Multimedia **A**uthoring and **M**anagement using your **E**yes and **M**ind

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D6.3(P1)- Clinical trials protocol & Ethics audit

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Abstract: The scope of D6.3 is twofold. First, to describe the protocol that will be followed during MAMEM's clinical trials and second to report on the ethics auditing process that has been performed for the activities covering the first twelve months of the project. The clinical protocol has been created according to the definition of the clinical trials outlined in D6.2 and will be submitted in all clinical centres, so as to be reviewed and approved by the respective institutional review boards ("Helsinki approval"). The ethics auditing process has been performed by the project's internal ethics advisor that evaluated and reported on the compliance of MAMEM's activities with the ethical rules and commitments established in the project's description of actions.

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Executive Summary

D6.3 reports on two parallel activities that have taken place in the context of WP6: a) the development of an elaborated protocol for the project's clinical trials that will translated and submitted for approval in the ethical committee of each clinical site, and b) the ethics auditing process that has been carried out on the activities that took place during the first twelve months of the project.

In what refers to the clinical protocol, although the project's phase on clinical trials is only expected to begin at M18, certain aspects of the protocol were already outlined as part of the previous WP6 deliverables (D6.1 & D6.2). However, as the project activities advances it is now possible to portray the clinical protocol more accurately and with sufficient detail for requesting a "Helsinki Approval" (i.e. ethical approval). In particular, the protocol elaborates on the definition of the clinical trials outlined in D6.2 and has been designed to follow the guidelines of ICH-GCP65 [3]. These guidelines provide "an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects". The clinical trials protocol (as presented in this document) will be translated to Greek and Hebrew and will be submitted (along with the accompanying supporting material) in the ethical committee of each clinical site so as to get the necessary approval.

More specifically, the clinical trials will be divided into two phases. The first phase is designed to test the platform in a controlled environment to address its feasibility and usability. Those will be demonstrated with the participation of able-bodies individuals (total of 18), and patients with spinal cord injury (n=5), Parkinson's disease (n=5) and Neuromuscular disorders (n=5), in the respective clinical sites (i.e., Sheba, MDA HELLAS and AUTH). These participants will be trained to use the platform and will be asked to preform dictated tasks for controlling the computer with their eyes and mind. Later, during an interim stage, if needed, changes will be incorporated in the platform based on the conclusions of the first stage. Then, the second phase will start. The second phase will assess the impact of the new platform on the patients' social activity as affected by their newly acquired ability to generate and share multi-media content. This will be done in the patients' homes. By installing the platform in the homes of 10 patients with spinal cord injury, 10 patients with Parkinson's disease and 10 patients with Neuromuscular disorders, for one week, we will test to what extent social communications were enhanced at that period of time, in comparison to the period prior to the experiment. Section 2 provides the necessary details for theses phases by setting the objectives, identifying the inclusion/exclusion criteria, specifying the apparatus of the utilized platform, describing the procedure and its expected outcome measures.

Finally, Section 3 describes the process that has been followed so as by the consortium to provide the ethics auditor with the information necessary to perform the ethics audit, as well as the assessment scales that have been used by the auditor to judge the appropriateness of the undertaken actions. The outcome of the ethics auditing process is provided as an appendix of this document.

Abbreviations and Acronyms

EEG	ElectroEncephaloGram
GSR	Galvanic Skin Response
PD	Parkinson Disease
SCI	Spinal Cord Injury
COPM	Canadian Occupational Performance Measure
NMD	Neuro muscular disease
DBS	Deep Brain Stimulation
SNS	Social Networking Sites
DOA	Description of Activities

Table of Contents

List of Figures

List of Tables

1 Introduction

The overarching goal of MAMEM is "to integrate people with disability back into society by endowing them with the critical skill of managing and authoring multimedia content using novel and more natural interface channels". In order to do this, a platform will be developed by the technological partners and tested in the sites of the clinical partners.

In the first stage of the project, the habits, needs, and difficulties of the potential users (spinal cord injury, Parkinson's disease and Neuromuscular disorders) were assessed using literature surveys, as well as conducting focus groups with the participation of clinical experts and interviewing the patients with the use of structured questionnaires. The interviews were conducted after obtaining the necessary approval of the local institutional ethical committees of each clinical site (see appendix in [1]). The data that were gathered using these methods was translated into specific clinical requirements that were presented in two MAMEM project deliverables (i.e., D6.1, D6.2; [1, 2]). These outcomes were part of the considerations that were made by MAMEM's technological partners in design the architecture and implementing the algorithms of the platform. The clinical partners, congruently, elaborated the design of the clinical trials protocol which describes the way to demonstrate the feasibility, usability and the efficacy of the platform among the potential users. In order to obtain an ethical approval for the trials, it is important to specify the design and procedure of the trials, the apparatuses that will be used in the trials, the primary and secondary outcomes and the methods that will be used to assess these outcomes.

The clinical trials have two objectives: (1) to assess the feasibility and usability of the system among the potential users: spinal cord injury (SCI), neuromuscular disorders (NMD) and Parkinson's disease (PD). These patients are in different clinical conditions and therefore may have certain requirements that need to be met. These requirements were assessed indirectly during the previous stages, yet in the clinical trials they will be also assessed directly. (2) To test the ability of the platform to enhance the social communication activities of the patients in real-world conditions, i.e. the patient's homes. This is the main outcome of the project and it should be tested only after making sure that the platform can be usable by the patients in their daily activities.

With these two objectives in mind, the clinical trials will be divided into two phases. The first phase is designed to test the platform in a controlled environment to address its feasibility and usability. The second phase is designed to assess the impact of the new platform on the core target variable of the project, which is to foster social integration by allowing to author and manage multimedia content. In total, there will be 63 subjects that will participate, i.e., 21 participants in each of the three clinical sites (6 healthy + 5 patients during the first phase, and 10 patients in the second phase). The primary endpoints of the first phase are accuracy, completion time and learning curves (i.e., rate of progress in the efficiency of operating the system) describing the performance of the subjects of the participants while preforming dictated computer operation tasks. The primary endpoints of the second phase are the activities done and usage time of the platform measured by designated software tools. The first phase will be open and non-randomized and will include three groups of patients and three matched groups of able-bodied individuals. The second phase will be open and non-randomized with three groups of patients (SCI, NMD and PD).

The apparatuses in these trials consist of a number of already approved and widely used instruments which allow electroencephalography (EEG) reading, gaze analyses and capturing the galvanic skin response. This clinical trial protocol was developed and structured in accordance to the guideline of ICH-GCP65 [3], which provides “an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects”.

Finally, in addition to presenting the clinical trials protocol, this deliverable also contains an ethics audit report. The MAMEM project gives specific attention to any ethical issues that will arise and addresses them in a professional way following very closely established EU regulations and corresponding national laws about user privacy, confidentiality and consent. Since a considerable period of time has passed since the project’s start, an ethic audit was performed to ensure the actions done so far in the project are consistent with the ethic regulation and laws. The report consists of MAMEM’s ethics obligation as derived from the projects’ Description of Activities (DOA) [11], the activities (or plans) that have been undertaken to address them and the auditor’s assessment.

2 Clinical trials protocol

The following description of the clinical trials follows the structure of clinical protocols as defined by the guidelines of ICH-GCP65 [3].

2.1 Background

The MAMEM project's overarching goal is to "integrate people with disability back into society by endowing them with the critical skill of managing and authoring multimedia content using novel and more natural interface channels. These channels will be controlled by eye-movements and mental commands, significantly increasing the potential for communication and exchange in leisure (e.g. social networks) and non-leisure context (e.g. workplace)".

In a digitized world, where multimedia-related tasks occupy a large portion of our every-day activities in leisure and non-leisure contexts, and nowadays that children grow accompanied by computerized devices, the skill to manage and author multimedia content is particularly important in becoming more socially integrated. This assertion has more vigour, when disabled people are concerned.

The meaning of multimedia content as part of a communication process has been studied [4] with the most encouraging finding being the importance of sharing as one of the main goals for generating and working with multimedia. Motivated by this fact, MAMEM takes a radical perspective on natural computer interaction with the aim to deliver the technology that will allow people with disability to operate software applications and execute multimedia-related tasks using their eyes and mind. In this way, the MAMEM's project technology can help to enhance the social participation of people with disabilities because of their newly acquired ability to manage and author multimedia content.

MAMEM, therefore, delivers the technology to enable interface channels that can be controlled through eye-movements and mental commands. This is accomplished by extending current applications with advanced abilities to use signals captured by an eye-tracker, an EEG-recorder and bio-measurement sensors. Then, pattern recognition and tracking algorithms are employed to jointly translate these signals into meaningful control and enable a set of novel paradigms for multimodal interaction. These paradigms will allow for low- (e.g., move a mouse), meso- (e.g., tick a box) and high-level (e.g., select n-out-of-m items) control of interface applications through the control of the eyes and the mind.

MAMEM will engage three different cohorts of disabled (i.e. Parkinson's disease, neuromuscular disease, and tetraplegia) that will be asked to test a set of prototype applications dealing with multimedia authoring and management. MAMEM's final objective is to assess the impact of this technology in making these people more socially integrated by, for instance, becoming more active in sharing content through social networks and communicating with their friends and family.

MAMEM's approach is structured around three pillars: a) deliver the necessary technology for developing novel interaction paradigms that shift the source of "control" from hands, fingers and spoken words, to eye-movements, brain electrical signals and bio-measurements, b) validate the technology by setting up a number of clinically oriented pilot

trials and usage scenarios with end-user groups, which are diverse with respect to the cause of their disability but all sharing the degeneration of their neuromuscular system, c) assess the impact of using this technology and as a consequence their newly acquired ability to manage, generate and share multimedia content in becoming more integrated with the rest of the society.

MAMEM is planned as a 36-month project. 7 months for the analysis of the requirements that will take place in parallel with middleware's architecture design, 13 months of research and development, 5 months for pilot trials, 9 months of an interim stage of additional research and development and finally 4 months of additional pilot trials.

According to this timeline, in the first stage of the project, the habits, needs, and difficulties of the potential users (spinal cord injury, Parkinson's disease and Neuromuscular disorders patients) were assessed using literature surveys, focus groups and questionnaires. The questionnaires' trials were approved in an early study (see appendix in [1]) by the local institutional ethical committees of each clinical site. The data that was gathered using these methods was translated into specific requirements that were presented in two MAMEM project deliverables of WP6 [1, 2] that were circulated to the entire consortium, including the technological partners. In the following months, the technical features of the platform were defined and designed according to these requirements. Following these, clinical trials are to be conducted in order to demonstrate feasibility and usability of the platform among the potential users

2.2 Trial design, objective and purpose

The trials will be divided into two phases. The first phase is designed to test the platform in a controlled environment to address its feasibility and usability. The second phase is designed to assess the impact of the new platform on the core target variable of the project, which is to foster social integration by allowing to author and manage multimedia content. This will be done in less controlled settings, i.e. the patient's homes. In total, there will be 63 subjects that will participate, i.e., 21 participants in each of the three clinical sites (6 healthy + 5 patients during the first phase, and 10 additional patients in the second phase). The duration of phase I, will last approximately 5-6 months. The duration of the second phase will last approximately 4-6 months (with dependency on the number of platforms available for the trials). The following pages describe both of these phases in regards to their objectives, participants, procedure etc. The primary endpoints of the first phase are accuracy, completion time and learning curves of the participants while preforming dictated tasks. The primary endpoints of the second phase are the activities done and usage time with the platform measured by designated software. The first phase will be open and non-randomized and will include three groups of patients and three matched groups of able-bodied individuals. The second phase will be open and non-randomized with three groups of patients. The expected participation duration of the participants in the first phase will be approximately half a day. In the second phase, the social activities will be monitored for two months prior to actual participation, there will be half a day of training and testing and the monitoring period will be one week. There will be no follow up on the participants in both phases.

2.3 Phase I - feasibility and usability assessment in a controlled environment

2.3.1 Objective

The objective of Phase I is to test the platform in a controlled environment and address its feasibility and usability aspects. This phase is targeted on closely examining the use of MAMEM platform by actual potential users, as well as on maximizing the ability to adjust and calibrate the platform to their needs. The adjustments and calibration will be done in a period between Phase I and II, aimed specifically for this objective. Therefore, Phase I will take place in a controlled environment which will allow us to assess the platform as systematically as possible. The amendments done in the interim period will maximize the platforms' feasibility and usability for Phase II, where the platforms' capabilities to foster multimedia management and authoring will be assessed.

2.3.2 Selection and Withdrawal of Subjects

Phase I will consist of testing, in each clinical site, 6 healthy participants and 5 patients. The rational of recruiting 6 healthy participants is to assess MAMEM's feasibility and usability among able – body participants free from any medical condition that may affect brain-computer interfaces and gaze behaviour analysis [5]. Then, 5 patients, age and gender matched to the healthy participants will be recruited.

In the following we provide the criteria for including, excluding and withdrawing participants from the clinical trials:

Inclusion criteria:

Inclusion criteria for healthy subjects:

- Men and women aged 18-80

Inclusion criteria for SCI patients:

- Men and women aged 18-80
- Suffering from a complete or incomplete spinal cord injury from C5 and above

Inclusion criteria for PD patients:

- Men and women aged 45-75
- Diagnosed with Parkinson's disease

Inclusion criteria for NMD patients:

- Men and women aged 18-35
- Suffering from a NMD (Duchenne, SMA, SMA II, Tunesian, ALS, Arthrogryposis)

Exclusion criteria:

Exclusion criteria for SCI patients and healthy controls:

- Involuntary eye movements

- Implanted devices that may interfere with the brain electrical activity recorded by the EEG sensor
- Medical conditions that may induce seizures
- Brain conditions such as brain trauma, brain surgery, stroke that may interfere with the brain electrical activity recorded by the EEG sensor
- Any psychiatric (e.g., major depression) or cognitive conditions that may interfere with understanding the instructions or with participant cooperation
- Drugs or alcohol abuse

Exclusion criteria for PD patients and healthy controls:

- Presence of involuntary eye movements
- Any psychiatric or cognitive condition that may interfere with understanding the instructions (including PD patients with dementia)
- Implanted devices (DBS and other electrical medical devices) that may interfere with the brain electrical activity recorded by the EEG sensor
- Brain disorders, such as trauma, stroke, surgery etc, that may interfere the brain electrical activity recorded by the EEG sensor
- Diminished visual acuity
- Very severe body involuntary movements/dyskinesias for PD patients
- Medical conditions that may induce seizures
- Prominent EEG abnormalities, such as continuous slowing, epileptiform discharges

Exclusion criteria for NMD patients and healthy controls:

- Involuntary eye movements and twitches
- Implanted devices (pacemaker) that may interfere with the absorption of EEG waves
- Medical conditions that can cause seizures, such as epilepsy
- Brain conditions that may affect EEG waves
- Any psychiatric or cognitive conditions that may interfere with understanding instructions or with cooperation
- bedridden

Withdrawal criteria:

Removal from study criteria for all participants:

- Do not understand the instructions of the study's personnel
- Inability to complete at least 50% of the protocol
- Unable to use the MAMEM platform; e.g. unable to control the computer with brain or eyes after the 1-2 hours of practice
- Lack of cooperation with the study's personnel

Participants that are withdrawn from the study will be replaced in the case where the withdrawal takes place in the first two hours of the participation. There will be no follow up for the withdrawn participants.

2.3.3 Apparatus and Specifications

The apparatus of Phase I will include the MAMEM platform and a standard desktop computer. The MAMEM platform will be set-up by an investigator or a research assistant who will be trained to operate the platform.

The MAMEM apparatus EEG part will include the EBNeuro's EEG device which consists of a BePlusLTM Bioelectric Signal Amplifier (64 channels) together with an EEG prewired headcap in elastic fabric (61+2 channels: 10-10 ICNS system + Ref. and GND), able to read EEG signals. Alternatively, the EGI 300 Geodesic EEG System (GES 300), using a 256-channel HydroCel Geodesic Sensor Net (HCGSN) may be also used. Both devices are commercial products that have been certified to conform to the medical and safety regulations across the globe.

The MAMEM gaze reading part will include an eye tracking system used for gaze behaviour analysis (SMI REDn Scientific) also used regularly in research and medical facilities around the world (e.g. Harvard University, Yale University, Carnegie Mellon University, Technische Universität München, Peking University, ETH Zurich, Macquarie University Sidney, Bausch & Lomb, Carl Zeiss Meditech, Alcon, Samsung Medical Center and many others). The SMI REDn Scientific eye-tracker is a commercial product that conforms to the medical and safety regulation across Europe and rest of the globe.

Finally, the MAMEM platform will also include a galvanic skin response measuring system. This will be the Shimmer3 GSR+ Unit, which is also a commercial product that has received the necessary medical and safety regulations.

See Appendix A.1 for more information on the specifications of each of the aforementioned devices (i.e. investigator brochures), as well as their certifications (i.e. declarations of conformance).

2.3.4 Procedure

MAMEM platform will be tested in a dedicated room. Phase I trials will take approximately a half day visit. Travel expenses will be reimbursed to the participants and they will be also paid for their time. In order to withstand the study protocol the participants will be given several breaks. If needed, subjects will be invited for a second visit to complete the protocol. In each clinical site, the procedure for the first 6 healthy participants will be identical to the procedure for the next 5 patient. This way, the data of healthy participants will serve as a baseline of which the patients' data can be compared to.

The test day of Phase I will be divided as well into two parts. The first part will be 1-2 hours of setup and training. This will include an introduction to the platform, putting on all necessary wearables to the participants and training them using a learning curve. Learning curves are useful learning performance measures, and enable us to understand if the subject exhausted his/her capacity to learn [12]. For example, the more the person becomes skilful in performing an action, his execution time and error rate during the trial, will decrease. If it is noticed that execution time does not reduce any more from trial to trial, or the error rate

does not improve, one can conclude that the subjects reached a 'plateau' in his/her capacity to improve the performance.

Part 1 – Training:

The training part will continue until a predefined threshold is passed, which will indicate the subject operates in a satisfactory level (e.g., minimal errors, sufficient low values of execution time). The number of trials for each participant will be roughly determined according to the calculated learning curves of the first 6 healthy participants. In the case of a participant not being able to pass the threshold after a predefined number of attempts, his/her participation in the study will be terminated.

The training part will be composed of a training session with the EEG element, a training session with the gaze element, a training session with galvanic skin response element and a training session with all elements. Some of the tasks presented in Table 1 will be specific for the EEG element, some will be specific for the gaze element and some will be for all of them. In order to create the learning curves, for each task, measurements of accuracy and execution time will be recorded in the platform and then plotted (see outcome measures – Section 2.3.5). Table 1 presents an extensive list of the training tasks that will be considered in Phase I. The final list will be decided by further considering the limitations that may arise during the platform's technical implementation.

Table 1: Training tasks

Training tasks	Suggested task using MAMEM platform
Cursor – basic	Select: Click the left button Click the right button Activate: Double click the left button Move the cursor around the edges of the screen Zoom in / out Copy and move Scroll bar- scroll down and up, change pages
Windows' operations	Menu – select text, open category and select "copy" Switching between windows/tabs Open an application Typing with and without text prediction
Keyboard operations	Using frequent key combinations (in one action)

Once reaching a satisfactory level according to the learning curves, the second part will begin.

Part 2 - Dictated tasks for advanced usage scenarios

In this part, the feasibility and usability of the MAMEM platform for multimedia management, authoring and sharing will be tested using dictated tasks (see Table 2). These tasks will include advanced usage scenarios for managing, authoring and sharing multimedia content. They will be communicated using a designated software that will present the task, its objectives and necessary steps, and the participant's performance will be assessed by measuring: a) success rate (including mistakes), b) time to complete each step, and c) number of successful completed steps (see also the outcome measures - Section 2.3.5). As in the previous case, Table 2 presents an extensive list of the tasks that will be considered in this part of training. The final list will be decided by further considering the limitations that may arise during the platform's technical implementation.

Table 2: Dictated tasks

Dictated task (communication)	Suggested task using MAMEM platform
Writing an e-mail	Open an email client software, write and send an email
Photo editing	Open an image editing software, resize or re-colour picture, save it
Sharing information	Post text and pictures in a social network, e.g. Facebook
Searching the internet	Use a search engine to find specific information including navigating to the pages and scrolling (e.g. getting to the bottom of the information on a long page)
Instant messaging	Use an Instant messaging app, e.g. The Facebook's Instant messaging app
Watching a movie online	Search for a video on YouTube, and watch it (e.g. ability to start and pause the video)
Managing music library	Arrange several music files into a playlist
Writing /editing text	Write a few sentences in word /create one slide in PowerPoint

2.3.5 Outcome measures

The outcome measures of both training parts during Phase I will be measured by a desktop monitoring software that will monitor the user activities that are taking place in the computer (see appendix A.3). To allow privacy, the participants will be able to turn off the monitoring software. The software will automatically grade the actions (each step of each task) undertaken by the subject: as a Success (S) or a failure (F). In addition, the time to finish (seconds) and the number of mistakes will be measured. Based on these measures, a composite score and the corresponding learning curve will be calculated. In addition, patient and caregiver perceived usability and user satisfaction would be measured using a standard usability questionnaire (SUS, [6]) and a user satisfaction questionnaire (QUEST 2.0 [7]). Below we outline the primary and secondary outcome measures that will be used in Phase I.

Primary outcome measure:

- Accuracy – percent of successes in attempts to perform each step of each task.
- Time – taken to complete each step of each task

- A composite score based on accuracy and time.
- Learning curves

Secondary outcome measure:

- Perceived usability
- User satisfaction

2.3.6 Statistics

We will use conventional descriptive statistic methods using box plots, means, standard deviations and 95% confidence intervals for continuous variables, median and inter-quartile ranges for non-normal continuous or ordinal data and percentages for categorical data. Analysis will evaluate outlying values and homogeneity. Dependent variables will be checked for normality and homoscedasticity, and data will be log transformed (if not normal). The major tool will be within-subject comparison models (e.g., Analysis of Variance - ANOVA). Whenever suited, we will add analysis of covariance (ANCOVA) to adjust the comparison for potential covariates (e.g., disease severity). Multiple imputations will be used to deal with missing outcome data. Measures will be compared within and across patient cohorts (healthy, PD, SCI, NMD).

In order to assess the MAMEM platform's feasibility and usability by the clinical cohorts, the primary and secondary outcome measures in the dictated tasks of the patients will be compared to the primary and secondary outcome measures of the healthy participants using multiple t-tests, adjusted for multiple comparisons. Non-significant deviations would suggest that the clinical cohorts could use the platform at a satisfactory level without the need for modifications. Significant deviations would warrant additional modification to the platform and/or changing the protocol, during the interim assessment stage between the two clinical trials' phases.

The data from all subjects who finished both parts of this phase will be used in the analyses. A p value of 0.05 will be used in all of the statistical analyses. In addition to the p values, the effect size will also be reported.

2.4 Phase II – Assessing the impact of MAMEM in less controlled environments

In the second phase, the participants will go over the same protocol as in the first phase, but this time in their home environment (and using the lightweight installation – see D4.1 [8]). The platform will be given to them for a fixed period (i.e. a week) in which they will be encouraged to use it. Since the number of platforms to be distributed is limited, the devices will be given in a rotational process that will accommodate the time restrictions of the project. During this phase, apart from the software monitoring the user's activities that are performed in the computer (see Appendix A.3), an additional monitoring software will be used to monitor their **public** online activities, as shared through their social network accounts (see Appendix A.2). The monitoring process will start two months prior to the trial (so as to obtain a baseline) and will continue throughout and after the trial. To allow privacy, the participants will be able to turn off both monitoring tools.

2.4.1 Objective

The objective of Phase II is to assess the impact of the new platform on the core target variable, which is to foster social integration by allowing to author and manage multimedia content. This will be done in less controlled settings, i.e. the patient's homes. This phase is generally targeted to assess the actual effect of the MAMEM platform on the social activities of the patients in case they will own it in the future. In order to do this, the public social activities of the participants will be monitored before and while using the platform and a significant change will be the indicator for a significant impact.

2.4.2 Selection and Withdrawal of Subjects

For this phase, in each clinical site, 10 additional patients will be recruited. Efforts will be made that the 5 patients who participated in Phase I will also participate in Phase II. This will enable to shorten the training period and assess the platform's learning effect over time, by offering a baseline to which these patients performance will be compared.

The inclusion/exclusion/withdrawn criteria of the patients during this stage will be almost identical to the previous phase (see 2.3.2), with the necessary modifications regarding the procedure. More specifically, not owning or using a computer will not be an exclusion criteria since some patients find it too difficult for them to use one and thus redundant to own one. Patients who do not own a computer will be encouraged to acquire one before the participation in the study.

2.4.3 Apparatus and specifications

The apparatus of this phase will be almost identical to Phase I (see 2.3.3) and will include the MAMEM platform and a computer used by the patient. The difference will be the fact that during this Phase, a lightweight installation (see D4.1 [8]) will be used. In particular, the EEG headset of the system will be the Emotiv EPOC/EPOC+, a 14 channels, high resolution, multi-channel, portable system which has been designed for practical research applications (see appendix A.1 for specifications). Equivalently, the eye-tracking device of the system will be the device myGaze Assistive 2, which is a lightweight and portable eye-tracking systems that

incorporates the eye-tracking algorithms developed by SMI. myGaze Assistive 2 conforms to the same medical and safety regulations as the SMI REDn Scientific.

2.4.4 Procedure

Two months before receiving the platform to their homes, the subject's public online social activities will be measured using software designed for this purpose (see Appendix A.2). This software will monitor the social activity externally by following the participants' social accounts, after giving their consent. Using these data, the impact of MAMEM on the social integration status of the participants could be later assessed.

Phase II procedure will include a half day visit to the patient's house for setup and training (identical to Phase I, see 2.3.4) and leaving the MAMEM platform on the patient's home for a fixed period (e.g. one week). The half day visit will demand bringing all the necessary equipment and setting it up by an investigator or a research assistant trained to do so. In case the patient has a computer that covers the requirements of the platform (see D4.1 [8]), the platform will be connected to it (for ecological validity reasons). In case there are technical issues connecting to the local computer or if the participant has no computer, a computer will be provided for the fixed period. During this period, if needed, technical support will arrive to the patient's homes. In case some participants will have difficulties using the computer with the platform due to lack of experience, technical support will assist them, when possible, over the phone.

2.4.5 Outcome measures

The outcome measures of the first half day visit to the participants' home will be identical to the outcome measures in Phase I (see 2.3.5). As already mentioned, the subject's online social activities will be monitored externally (see Appendix A.3). To assess the usage of the MAMEM platform, designated software will monitor only the usage time and the activities done with the platform (see Appendix A.2). The monitoring software will have an easy to track on/off switch, enabling the participants to turn it off if they should choose to do so. Finally, the participants and their caregiver/family members will be asked to fill out the user satisfaction, social inclusion and self-report technical-problems questionnaires.

Primary outcome measure

- Public activities per day in social media
- Time spent using the MAMEM platform per day
- Number of MAMEM platform activities - e.g. using the search engine, entering the email etc.

Secondary outcome measure

- Self-reported satisfaction of using MAMEM for various activities –similar to the Canadian Occupational Performance Measure (COPM) [9]. The questionnaire will query about the use of MAMEM for social authoring; each participant will rate his/her performance and satisfaction from the MAMEM on a scale of 1-5.
- Self-reported Technical problems

2.4.6 Statistics

All data from the half day of setup and training will be handled the same way as in Phase I (see section 2.3.6). The number of online social multimedia authoring activities will be compared to these activities before the fixed period using repeated measures analyses. Perceived usability and user satisfaction will also be compared across cohorts, patients and caregivers using multiple ANOVA tests.

The secondary outcome measures will be analysed using repeated measures analysis of variance (RMANOVA) to assess differences between cohorts and across time for each group of participants and then compared across groups. All secondary analyses will be adjusted for multiple comparisons.

A p value of 0.05 will be used in all of the statistical analyses to assert statistical significance. In addition to the p values, the effect size will also be reported.

2.5 Handling and record keeping of social data

More and more individuals are making use of Social Networking Sites (SNSs) to stay in touch with family and friends, to engage in professional networking or to connect around shared interests and ideas. But users are not the only ones who are interested in SNSs. SNSs have come to attract a wide range of actors, which include application developers, web trackers, third-party websites, data brokers and other observers.

As the number of actors engaging with SNSs and SNS data increases, so does the risk for potential privacy infringements. It should first be noted that different categories of data are disclosed via SNSs. Take for instance:

a) **Disclosed data:** data that is posted by SNS users on their own profile pages (e.g., blog entry, picture, video);
b) **Entrusted data:** data that is posted by SNS users on the profile pages of other SNS users (e.g., a wall post, comment);
c) **Derived data:** data which is inferred from (other) SNS data (e.g., membership of group X implies attribute Y);
d) **Incidental data:** data about an SNS user which has been uploaded by another SNS user (e.g., a picture);
e) **Behavioural data:** data regarding the activities of SNS users within the SNS (e.g., who they interact with and how).

Each of these social networking data will qualify as personal data insofar as they relate to an identified or identifiable individual. In the context of MAMEM we are primarily interested in behavioural data, which is the kind of data that will allow us to spot changes in the social integration status of the subjects. The treatment of these data will be done in accordance with the guidelines set in MAMEM's data management plan, D1.4 [10].

More specifically, in the context of MAMEM we will only use the social network data that have been shared as public, which implies that the users' consent for their processing has been already provided. Nevertheless, additional provisions will be made so as the processing of such data would still be fair and lawful. This will be accomplished by ensuring that all

organizations involved in the processing of data obtained from social networks will comply with the applicable laws on data protection.

Another important aspect has to do with the fact that personal data must be processed for a specified, explicit and legitimate purpose. We should, however, differentiate between the purpose of the social network provider and the purpose of any third party re-using the posted personal data. These two might coincide but they might as well have nothing to do with each other. Any further processing of personal data by third parties requires a legitimate reason for it as well as a clearly defined purpose. In this respect, MAMEM foresees the generation of an inform consent that will extent the purpose of use, originally envisaged by the SNS provider, towards exploiting the subject's behavioural data for detecting any changes in its social integration status. This consent will be delivered and singed as part of the process installing the social media monitoring software (see Appendix A.2). In addition, we will make sure to satisfy the minimisation principle, which states that the processing of personal data from SNSs should not include more data than necessary to achieve the legitimate purpose. In this respect, as we progress with the development of the mechanism for monitoring the activity in social media, we will specify, for each social network, the types of data that need to be collected and processed.

2.6 Quality Control and Quality Assurance

The planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) include:

- Training the personnel involved in the experiments. Each of every one should be familiar with all details of the trial protocols.
- Using pre-defined case report forms (CRFs) to be followed in the process of recording the data
- Nominating a personal (study coordinator) who will monitor the organization of the collected data. Such person will be nominated in each clinical site.
- Verifying (with at least one more clinician) the adherence of all recruited subjects to the inclusion – exclusion criteria.
- Weekly backups of data sets
- Repeat of statistical analysis

2.7 Ethics

Clinical trials protocols are conducted in accordance to the guideline of guideline of ICH-GCP65 [3]. A policy of strict compliance with the trial protocol will be adopted. The researchers will place particular attention to any ethical issues that will arise and will address them in a professional way following very closely established EU regulations and corresponding national laws about user privacy, confidentiality and consent. Briefly, the adopted ethical practices include (as described fully in the DoA [11]): a) Protecting the rights of the participants, b) Protecting safety of the participants, c) Protection privacy of the participants, and d) employ non-discriminative policies. Finally, as already mentioned, MAMEM's clinical protocol will be submitted to the ethical committee of each institution so as to receive the necessary approval. This process will be also audited on a yearly basis.

2.8 Financing and insurance

The financing of the trials will be done by EU dedicated grants for the MAMEM project which the institutions in charge of conducting them received for this purpose. The participants will be insured in both Phases of the trials following the typical procedure employed by the institutions conducting the clinical trials in both institutions.

2.9 Publication Policy

The MAMEM project seeks to dissimilate the results of the clinical trials. Reliable reports, reflecting accurately the design and the results of the clinical trials will be prepared for publication in suitable scientific conferences and journals. The policy employ for publishing the results derived from the clinical trials will be fully aligned with the guidelines for "Knowledge management and intellectual property" as specified in Section 2.2.3 of the DoA[11], as well as with the guidelines that will be agreed within the consortium as part of the consortium IPR plan (i.e. deliverable D1.5 due on M18).

3 Ethics audit

As specified in the DoA [11], and specifically in the part related to Ethics (Section 5), ethical committees will have to approve the procedure in each of the countries conducting pilot trials. This has already taken place for the purpose of conducting the focus groups and delivering the questionnaires (i.e. the approvals have been incorporated as part of D6.1). The same process will be repeated immediately after finalizing D6.3, by submitting the clinical protocol described in Section 2 to obtain the necessary approvals for conducting the pilot trials.

Moreover, in order to ensure the compliance of MAMEM activities with the ethical rules, we have appointed an internal ethic auditor, so as to perform an ethics review of MAMEM activities in each 12-month period. More specifically, in line with our commitments in the DoA [11], Prof. Georgios Kiriazis has been appointed to carry out the ethics auditing process for the first 12 months of MAMEM's activities. Prof. Georgios Kiriazis has been a regular member of the Ethics Committee in the Faculty of Health Sciences (Aristotle University of Thessaloniki) and is fully qualified to serve as MAMEM's ethics auditor. In the following, we provide further details about the ethics auditing process that has been carried out for the first 12 months of the project.

Initially, the ethics auditor was provided with the DoA [11] so as identify the project obligations with respect to ethics. Subsequently, a set of obligations were delivered to MAMEM consortium as those derived from the DoA [11], along with a request to describe the activities that have been undertaken to address each of these obligations. A table was created in return, including the activities that were made to comply with the obligations. Furthermore, evidence was provided to justify these activities in the form of protocols, approvals and provisions that have been made available as part of MAMEM's deliverables. Finally, based on the provided information the auditor was able to identify which of the obligations have been sufficiently addressed and which are still pending.

More specifically, the auditor decided to use three scales of assessment: a) **Addressed**, characterizing the obligations that have been fully addressed; b) **Partly addressed**, characterizing the obligations where sufficient actions have been taken, covering the auditing period, but obligations will have to be re-evaluated during the next audit; c) **Not addressed**, characterizing the obligations that require immediate action from the consortium, as they have not been yet addressed.

The filled in table serving as the ethics audit report that has been signed by Prof. Kiriazis is included in Appendix A.4 of this document.

4 Conclusions

D6.3 has been structured to serve a twofold purpose: a) to elaborate on the protocol of the clinical trials that will be carried out in the context of MAMEM and specify the details necessary to submit this protocol for ethical review, b) to report on the activities that have taken place to ensure the compliance of MAMEM activities with the ethical rules established in the Description of Activities (DoA) and provide the corresponding ethics audit.

With respect to the former, our protocol has been designed to follow the guidelines of ICH-GCP65 [3] that are considered as "an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects". More specifically, we have specified for the trials to take place in two Phases and for each of these phases we have provided details about the: i) objectives, ii) inclusion/exclusion/withdrawal criteria for each patient cohort, iii) apparatus and specifications of the platform's components, iv) procedure to be followed, v) outcome measures, and vi) statistical means that will be used to evaluate the outcomes. In its current form, the protocol already provides a significant amount of details with respect to the pilot trials and will be further refined by considering the limitations that may arise during the platform's technical implementation.

With respect to later, the ethics audit has taken the form of an extended table including information about: i) the obligation of MAMEM consortium as those derived from the DoA, ii) the actions that have been undertaken to address them, iii) the evidence verifying these actions, and iv) the auditor's assessment indicating whether the obligations have been sufficiently addressed, should be re-evaluated in the future, or immediate actions are needed. The ethics audit has been provided as an Appendix of this document.

5 References

[1] D6.1 - Clinical requirements for the MAMEM platform for each of the patient cohort, MAMEM Consortium, August 2015. url: **http://www.mamem.eu/wp-content/uploads/2015/09/D6.1_Clinical_requirements_Final.pdf**

[2] D6.2 - Definition of pilot trials with the participation of patients, MAMEM Consortium, November 2015. url: http://www.mamem.eu/wp-content/uploads/2015/11/D6.2_ClinicalRequirements_PilotTrialsDefinition_Final.pdf

[3] **http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/good-clinical-practice.html**).

[4] Frohlich, D, et al., (2002). Requirements for photoware." In Proc. of the 2002 ACM Conf. on Computer supported cooperative work, pp. 166-175

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[8] D4.1 - Report on the middleware architecture and technical requirements, MAMEM Consortium, November 2015, url: **http://www.mamem.eu/wp-content/uploads/2015/11/D4.1_Architecture_and_Technical_Requirements_Final.pdf**

[9] Law, M., Baptiste, S., McColl, M., Opzoomer, A., Polatajko, H., & Pollock, N. (1990). The Canadian occupational performance measure: an outcome measure for occupational therapy. *Canadian Journal of Occupational Therapy*, *57*(2), 82-87.

[10] D1.4 – Data management plan, MAMEM consortium, November 2015, url: **http://www.mamem.eu/wp-content/uploads/2015/11/D1.4_DataManagementPlan_Final.pdf**

[11] “MAMEM Project Description of Actions – PartB,” 2015. - Readable form (requires authentication): **http://mklab.iti.gr/mamem/images/3/32/PartB_MAMEM.pdf**

[12] Ritter, F. E., & Schooler, L. J. (2002) The learning curve. In International Encyclopedia of the Social and Behavioral Sciences (2002), 8602-8605. Amsterdam: Pergamon

A. Appendix

A.1. Technical specifications, safety approvals, user manuals of MAMEM components.

In the following, we provide links to a set of documents summarizing the specifications, the operator manuals and the Declarations of Conformity for the different components of the MAMEM platform. These are presented in order to demonstrate that MAMEM platform consists of already approved components that are all in regular use and therefore no new untested apparatus will be used in these trials. Considering size and length reasons, the following are links to PDF files uploaded in the MAMEM projects' WIKI (requires authentication to MAMEM wiki):

Be Plus LTM (EB Neuro's EEG device)

1. Be plus 2 EB Neuro-CE Approval
2. Be plus EB Neuro-CE Approval
3. BE plus operator manual
4. EEG EB Neuro-CE Approval

Head cap component

5. EEG head cap EB Neuro-CE Approval
6. head cap instructions

EGI 300 Geodesic EEG System (GES 300)

7. EEG system CE Approval

Lightweight installation (EEG)

8. Emotiv - CE Approval
9. Emotiv EPOC Specifications

Gaze reading component

10. Eye tracking - CE Approval

GSR component

11. GSR Specifications
12. Net Station - Manual

A.2. Social Media Monitoring Software

We plan to rely on an easy-to-use web-based tool that enables real-time monitoring and analysis of a variety of popular social media platforms (Twitter, Facebook, Instagram, etc.) in order to track the social activity of our subjects and derive conclusions with respect to their level of social integration.

The monitoring tool is configured to keep track of content that is posted around specific keywords and/or accounts/sources of interest. For instance, these could include a set of keywords that are indicative of a certain topic and a number of accounts that often post messages related to this topic. Having these keywords and accounts in place, we will then be able to browse through a stream of social media items that have been posted in relation to them. Such a stream is illustrated in Figure 1, where the tool presents social media content related to the brand "Liebherr" (in this case the tool has been used for the task of brand monitoring).

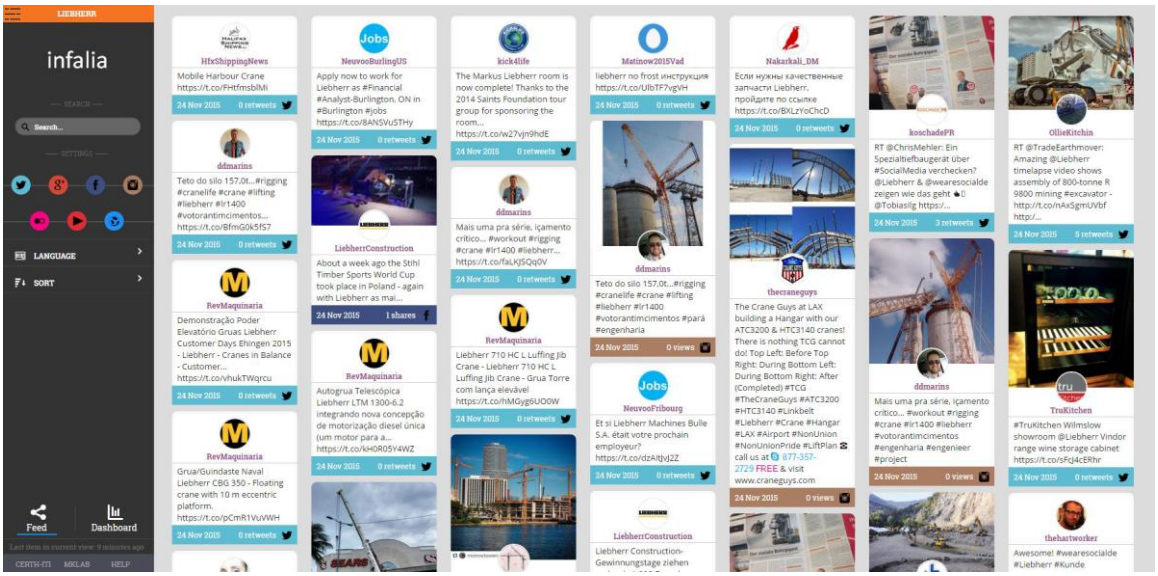


Figure 1: Browsing through a stream ("feed") of social media posts around the brand "Liebherr".

The stream (or feed) view enables users to also filter the monitored items by keyword, source (e.g. show only posts from Twitter), and language, and to also rank them by recency (i.e. first the most recent ones) or popularity (e.g. first the ones with the largest number of retweets).

Browsing the messages that social media users post around a topic or entity of interest is definitely useful for discovering points of view, complaints and positive comments about the topic of interest. However, the real power of the tool is the capability to provide quantitative views and statistics about the monitored content. This is exposed to users through the "dashboard" view, which is illustrated in Figure 2.

The dashboard consists of a number of "widgets", i.e. visualization elements that depict a specific piece of information in an easy-to-grasp way. Each widget or any combination of them can be embedded in a third-party website on demand.

The first row of widgets concerns the activity and impact measurement of the monitored topic in terms of activity (number of posts), user base (number of users posting), reach (number of users reached) and endorsement (number of users liking the posted content).

Figure 2: Dashboard offering several statistics and visualizations around the brand "Liebherr" (again the example above is used in an example for brank monitoring).

Another widget depicts the contribution of each social media source (Twitter, Instagram, etc.) to the overall activity about the topic. A timeline widget illustrates the activity around the most important keywords over time. There are also two map widgets: a) a heatmap widget showing the levels of activity across the globe based on the location of geotagged posts (i.e. when users chose to share the location of their posts), b) a world map depicting the location of users (by geo-parsing the location field that users have entered in their public user profile page). Finally, there is a histogram widget that shows the most active users around the topic and a keyword bubble widget that depicts the most important keywords

around the topic. Relying on the functionality of the aforementioned tool and making best use of the available widgets we will manage to derive the information necessary to spot any change in the social integration status of our subjects.

A.3. Desktop Monitoring Software

User's activities taking place in the computer will be monitored using a desktop monitoring software. In the context of MAMEM our intention is to employ iSafe Free Keylogger[1], which is a free software that provides a set of features that can be used to monitor user's activities as they operate the computer, at any given time.

More specifically, iSafe Free Keylogger can be used to capture the user's screen at a specified frequency, giving insight about the applications operated by the user. Furthermore, it has the ability to record every keystroke typed, including all special characters, while being language independent as it includes a wide variety of input languages. As a consequence, it is trivial to recognize all visited websites irrespectively of the web browser that has been used to serve these websites. One extra feature that can be applied based on recorded keystrokes is monitoring any kind of chat the user participates to, such as skype, facebook or mail. In addition, mouse activity can be listed in log files, with every click being stored in these files. Last but not least, iSafe Free Keylogger provides a rather rare feature that grants access to input and output devices. All printing processes can be identified and registered, the insertion of a usb drive can also be reckoned and the voice input from the microphone can be recorded as well. Figure 3 provides a screenshot for the dashboard view of the monitoring application.

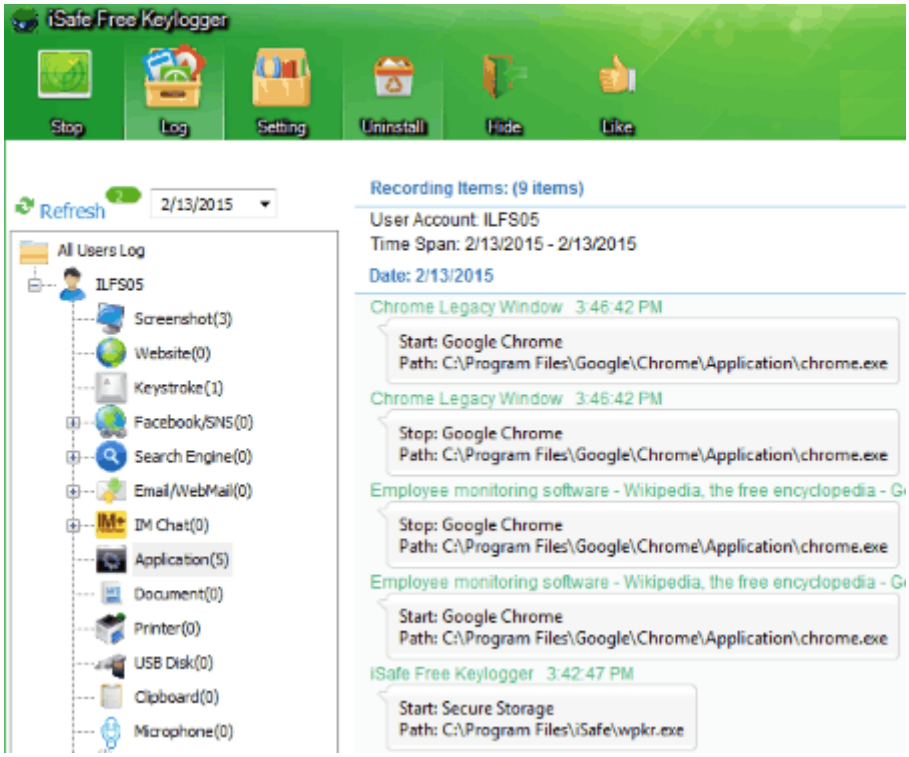


Figure 3: iSafe Free Keylogger Interface

The process of installing iSafe Free Keylogger is straight-forward and allows to easily configure the set of features that will be enabled for monitoring the user's activities. After the installation is completed, the keylogger becomes totally transparent to the user so as to avoid any disturbance.

[1] http://www.isafesoft.com/free-keylogger/index.htm

A.4. Ethics audit

In the following pages we provide the table serving as the ethics audit report, as it has been filled and signed by MAMEM's ethics auditor Prof. George Kiriazis. The process of structuring and filling-up this table has been explained in Section 3.

Appendix II: Ethics Audit

In the following we provide MAMEM's ethics obligation as derived from the Description of Actitivies (DoA), as well as the activities (or plans) that have been undertaken to address them. The goal of this table is to serve as a reference for MAMEM's Ethics Auditor to identify which of the obligations have been already addressed and which are pending. Auditor's feedback is provided in the following forms:

- **Addressed:** For obligations that have been fully addressed.
- **Partly addressed:** Certain actions have been taken, covering the auditing period but the obligation will have to be re-evaluated during the next audit.
- **Not addressed:** For obligations that have not been addresses and require immediate actions from the consortium.

Ethic's Obligations as derived from MAMEM's DoA	Explicit reference in the DoA	Activities	Evidence	Auditor assessment
MAMEM Ethical Protocol • Protect the rights, safety and well-being of research participants • Provide ethical framework	PartB_MAMEM_DoA Page: 95 Chapter: 5.1.1	The first version of MAMEM's Ethical Protocol has been developed in the context of D6.1 so as to obtain the ethical approval to conduct the questionnaire-based study	Deliverable D6.1 (Section 10.1) -> Ethical Protocol	**Addressed**
Minimal Risk • Applications should not expose participants to more than minimal risk (psychological/sociological)	PartB_MAMEM_DoA Page: 95 Chapter: 5.1.1	According to MAMEM's clinical protocol included in D6.3 (see this document) participants will not be exposed to more than minimal risk.	Deliverable D6.3	**Addressed**
Recruitment of Participants • Subject inclusion criteria • Subject exclusion criteria • Subject withdrawal criteria • Handle the participants properly to avoid stigmatization	PartB_MAMEM_DoA Page: 95 Chapter: 5.1.1	All information concerning the inclusion/exclusion/withdrawal criteria of the subjects have been included in D6.2 and are further updated in this document (D6.3). The same documents incorporate also information on how to avoid	Deliverables D6.2, D6.3	**Addressed**

		stigmatization.		
Protect participants from physical danger	PartB_MAMEM_DoA Page: 97 Chapter: 5.1.1	Until M12, experiments have been performed only on healthy subjects. The experiments have taken place in a fully controlled laboratory environment.	Report(s) on accompanying the release of MAMEM datasets [1] and [2]. Check these download links to get the reports	**Partly addressed** This obligation will have to be re-evaluated in the next audit, when the experiments will have been performed on real participants and not only on healthy subjects.
Inform participants • What the research is about • Why it is being conducted • Who it is being conducted for and who is funding it • Purpose of study and use of results • Where the results will appear and who is likely to have access to them • What will be expected of them and how long the participation will last • Right to withdraw from trial	PartB_MAMEM_DoA Page 97 Chapter: 5.1.1	Participants have been informed through the use of consent forms. Consent forms have been used both informing the participants before answering the questionnaires and participating to focus groups, as well as before undertaking any of MAMEM related experiments.	Deliverable D6.2 (Section 8.1) & EthicsMaterial Folder -> EEG_Consent_Form	**Addressed**
Ensure voluntary participation • Take into consideration	PartB_MAMEM_DoA Page 97	In the process of gathering requirements and identifying the	Deliverables D6.1 and D6.2	**Addressed**

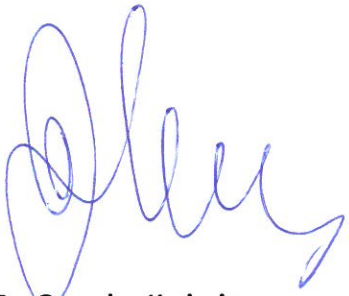
whether the individual is in a position to decide and whether participation could pose a danger to this person • Encourage participants to discuss the research with others before agreeing to participate • Do not rush the participants while reading the form	Chapter: 5.1.1	scenarios, the established recruitment process has ensured the volunteering nature of the participants. Given that the same recruitments process will be followed for recruiting participants for the trials, the aspect of volunteerism should still be prevalent.		
Ethical commissions will have to approve the procedure, in each of the countries conducting pilot studies and copies of the obtained approvals will be submitted to the European Commission	PartB_MAMEM_DoA Page 98 Chapter: 5.1.1	Before conducting the focus group studies and delivering the questionnaires for soliciting the feedback of research participants we have obtained ethical approvals from an ethics committe of each country. A copy of those approvals has been provided as part of D6.1 (Section 10.2). For the purpose of conducting the trials a similar process will be followed using the description of the clinical trials included in D6.3 as the base to form the ethical protocols that will be submitted for approval.	Deliverables D6.1 and D6.3 (current document) Ethical approvals (Deliverable D6.1 – Section 10.2)	**Addressed**
Data collection, storage, transmition and retention	PartB_MAMEM_DoA Page 98	MAMEM's policy on data management has been articulated	Deliverable D1.4 - Data management plan	**Addressed**

	Chapter: 5.1.1	in deliverable D1.4. In this deliverable we specify the kind of data that will be collected in the context of MAMEM, as well as aspects related to their anonymization, sharing between partners, right to delete, retention strategies and underlying legal framework for maintaining the data, authorized-only access and treatment with respect to privacy.		
Sensitive Data • Sensitive information that will be necessary for assessing the patient's eligibility for the pilot trials of MAMEM will be collected but other kind of data will not be collected	PartB_MAMEM_DoA Page 99 Chapter: 5.1.1	During the 1st year activities, the use of sensitive information became necessary only during the recruitment of patients for the questionnaire-based study. Thius, this information was only reveal to the appropriately trained personnel of MAMEM' clinical partners and has not be shared with the rest of the consortium.	Deliverables D6.1 and D6.2	**Addressed**
Usage • All clinical tests involving real patients will be performed by qualified medical staff, with the highest expertise in practice, which will guarantee a strict conformance with national and international ethics	PartB_MAMEM_DoA Page 99 Chapter: 5.1.1	During the 1st year there hasn't been any data collection from patients. For the data collection process that has been performed for engineering purposes by volunteers, the most experienced members of the stuff where employed. In addition, informed consents were signed by all participants, explicitly stating that	Report(s) accompanying the release of MAMEM datasets [1] and [2]. Check these download links to get the reports	**Addressed**

and regulations • The data collected will be strictly used for research purposes and will not be provided, given or sold to any third party		their data can be shared for research purposes.		
Non EU-countries • Imported data will be anonymized, using a code, with the key linking the actual identity with the code being in a locked cabinet in the PI's office • The eye-tracking, brain-electrical signals, biomeasurements and social data will be accessible through an 128-bit SSL that requires authentication • All studies will be conducted under the supervision of the "Israeli Ministry of Health – Pharmaceutical Division - Regulations" and approved by the Sheba Medical center Ethics committee	PartB_MAMEM_DoA Page 99 Chapter: 5.1.1	During the 1st year there hasn't been any imported data from non EU-counties. For the data that have been collected in Israel during the focus groups and questionnaire-based studies, ethical approvals have been obtained by the appropriate authorities.	Deliverable 6.1	**Addressed**
Incidental Findings • Recognize and cross-validate Incidental Findings	PartB_MAMEM_DoA Page 99 - 100	The informed consents that have used both for collecting the end-user requirements, as well as for	Deliverable D6.1 (Appendix-Informed Consent)	**Partly addressed,** because the list

• Define Incidental Findings in the consent forms and give the option to participants to decide whether they want to be notified about them	Chapter: 5.1.1	performing the preliminary data collection processes, make explicit references incidental findings and the options available to treat them.	EthicsMaterial Folder -> EEG_Consent_Form	of potential IFs is not very clear.
Gender Issues • Gender balance in the professionals related with the project • Gender balance in the participants for the pilot trials	PartB_MAMEM_DoA Page 100 - 101 Chapter: 5.1.3	In assembling the cohorts special care has been placed on creating gender and age-balanced groups, always with respect to the particularities of the disease.	Deliverable 6.2	**Addressed**

[1] https://dx.doi.org/10.6084/m9.figshare.2068677
[2] https://dx.doi.org/10.6084/m9.figshare.3153409



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Ethics Audit
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