PROMETEUS – Preterm Brain-Oxygenation and Metabolic EU-Sensing: Feed the Brain

Grant Agreement Number 101099093

PROMETEUS IN PRESENCE MEETING MINUTE

Date and time: **July, 5th 2023, 10.30 am CET**

Meeting location: University of Padova Language Centre, Padova, Via Venezia 16, Padova, Italy

Meeting Chair: Sabrina BRIGADOI - *Unipd*

Participants:

- Steering Committee members,
- Executive Board members,
- Other project participants

Staff and Guests:

- Sara Casadesús Anglada – *UdG*, Project Manager
- Marta POZZA - *Unipd*, administrative staff

Objective

- Update from each WP leader and other partners on the activities of the WPs in which they're involved;
- Information and agreement on a way to manage continuous reporting and internal monitoring activities;
- Potential new partners' applications to join the consortium in response to the call HORIZON-WIDERA-2023-ACCESS-06;
- Updates regarding the selection of an Ethics Advisor for the project;
- Change of PI contact person for a few months;
- Scheduling of next meetings, workshops, and seminars;
- Discussion about the creation of the Prometeus Exploitation Committee (PEC).

Meeting Agenda

Time	***Item***	***Leads***
10.30-10.45	Welcome speech	Sabrina BRIGADOI - *Unipd*
10.45-12.00	WP leader and partner update on the ongoing activities	Davide CONTINI – *Polimi* Berta Ben Shachar – *QLAB* Jacopo BONET – *UNIPD* Emmanuel BARBIER – *UGA* Alberto SCARPA – *DAVE* Paola RIGO – *Unipd* Sabrina BRIGADOI - *Unipd*

12.00-12.45	WP6 Ethics requirements and procedures	Sabrina BRIGADOI - *Unipd*
14.00-14.30	▪ Continuous reporting and internal monitoring procedures; ▪ Main characteristics of HORIZON-WIDERA-2023-ACCESS-06 call	Marta POZZA - *Unipd*
14.30-15.45	▪ How to deal with potential new partners' applications to join the Consortium in response to the call HORIZON-WIDERA-2023-ACCESS-06; ▪ Change of PI contact person for a few months; ▪ Updates regarding the selection of an Ethics Advisor for the project; ▪ Scheduling of next meetings, workshops, and seminars; ▪ Discussion about the creation of the Prometeus Exploitation Committee (PEC).	Sabrina BRIGADOI - *Unipd*

Meeting notes

Coordinator of the PROMETEUS project Sabrina Brigadoi, University of Padua, welcomed the participants, presented the agenda of the meeting, and opened the meeting by asking all the participants to briefly introduce themselves, leaving the stage to each WP leader and partner representative involved in the ongoing activities.

1. WP leader and partner update on the ongoing activities

1.1 WP1

WP 1 leader, Davide Contini, presents the partners who are working on WP 1 for the realisation of neo-opticap (Polimi, PIONIRS, ICFO, UCL), and who have provided suggestions from the activities planned in other WPs (UCC, DAVE, UNIPD), together with the list of tasks and the timeframe foreseen for their achievement. He lists the deliverables that are due over time and the connections with the other WPs.

During the first month, work focused mainly on defining, together with the other partners, the design and layout aspects of the instrument and which measurements to consider.

Two prototypes will be developed, one for each study site at the NICUs.

He then goes on to talk about what studies are underway with the ICFO partner to determine what characteristics the instrument must have and the best places to direct the fibres to take measurements.

Together with UCL, Polimi worked on the patient interface. The system is skin-safe, but the aim is to create a product that is also eye-safe, a feature that would make it suitable for classification as a CE class 1 medical device.

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He then informs the partners that a slight delay is due to the fact that the Associated Partner, UCL, is still waiting for UKRI's approval of alternative funding to that of the EU and this has led to difficulties in recruiting staff to work on the project. However, the current delay can be made up rather easily and does not cause any concern.

1.2 WP 2

QULAB is represented by Berta Ben Shachar, who shows those present what the company is currently working on. It is a minimally invasive sensor for detecting glucose, lactate and beta-hydroxybutyrate (BHB) levels, a technology that will be patented.

The first planned activities were completed, and the application for ethical approval of the experimental protocol on pigs was accepted. Therefore, studies to test the safety of the sensor have started. The first-in-man study should be initiated towards the end of this year.

The equipment used now consists of a large applicator, which will be made smaller, and a sensor that detects three different parameters but can hold up to six.

The sensor developed by QULAB penetrates only 1 mm into the dermis and is therefore minimally invasive and less painful compared to others on the market.

The study carried out so far on pigs gave good results and was an application-related safety study, without any data collection.

A central aspect of the new continuous glucose monitoring (CGM) device lies in the material: silicon on a patented stainless-steel support (QULAB's patented technology), which, even if it were to break, would leave no silicon in the body.

Currently, the prototype sensor built is large enough to be manipulated in studies, but its sensitive part is about 1/500 the size of conventional sensors.

Josep Vehi from the University of Girona and Daniele Trevisanuto from the University of Padua spoke to ask what the size of the sensor will be as a final product and how much of an impact it will have on preterm infants, also in terms of location (currently the thigh). Daniele Trevisanuto also suggested performing a joint clinical study of the device to test its usability and efficacy in his department.

1.3 WP3

Jacopo Bonet, representing the team at the University of Padua that is working on the metabolic model, together with UGA, presents the preparatory work done so far on data (lactate and glucose) from other studies on premature infants.

However, the data are too small in terms of sample size and different from those to be collected. For this reason, it is currently difficult to begin to outline the features of a model that identifies the interrelationships between the significant variables, positive and negative trends, and whether there are correlations with other variables that could lead to complications.

For the research group at the University of Grenoble Alpes, Emmanuel Barbier reports that a PhD student has been recruited and will start working on the project in September. In addition, a researcher with expertise in bioengineering is expected to be recruited later.

Regarding the experimental study on rats, he describes to the participants how it will be carried out and what aspects will have to be decided upon. The proposal for the execution of the clinical

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study to be submitted to the competent authority is now ready, after a careful study of the literature, and will be sent at the end of the month.

It is usually necessary to wait two to three months before receiving a response from the competent authority, and in the meantime, they will be able to begin some optimisation steps on mice, under the authorisation of existing ethical approvals.

The rats on which the experiments will be carried out will be 14 days old. One aspect to be optimised is the feeding mode and type of diet of the rats away from the mother.

In addition, it will be necessary to set up the animal model of hyper- and hypo-glycaemia and to adjust the injection of glucose, lactate and BHB tracers.

Data will be acquired by MRI and by measuring the effects of nutrition and blood sugar on glucose, lactate and BHB consumption in the blood and brain.

The data acquired will be the basis on which the University of Padua team will work on the metabolic model.

Davide Contini and Alessandro Torricelli, propose the combined use of the fNIRS technique in this experiment as well. The results could be useful, although it may not be easily given the size of the rats studied. Chiara Dalla Man, WP3 leader, agrees.

Sabrina Brigadoi adds that there are few publications dating back to the 1990s in which fNIRS technology and glycaemic analysis were combined to study their interaction. However, no model has ever been developed or researched.

1.4 WP4

No update from the WP4 leaders, whose activities will start in September 2023.

1.5 WP5

Alberto Scarpa, for DAVE, briefly presents the assigned WP and the project tasks. The first one has been completed and work is now proceeding on the second planned task, the preparation of the first prototype.

Towards the end of the first year, when they start receiving data from the other partners, they will be able to better integrate their work.

They have chosen the hardware, and the touchscreen and are working on the software and user interface.

He shows the user interface to the participants, still in the draft version, asking for the involvement of the project participants working in the clinical area for aspects such as shape, size and layout of the hardware as well as the contents of the interface.

Finally, he outlines the next deadlines:

- Edge-cloud communication architecture will be ready in September;
- in Novembre PoC of local app for partners;
- in December the deliverable 5.2 Cloud-app Prototype evaluation will be ready.

By December, with a simulation of the data, it will be possible to start using the device.

Davide Contini intervened, proposing to share sample data, to start entering them into it.

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1.6 WP7

WP7 leader Paola Rigo shows the participants the main activities planned in the WP:

- Assessment of the perception of prematurity and the impact of Prometeus neonatal medical devices;
- Visual and Oral Archive of Prematurity: longitudinal memory of the experience related to Prometeus devices and prematurity.

She describes the instrument "Integrated Patient Journey Mapping tool" which is generally used to incorporate the experience of the patient and family members into medical practice, to be supplemented by in-depth interviews to evaluate the impact of on-body monitoring devices on parents and HCP perception during NICU stay.

In addition, longitudinal narrative sessions will be realised to bring out spontaneous nuclei of meanings related to the parental and HCP experience of prematurity.

UCC and Unipd worked together to improve and adapt the instruments to the project as much as possible.

The work on longitudinal narrative sessions led to the development of a protocol, currently in the pilot phase, involving seven families with a history of premature birth. The narrative sessions were transcribed, and the data analysis phase began, to collect spontaneous meanings and those directly associated with the project.

At the next meeting, they will probably be able to report the results of this first study.

The narrative sessions will be collected by staff in the two locations (Italy and Ireland) and subtitled and made available on the project website as a visual and oral archive of prematurity.

An aspect that might be of interest is the parents' perception of the interface of the Prometheus tool.

1.7 WP8

The PI, Sabrina Brigadoi, briefly updates those present on the deliverables submitted and those on which she is working, and which are due at the end of July:

- Plan for Dissemination and Exploitation Including Communication Activities;
- Data Management Plan

In the absence of the WP6 leader, she invites the participants to discuss the issue of approval by the relevant regulatory authorities and ethics committees of the study in humans.

The study could be considered clinical or research and is conducted with a group of devices, all without CE class 1 certification. The population on which the study is proposed also poses other important ethical issues to be carefully examined.

As discussed at the last WP leaders' meeting, it might be important to define the Country from which to start the application for approval.

Davide Contini intervenes to point out how the neo-opticap equipment can still be considered non-invasive since it uses skin-safe light, which can also be further improved from a hardware

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perspective making it eye safe as well. Although the CMM sensor reduces its degree of invasivity compared to current devices on the market, it is still considered minimally invasive.

They wonder whether it will be necessary to take the request to the Ministry of Health for approval.

Daniele Trevisanuto reports that the regulations have changed recently and that the Ethics Committees are divided by area. Generally, due to previous experience in similar research activities, it is also necessary, after obtaining the Ethics Committee's approval, for the device to be CE-marked for medical use and, for this, the Ministry's approval is crucial. This may take 3-4 months.

The activities carried out within the framework of WP7, on the other hand, as they do not directly address premature infants and take place outside the hospital, only require the approval of the internal ethics committees. The approval has already been obtained at UNIPD.

Michele Lacerenza reports that, from recent experience, the Ethics Committees usually refer to the Ministry of Health if the study involves the use of devices, and the Ministry tends to classify this type of activity as a clinical study, with a request that the devices used have the CE mark. He suggests submitting the study as a research activity because the time for approval of a study with a medical device is long.

Rob Cooper adds that in the UK too, if a device is used as a diagnostic tool, then it must be CE marked.

Sabrina Brigadoi reminds us that the Prometeus device will not be a substitute for a clinical decision, but a supplement and that, for this reason, it may not be classified as a diagnostic tool.

QLAB had no plans to apply for a CE mark for the sensor.

Alessandro Torricelli adds that universities cannot be considered manufacturers, and this leads to obstacles when applying for CE marking.

They suggest getting in touch with the local ethics committee to start exploring which is the most appropriate way to proceed.

The participants then discuss the characteristics of the device and its interface, such as the length of the optical fibre, and the clinical information that the display will show.

Daniele Trevisanuto intervenes by saying that it may make sense for the information in the Prometeus device to be synthesised and not redundant with the other instruments already present in the NICU. In the study phase, however, it would be useful for all of them to be visible because this would allow healthcare professionals to understand the meaning of the study itself.

Davide Contini adds that one could think of a project mode and an end-user mode.

The family interface could be more focused on the actions taken and the good health of the child, adds Paola Rigo.

Daniele Trevisanuto suggests that the members of the UGA group simulate clinical conditions in the rat trial to extract data that can shed light on antecedents, predictive factors, and consequences.

2. Continuous reporting and internal monitoring procedures and main characteristics of HORIZON-WIDERA-2023-ACCESS-06 call

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Marta Pozza, an administrative staff member of the Coordinator, presents to participants information on the continuous reporting that the funder requires during the course of the project, showing the areas in the Continuous Reporting module of the Participant Portal, highlighting its contents and identifying which information the Coordinator can enter and which the partners can insert on their own.

In addition, she recalls that initial monitoring of the activities carried out and the expenses incurred during the first half of the year has been arranged, with the request to send the data between the end of August and the beginning of September 2023.

Davide Contini takes the floor to suggest that it is the Coordinator, after collecting data from each partner, who enters them into the portal, to avoid overlapping, duplicate information and to facilitate monitoring.

Marta Pozza then presents the main features of the HORIZON-WIDERA-2023-ACCESS-06 call, for which the Consortium received six proposals from different actors, both representatives of universities and SMEs.

Berta Ben Shachar of QLAB asks how flexible the budget is and what changes can be made.

The representatives of PIONIRS ask how they can arrange for the inclusion of possible unit costs among the personnel costs to be declared, which were not defined at the proposal stage.

3. How to deal with potential new partners' applications to join the Consortium in response to the call HORIZON-WIDERA-2023-ACCESS-06

The PI takes the floor to briefly describe the consortium membership proposals collected so far and to ask the partners if there is any interest in accepting them.

The members of the Steering Committee ask to be allowed to examine them in detail, although they do not identify any expertise that would bring added value to the project among the listed proposals.

The coordinator will send the full proposals to the members of the Steering Committee and, for information, the Executive Board and ask them to respond within 15 days.

All Steering Committee members unanimously approve the proposal.

4. Change of IP contact person for a few months

The Coordinator, Sabrina Brigadoi, informs the partners that from the end of August until the end of January she will be on maternity leave. She proposes that during that period Chiara Dalla Man be the scientific and technical point of contact for the Coordinator.

All partners agree.

5. Updates regarding the selection of an Ethics Advisor for the project

The PI reports to the members of the Steering Committee and to the participants that the search for a consultant who could take on the role of Ethics Advisor for the project has so far led to only one name, Prof. Roberto Cippitanti, whose previous experience and expertise she summarises.

Although he is not an expert in neonatology, Prof. Cippitani has expertise in the legal field and has worked as an Ethics Advisor and Legal Advisor for Universities and Research Centres, as well

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as holding several courses in the context of PhD and MSc courses on ethical and bioethical aspects of research. He has an in-depth knowledge of the Horizon Europe Funding Programme, having also worked as an expert evaluator. He is and has been involved in numerous projects also as an ethics manager and advisor.

He could then be assisted by the members of the Advisory Board in purely clinical aspects.

The partners attending note a potential conflict of interest in the fact that Legal Firm Cippitani, Di Gioacchino & Iozzolino, of which it is a partner, is entrusted with the task of auditing some of the projects implemented by the Politecnico di Milano.

Sabrina Brigadoi also recalls that the appointment of an Ethics Advisor is foreseen by the GA as a necessary requirement for the project and that the advisor's activity must be rewarded. She, therefore, proposes that the Coordinator should appoint the Ethics Advisor, but that the expense should be shared among the various partners who have received EU funding to implement the project.

Participants propose to initiate contacts to look for other possible candidates and ask for a quote and an estimate of the cost each partner would incur.

6. Scheduling of next meetings, workshops, and seminars

About the organisation of the next project meetings, Sabrina Brigadoi proposes that an online meeting between the members of the executive board be planned in December, in which the members of the advisory board will also be invited to participate. The minutes will also be shared with the Steering Committee.

For the next face-to-face meeting, he proposes that the PIs submit their availability: UGA, UdG and Polimi are available to host the next project meeting and the choice will also take into consideration the results achieved in the project and the possibility to show them in person to the participants.

The project also envisages the realisation of one seminar per year for each participating country, the first to be held by the end of January 2024.

Brigadoi suggests that for the first year, each partner should make a short video describing their activities and their role in the project. That the videos realised be subtitled in all the languages the Consortium represents and disseminated through the project website and contacts with associations of families of premature infants, healthcare professionals, and other sponsoring channels.

Alessandro Torricelli proposes to use this format later, even at the second face-to-face meeting, to make the presentations homogeneous and the recording mode and setting uniform.

Torricelli and Contini, as an alternative, propose the production of a cartoon video describing the project, to be made by specialised professionals.

Brigadoi, finally, proposes that the four workshops to be held in Italy and Ireland be targeted so as to involve each a distinct and specific audience between industry, families and societies, and neonatologists, and that they be held indicatively the first at the end of 2024, the second at the end of 2025, the third in mid-2026 and the last at the end of the project, in January 2027.

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She invites participants to identify conferences, trade fairs, and industry events where workshops can be held.

7. Discussion about the creation of the Prometeus Exploitation Committee (PEC)

The project PI recalls that a Committee has been foreseen that can focus on all aspects of the chain ranging from intellectual property management to freedom-to-operate and market analyses, to the management of regulatory approvals, to product and service profiling in liaison with industry, academia, and end-users.

She encourages SMEs and university partners with greater involvement in aspects related to the creation of devices, models, and software to contact their relevant offices to set up the committee.

Unipd can, through its competent office, take part in an initial meeting with the SME partners and the Universities and Research Institutes involved in industrial property and technology transfer and intervene punctually in questions that may arise on these issues.

She, therefore, asks the partners to give feedback by the end of September.

Decisions Taken

- Chiara Dalla Man Coordinator's new point of contact during Sabrina Brigadoi's maternity leave;
- Organise the first online seminar in remote mode (cartoon or video);
- Plan and organise 4 workshops as described in point 6.

Actions/To-Do Items

Description	Status (Open/In progress/Closed/On hold)	Schedule	Lead person in charge
Collect continuous monitoring data from partners	In progress	10th September	Marta Pozza, Unipd
Send to SC members complete applications for consortium participation under HORIZON-WIDERA-2023-ACCESS-06 and take a decision on their participation	In progress	26th July	Sabrina Brigadoi, Unipd
Explore new potential candidates to be appointed as Ethics Advisor	In progress	As soon as possible and within the end of the year 2023	All partners
Send the quote of the proposed candidate in the role of Ethics Advisor with a breakdown of the cost per participant	Open	As soon as possibile	Sabrina Brigadoi, Unipd

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Request quotes and content to realise a cartoon video for the first seminar planned as part of the project	Open	As soon as possible and within the end of 2023	Sabrina Brigadoi, Unipd, all WP leaders as regard the content
Identifying a venue for the second in-person meeting	Open	By the end of 2023	All partners
Investigate the availability of EMSs and industrial property, patent, and technology transfer offices of the universities of the partners most involved in these aspects to appoint the Prometeus Exploitation Committee	Open	By the end of September 2023	DAVE, Polimi, PIONIRS, QLAB, Unipd

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Proposed date for next meetings

- December 2023 Executive Board meeting + Advisory Board meeting;
- July 2024 in person plenary meeting + Steering Committee meeting + Executive Board meeting.

Related documents

- Prometeus_presentations_05.07.2023 meeting - https://www.prometeus-eic.eu/reserved-area/.

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