Mobile Assistance for Groups and Individuals within the Community – Stroke

End of Phase 1 Ethics and Research Governance Advice for Suppliers to assist with the planning of Phases 2 and 3: Information for Suppliers

Horizon 2020
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Contents

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1. Introduction

This document is designed to build upon the information already available on the MAGIC-PCP Website entitled “Requirements for ethical review of MAGIC projects: Information for Suppliers”, the information published in the Phase 1 Call for Tender and has been written to assist the Phase 1 Suppliers with their planning of Phases 2 and 3.

Summary of topics known by Suppliers and Buyers Group thus far…

1. Each supplier has been informed, in the Call for Tender, that they will have to conduct a field trial which is split across two sites concurrently i.e. 1 site in Italy the other in NI
2. For planning purposes the Call for Tender advised bidders, “The purchase of a set of prototype(s) or first test products or services resulting from the R&D, are needed for R&D purposes and it is reasonable to assume trial will consist of a minimum of 150 patients in 2 cycles of 6-months of 75 patients involved in each region concurrently and the equipment is expected to remain in situ for ongoing post project testing.”
3. Each supplier who is awarded a Phase 2 contract, will have to design the field trial and seek approval from the appropriate authorities in both Italy and NI. This activity will occur during Phase 2 so that suppliers who are then awarded a Phase 3 contract will be ready to commence the trial from the Phase 3 contract ‘go live’.
4. Each supplier has been acquainted with the Buyers Group, local research and development units and go-to clinicians all of who can give advice with regard to trial design and that these costs are not recharged to suppliers. Such contributions are ‘in-kind’.
5. Each supplier knows, from Call for Tender, to set aside resources to fund a research nurse in each of the two trial sites in Phase 3.
6. A research nurse, dedicated to each supplier, must be able to consistently identify participants, consent them into the study, give the participants the solution, train in use of the solution, track progress, record metrics and feed findings and results back to the supplier; their activity must at all times follow the approved research governance protocol.
7. Each supplier must be treated equitably and receive the same support cost pricing schedule as all other providers.
8. A research intensity tool can be applied to a research protocol to determine research nurse time requirement.

2. Definitions

It is important that we all use the same terms and have a common understanding of the language of good research governance when thinking about the planning of the field trials. The following words and phrases have the following meanings:

Term	Definition
Chief Investigator	The person who takes overall responsibility for the design, conduct and reporting of the Study; or if a Multi-Site Study, the person who takes primary responsibility for the design, conduct and reporting of the entire Multi-Site Study, whether or not the person is an investigator at any particular site.

Multi-Site Study	Where the Study is part of a study being carried out by or on behalf of the Sponsor at different sites.
NHS Organisation	The NHS contracting body carrying out the research, including Health and Social Care (HSC) Organisations established in Northern Ireland.
SSN and SSR	SSN is the acronym of public Italian National Healthcare Service whereas SSR is the acronym of public Regional Healthcare Service. Study must be implemented according to the regulation of both SSN and SSR
Principal Investigator	The leader responsible for a team of individuals conducting the Study.
Participant	Patient, service user, carer, relative of the deceased, professional carer, employee, or member of the public, who consents to take part in the Study. All references to Participants refer to those recruited at or through the Site.
Protocol	The description of the Study as contained in Schedule 1 and all amendments thereto. Such amendments will form part of this Agreement.
Results	All discoveries, data, information, theories, methods, computer programs, format of presentations and applications of the same and all manifestations or expressions of the same in physical, chemical, biological, molecular, electronic or written form.
Site	Any premises occupied by the NHS Organisation in which or through which the Study will be conducted.
Study	The clinical research study being carried out by the NHS Organisation at the Site.

Nurse research	Nurse with a specialization in clinical research (master, degree, etc.)
Azienda Sanitaria Locale	Public Health Authorities are responsible for the management of all health services in a specific territory or Region.

3. Scope

MAGIC focuses upon the development and implementation of technology based solutions for patients who have experienced a stroke. The solutions will be tested in two European countries that are represented in the Buyers Group – Northern Ireland and Italy. The sites the Phase 3 field trials will be planned in Phase 2 but for guidance in NI there is a zoned regional approach being adopted and in Italy there are 3 distinct Italian Buyers Group locations each of which will host one trial.

4. Timeframe

MAGIC commenced on 1st January 2016 and will run for 52 months, finishing at the end of April 2020. It will be comprised of 4 Phases 0, 1, 2 and 3. Phase 1 and 2 will each last for 6-months with the Phase 2 Call for Tender expected to be issued in August 2017 so that contracts should be able to be awarded and enable Phase 2 to 'go live' on 1st November 2017. If this timeframe is maintained then favourable opinion from research governance/ ethic committees should have been given by the end of April 2018.

5. Cost of Research Nurse

To help the supplier plan the resource allocation the following table has been populated to it show unit price and hours worked in both regions so that all suppliers know that they are being treated equitably. Moreover, it is not simply appropriate to say, at this stage, that each supplier should simply subcontract with the site hosts for 1.0 whole time equivalent (wte) Clinical Research Nurse (CRN) in each of the two sites as each proposed trial should be assessed during design phase to calculate the research intensity and therefore the volume of CRN time required to execute the trial in each site. Since in Italy does not exist a specific profile named CRN for trials implemented in Italy it will be considered a similar profile with research competencies

Information Field	Northern Ireland	Italy
Grade of Clinical Research Nurse	Top Point Band 6	Not lower than Level D
Number Hours worked per week	37.5 hours	36 hours
Hours that Constitute 0.1wte (Whole Time Equivalent) i.e. a morning or afternoon session.	3.75 hours	1 day
Cost of 0.1wte/ session	£24.59	€ (60.000/210 days)= 286
Cost of 0.1wte/ hour	£92.19	€ (60.000/210 days/6hours per day)= 47.62
Cost of 1.0wte/ 12-months	£44,250.70	€ 60,000
Cost of 1.0wte/ 18-months	£66,376.00	€ 90,000

The Research Intensity tool will be provided by the Northern Ireland Clinical Research Network (NICRN) Manager in Phase 2 once the supplier has designed their proposed trial.

6. Solution Safety Prior to Field Trial

It is essential that each supplier ensures the safety of any solution to be utilised with participants. As the participants will have had a stroke, live at home and possibly alone they may be considered as vulnerable and for any favourable opinion relating to research governance/ ethics the committees must be clear that participants will not be exposed to risks and safety will be paramount. Suppliers are advised to seek advice and pay attention to device safety, CE marking and classification of the solution will be important. If a device is classified as a medical device then the solution may require more vigorous approvals to be in place in advance of a favourable opinion being given.

Suppliers are strongly advised to seek guidance from the Medicines and Healthcare products Regulatory Agency. (MHRA)
https://www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device

For clinical trials implemented in Marche Region suppliers are strongly advised to seek guidance from Marche Region Ethics Committee
http://www.ospedaliriuniti.marche.it/portale/archivio13_cerm-ancona_0_446_1.html

7. Ethics and Security

Each consortium member organisation, within the Buyers Group, will ensure the ethics regulations and protocols within their geographical area will be adhered to with regard to the issue of ethics before any task or interventions are carried out on Stroke patients.

It is a policy requirement in the United Kingdom and Italy that any new research study which involves patients directly or their data obtains a favourable ethics opinion from a recognised ethics committee in that country. Where the research involves patients in the UK, this will be a National Health Service or Health and Social Care Research Ethics Committee. In Italy this will be the relevant regional Research Ethics Committee.

Any technology deployment in Phase 3 cannot occur before full ethical review by the relevant ethics committee. If patient data is required in the earlier phases 1 or 2, these proposals will also require ethical approval. The ethics committee has a duty to determine if the supplier's project meets the national legal and ethical requirements of the particular country where the tasks with patients will be carried out.

The suppliers may start testing with patients only when a favourable ethical opinion is in place. They will also be obligated to notify the research ethics committee after the start of the project of any substantial changes to design or patient consent. Therefore, the MAGIC PCP Buyers Group would expect the successful Phase 2 suppliers to be applying for ethical approval to ensure that the necessary permissions to operate field trials in Phase 3 are in place in advance of the start of Phase 3.

The ethics committee will focus on the patient's ability to consent, level of burden, the patient's understanding of risks and burdens of the project, what participating in the field testing means for standard care, what happens at the end of the study, safety and reporting issues, the expertise and experience of the company personnel dealing with the patients in the field testing. The ethics committee will also be concerned that the study design is of high quality and will expect that in the design of any technology that there has been patient public involvement. The IRAS application form will prompt the ethics applicant to answer a series of ethical questions and prepare the necessary field testing paperwork such as consent forms and information sheets for the patients and/or their carers.

7.1 Funding and Roles within Ethics and Security

- If a supplier where to apply for ethical approval a research sponsor would need to be identified and that sponsor would identify a CI and support staff.

- So if the research sponsor is the MAGIC Phase 2 supplier they would identify and fund the CI and support staff.

- Normally that supplier would have secured funding to do this; in this case, having been awarded a Phase 3 MAGIC PCP Contract, the funds would have been supplied through the contract from the Buyers Group to the Phase 3 supplier. It would not be the funder's responsibility to recruit these staff that would be the supplier's responsibility to ensure all is in order and staff are in

place. To be clear, the funding required to execute the trial would have been built into the contract price by the MAGIC PCP bidder.

- For the avoidance of doubt, the Research Nurse, for patient safety and Research Governance purposes, must be an employee of the host trial site. Therefore, each of the final three MAGIC PCP Phase 3 suppliers must subcontract with the trial host organisation. In Northern Ireland, the Northern Ireland Clinical Research Network based within the Belfast Trust will be the supplier's subcontractor for, and supplier of, the Research Nurse.

- Therefore, the MAGIC procurement process covered the cost of these staff and the resource is held by the successful Phase 3 supplier.

- The ethics committee would not get involved in the details of how these staff had been recruited and funded only that they are suitable for their roles within the project.

8. Guide to the necessary process for the supplier to follow to obtain the approval of the intervention by the relevant Ethics Committee.

The processes considered are those that are relevant in the two countries of the Buyers Group, Northern Ireland and Italy.

Northern Ireland

The ethics committees in Northern Ireland follow a national UK programme, where a standardised suite of documents are completed on-line through Integrated Research Application System (IRAS) will be followed https://www.myresearchproject.org.uk/ .

The IRAS 'my research project' website takes the research applicant through all elements of the proposed activity which is patient/ service user focused. The programme classifies the type of intervention and presents the applicant with the appropriate set of forms to complete. Whilst, this is a meticulous and thought provoking process it will be necessary to repeat for all activities that have an interaction with patients beyond their opinion of 'what type of service they would like to see in future'. Therefore, this process will be undertaken for each of the three phase 3 solutions prior to deployment along with the Work Package 6 impact evaluation.

The IRAS process will help shape the design of the testing in the natural environment to ensure all ethical dimensions are appropriately considered. This would require patient consent and so would need ethical and governance approvals undertaken through one ethics application to Office for Research Ethics Committees for NI (ORECNI) through the Integrated Research Application System (IRAS) and governance approvals in each Health and Social Care Trust.

It is important that the Research Managers in each of the regional Health and Social Care Provider Organisation are aware of any activity within their Trusts, Hospitals or Community Services. Within Northern Ireland Paul Biagioni, Senior Manager, Northern Ireland Clinical Research Network (NICRN) must be contacted in relation to the design of the trial. Paul will provide advice on conducting research in primary care. (Refer to Addendum 2 for contact details). In addition, Dr Siobhan McGrath, Head of the Office for Research Ethics Committees for NI, is best placed to provide further

advice to the MAGIC project prior to addressing all matters requiring ethical approval at each phase albeit that there will be no requirement placed upon the Suppliers to undertake patient/ service user testing in Phases 1 and 2.

Italy

The following process will be followed for MAGIC, to gain approval from the relevant Ethics Committee:

- The documentation regarding the MAGIC project will be sent to the Secretariat within 15 working days before the session.
- Administrative referents will send to the scientific group the opinion of the Committee.
- For the studies approved by others Ethics Committees, at the time of preparation of the first dossier should be produced, by the promoter through the Centre, all historical documentation, electronic media (CD or DVD), with all the views already acquired, both for the main study, and for any subsequent amendments.
- No documents should be sent directly to the Secretariat by the Founders, but only by the General and Health Directorates of the Centres, with a special letter of transmittal signed by both directors.
- The practice must be complete, that is including all the documents required by the annexes and perfected with the reports of the experimenters responsible for the feasibility statements (suitability of the experimental centre, the staff involved and cost analysis) and the approval of the General and Health Directorates competent for the centre that requires the evaluation (specific documentation of the centre).

Documentation should include:

- request for an opinion
- authorization request
- research protocol
- synopsis of the protocol
- information sheet for the patient
- informed consent form
- clinic tab for data collection
- list of participating centres
- statement by the proponent on the observational nature of the study
- opinion of the Ethics Committee of the coordinating centre
- curriculum vitae of the experimenter and collaborators
- economic aspects.

Detailed info for those clinical trials implemented in Marche Region suppliers are available at http://www.ospedaliriuniti.marche.it/portale/archivio13_cerm-ancona_0_446_1.html

9. Further Guidance on Consent Documents

Northern Ireland

Informed Consent - Explicit consent will be required from the participants of the pilot in accordance with Health and Social Care Research Ethics Committee procedures and

consent forms will be developed in accordance with National Research Ethics Service (NRES) and IRAS guidance.

Consent from guidance is available at

http://www.hra-decisiontools.org.uk/consent/examples.html

Italy

The procedures followed in the Italian regions involved follow a similar set of procedures to Northern Ireland. The subject, before sampling, must be informed about risks and benefits linked to the participation to MAGIC through informed consent that must be submitted to every patient involved. This document must be read/ understood and signed by the patient. It contains not only all risks/ benefits about their involvement but also all the patient information needed for this study.
Briefly, informed consent contains:

- clear and easy explanation of the scientific project for which patient is recruited,
- duration of the study and role of the patients
- risks and benefits linked to participation
- identity of contact person who answers about question on research, subject's rights; this person will be informed about any injury to the subject
- a statement describing the extent to which confidentiality of records identifying the subject will be maintained
- a statement that participation is voluntary
- personal records request (such as age, sex, birthplace, residence, telephone number, weight, height, occupation, any familiarities, etc)
- specific habits request
- clinical characteristics request

In the informed consent it is specified that the volunteer patient must be able to have their information removed at any time.
Four elements of informed consent (conditions of adequate information, understanding, voluntariness, and decisional capacity) should characterize the subject's authorization at every point of his/her participation in research.
The consent form used is based on that developed by the World Health Organisation Ethics Review Committee. (see attached document uploaded to the portal).

Each Clinical trial need a specific Informed Consent which approval is given by Ethic Committee. Detailed info for those clinical trials implemented in Marche Region suppliers are available at http://www.ospedaliriuniti.marche.it/portale/archivio13_cerm-ancona_0_446_1.html

10. The regulations that may affect the development of supplier technologies in MAGIC

Northern Ireland

In Northern Ireland UK, the research will be undergo ethical review and appraisal in accordance with the governance arrangements set out in the Northern Ireland Research Governance Framework 2007 and in the Governance Arrangements for

Research Ethics Committees UK (GAfREC, May 2011)
http://www.hra.nhs.uk/resources/research-legislation-and-governance/research-governance-frameworks/.
Other laws that apply are Public Health Act (Northern Ireland) 1967, the Data Protection Act 1998 and the Human Tissue Act 2004. This forms part of a national UK programme where a standardised suite of documents are completed on-line through Integrated Research Application System (IRAS):
https://www.myresearchproject.org.uk/

Italy

In Italy, the research will be undergo ethical review and appraisal in accordance with the governance arrangements set out in the provisions concerning the Regional Ethics Committee for the Marche region n.189/2012 and the corresponding Ethics Rules set out for the Piemonte Region.

Issue	***Action***
Research objectives (e.g. study of vulnerable populations, dual use, etc.)	This will be to examine the effectiveness of three, yet to be created, technological interventions where an individual has suffered a stroke and requires on-going support to attain their optimal level of functioning 6-months post stroke. There is likelihood that the participants may be vulnerable in that they may be frail, elderly and living alone. Not only will the interventions be tested and compared to existing data on patients who have just received traditional services but also the impact of the PCP MAGIC Project itself will be evaluated.
Research methodology (e.g. clinical trials, involvement of children and related consent procedures, protection of any data collected, etc.)	The specific design of the research methodology for the Impact Evaluation has been described in Work Package 6 by Dublin City University. However, there may be three different designs or research methodologies used; one for each of the three stage 3 solutions. The MAGIC Project will steer the research methods used to be as consistent as possible but thought will be given to a research approach fitting the type of intervention designed. As this is a pre-commercial procurement there is no way of pre-empting the research design and ethical ramifications at this stage but the MAGIC Project Team gives assurances that attention to detail with regard to Ethics will ensure the highest standards are maintained.
The potential impact of the research (e.g. dual use issues, environmental damage,	Early consideration has been given to potential impact even though the PCP

Issue	***Action***
stigmatisation of particular social groups, political or financial retaliation, benefit-sharing, malevolent use, etc.).	Project cannot predict, at this juncture, the type of intervention to be proposed by suppliers beyond the state of the art descriptions already given. However, the MAGIC Project team commit to ensure that the solutions commissioned will aim to minimise harm and maximise benefit. Moreover, as already stated the IRAS process will ensure that every element of the service deployment, research, development and evaluation will be considered to ensure the research activity does not burden practitioners, patients/ service users or their carers.

Detailed info for those clinical trials implemented in Marche Region suppliers are available at http://www.ospedaliriuniti.marche.it/portale/archivio13_cerm-ancona_0_446_1.html

ADDENDUM 1

UK Ethical Review Forms and Guidance Notes for use with research applications

Ethical Review Form (Lead Reviewer/REC Member)

The HRA has an established role to promote transparency, largely through RECs and the publication of research summaries; this will now be extended to include the publication of the summary of REC opinion.

The lead reviewer(s) should complete this form in preparation for the REC meeting. The form may also be used by other REC members. The REC Chair should use the headings as an aide memoire to structure the discussion at the meeting. Completed forms should be given to the REC Manager who will arrange for them to be destroyed once the minutes of the meeting have been ratified.

Meeting Date:

REC Reference Number:

Study Title:

Brief overview of study (optional depending on REC practice)

1. Social or scientific value; scientific design and conduct of the study (IRAS A6, A7-14, A 57-62, A75) Evaluation of a treatment, intervention, or theory that will improve health and well-being or increase knowledge. RECs should take into account the public interest in reliable evidence affecting health and social care. Use of accepted scientific principles and methods, including statistical techniques, to produce reliable and valid data. Is the research question important and necessary? Is the research design and proposed statistical analysis able to answer the question? Is there equipoise; are all treatment arms viable options for the research participants? Is there involvement of patients, service users, the public, in the design, management, and undertaking the research?
Comments/issues for discussion

2. Recruitment arrangements and access to health information, and fair research participant selection (IRAS A16, A 17-1, A17-2, A 27-29, A46, A47). Inclusion and exclusion of potential research participants. Selection of research participants so that vulnerable individuals are not targeted for risky research and the rich and socially powerful not favoured for potentially beneficial research. The benefits and risks of research should be distributed fairly among all social groups and classes, taking particular account of age, disability, gender, race, religion or belief and sexual orientation, as well as economic status and culture. How are research participants recruited? How does participation impact on their clinical care? Are compensation arrangements in place? Insurance (negligent/ non-negligent harm)**.**

Comments/issues for discussion:

3. Favourable risk benefit ratio; anticipated benefits/risks for research participants (present and future) (IRAS A 18- 25 & part B3 if radiation, and part B 5 if samples).Minimization of risks. Is there evidence of the consideration of any benefits/risk for individual research participants, past/future research participants, including whether the risk/intervention is sufficiently minimal to require no SSA. Are benefits/risk clearly identified for the research participant? Have steps been taken to minimise or eliminate the risk, hazards, discomfort, and distress and enhancement of potential benefits; risks to the research participant are proportionate to the benefits to the research participant and society? Is the balance between risk and benefit equitable?

Comments/issues for discussion:

4 Care and protection of research participants; respect for potential and enrolled research participants' welfare & dignity (IRAS A25, A50-53, A 76, A 77).
*permitting withdrawal from the research * protecting privacy through confidentiality *informing participants of newly discovered risks or benefits * informing participants of results of research *maintaining welfare of participants
*what will happen at the end of the study *provision of appropriate indemnity and insurance *trial registration arrangements in place? (note, this is a condition of the favourable opinion, mandatory for clinical trials).
Data protection & research participant's confidentiality (IRAS A 36 - 43) Where and how (anonymised/coded) and for how long will data be stored? What purpose will be served by the data? Who will access? Are research participants informed that access to their medical notes may be required? Arrangements made to deal with incidental disclosure?

Comments/issues for discussion:

5 Informed consent process and the adequacy and completeness of research participant information (A30 -34, A46, A49 & PIS).Provision of information to research participants about the purpose of the research, its procedures, potential risks, benefits, and alternatives, so that the individual understands this information and can make a voluntary

decision whether to enrol and continue to participate. Is the language used clear and understandable to the research participant it is aimed at? Does it include all the procedures as describe in the protocol? Have uncertainty and randomisation been explained to the research participant? Is consent taken as part of a process with research participants having adequate time to consider the information, and opportunity to ask questions? Is it clear to what the research participant consents or assents? Is there any inducement or coercion? Are vulnerable research participants involved? Is consent obtained to allow GP's to be informed? (Is the Welsh version an accurate translation of the given English version? Wales only)
Comments/issues for discussion:
6. Suitability of the applicant and supporting staff (investigator CV & IRAS question A47, A48) Applicant and supporting staff are suitably qualified and have experience relevant to the proposed research. Medical research involving human subjects must be conducted only by individuals with the appropriate scientific training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional. Are the local facilities and arrangements suitable? Have community issues been considered? Have any conflicts of interest been considered?
Comments/issues for discussion:

7. Independent review (IRAS A 54-56) Review of the design of the research trial, its proposed research participant population, and risk-benefit ratio by individuals unaffiliated with the research. The REC may be satisfied with credible assurances that the research has an identified sponsor and that it takes account of appropriate scientific peer review.
Comments/issues for discussion:

8. Suitability of supporting information E.g. GP letter, interview schedules, questionnaires, lone working policies etc.
Comments/issues for discussion:

9. Other general comments. E.g. missing information / typographical errors / application errors.

10. Consider and confirm the suitability of the summary of the study (IRAS A6-1). This summary will be published on the HRA website in this format together with the summary of the REC's ethical opinion.
Confirmed satisfactory **Changes requested**

Ethical Research issues and material available through research portal.

Within the UK and Northern Ireland in particular suppliers are guided to Integrated Research Application System (IRAS)
https://www.myresearchproject.org.uk/Signin.aspx

ADDENDUM 2

Model Agreement for non-commercial research in the Health Service Northern Ireland and Research & Development Contacts (R&D)

Please Access information relating to the agreement to be put into place between the Health and Social Care Trust in Northern Ireland and the MAGIC Supplier

http://www.ukcrc.org/regulation-governance/model-agreements/mnca/

The delivery and support for the Phase 3 trials will be coordinated and overseen by the Northern Ireland Clinical Research Network (NICRN) Manager albeit the will be local trial site co-ordination and approval will be delivered through the individual Trust's research Managers.

For reference, contact details are recorded below:

The Northern Ireland Clinical Research Network Manager
Paul Biagioni
NICRN Senior Manager
NICRN CC
Room 2007, 2nd Floor KEB
Royal Victoria Hospitals
BHSCT
Paul.Biagioni@nicrn.hscni.net

The Research & Development Managers in each Health and Social Care Trust are:

TRUST	NAME of R&D MANAGER	E-Mail ADDRESS
Northern Trust	Frances Johnston	Frances.Johnston@northerntrust.hscni.net
Belfast Trust	Alison Murphy	Alison.Murphy@belfasttrust.hscni.net
South Eastern Trust	Paul Carlin	Paul.Carlin@setrust.hscni.net
Western Trust	Sally Doherty	Sally.Doherty@westerntrust.hscni.net
Southern Trust	Irene Knox	Irene.Knox@southerntrust.hscni.net

Dr Siobhan McGrath, Head of the Office for Research Ethics Committees for NI, ORECNI, – email address: Siobhan.McGrath@hscni.net
http://www.hscbusiness.hscni.net/orecni.htm