication activities • IMI interim review meeting	NEURONET Project Leads	10:00
2	**Impact of COVID19 on projects** • Current challenges & obstacles • New opportunities • How could Neuronet help	All	10:15
Break			*11:00*

3	**Priorities for NEURONET**
	• New IMI call (biobank + data portal)
	• Neurodegeneration cohort (EPAD-LCS) follow-up
	• Collaborations across projects
	• Other initiatives and possibilities:
	  ○ Neuronet Academy
	  ○ Neuronet opinion paper
		All	11:15

4	**Wrap up and closing** • Immediate plans and concrete actions • Overall conclusions	NEURONET Project Leads	12:45
End of the meeting			*13:00*

6.2 5th SCB meeting agenda

NEURONET 5th Scientific Coordination Board meeting

Thursday 01/10/2020, from 10.00 till 13.00

No	Topic	Speakers	Time - CET

1	**Updates from NEURONET**
	• General updates
	• Results and recommendations from IMI interim review
	• Actions after last SCB meeting:
	  ○ Impact of COVID19 on IMI neurodegeneration portfolio and research funding
	  ○ Collaborations across projects
	• Impact analysis of IMI neurodegeneration portfolio
	• NEURONET Roundtable discussion @ AE conference
		Carlos Díaz, Lennert Steukers, Jacoline Bouvy, Jean Georges	10:00

Break			*11:15*
2	**Neurodegeneration research site network:** A network of European research centres working in the field of neurodegeneration.	All	11:30
3	**Neurodegeneration Summit 2021:** A Neuronet-driven cross-portfolio event	All	12:00
4	**Wrap up and closing** • Immediate plans and actions • Conclusions	Carlos Díaz, Lennert Steukers	12:45
End of the meeting			*13:00*

6.3 6th SCB meeting agenda

NEURONET 6th Scientific Coordination Board meeting

22/03/2021 1100 – 1400 CET

No	Topic	Speakers	Time - CET

1	**Brief introduction and general updates from NEURONET**
	• General updates
	• Review of actions completed after last SCB meeting
	• Asset Map and Knowledge Base
	• Landscape of initiatives and gap analysis: Perspectives of SCB members
	• Collaborations, EPAD-PHAGO, IDEA-FAST-MOBILISE-D
	• Future NEURONET Activities:
	  • *Neurodegeneration Summit*
	  • *Digital Endpoint Workshop*
		NEURONET Project Leads	11:00

2	**Neurodegeneration European Parent Cohort (NEURO-Cohort)**	NEURO Cohort TF	12:00
3	**Coming: European Platform for Neurodegenerative Diseases (EPND)**	PJ Visser	12:30
	Break		*13:00*
4	**EFPIA Survey**	All	13:15
5	**Evaluation and sustainability of NEURONET** • Asset-based view over project-based view • Presentation in preparation for a follow-up survey for formal evaluation	NEURONET Project Leads	13:30
	End of the meeting		*14:00*