MaGiCAD Constitution

CONTENTS

1. OVERVIEW

This document is intended to be a framework policy document for the running of the core MaGiCAD study. It is based on the policy document used by the Framingham study.

The MaGiCAD study consists of a Core Study, as described in MaGiCAD Core Study Management Protocol, as well as Peripheral Studies and Auxiliary Studies.

Peripheral Studies are run alongside the core MaGiCAD study and often require the collection of additional patients, data or samples over and above the Core Study. Peripheral Studies will have a member of the MaGiCAD Management Committee as the Principal Investigator, and each has its own policy document. The Peripheral Studies are listed in Appendix 1.

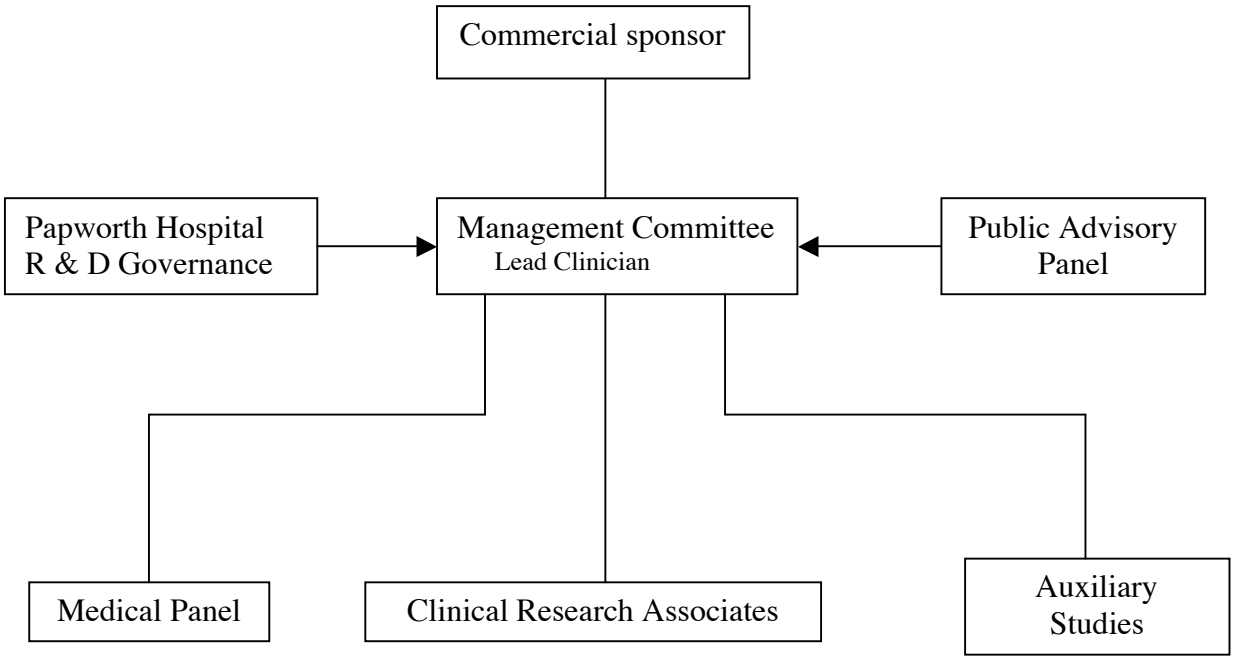
Auxiliary Studies differ from Peripheral Studies in that the Principal Investigator of the Auxiliary Study is not a member of the Management Committee. In addition, Auxiliary Studies will not require the collection additional samples or data by the MaGiCAD team. We welcome applications to run Auxiliary Studies under the MaGiCAD umbrella. Auxiliary Studies are listed in Appendix 2.

2. STRUCTURE OF MAGICAD

MaGiCAD is run at Papworth Hospital, near Cambridge in the UK with two aims:

1. Examine further the potential use of metabonomics and genomics as alternative diagnostics for coronary atherosclerosis to the angiogram.
2. Provide a large, well-characterised, bank of samples that can be used for basic science investigations into atherosclerosis.

A brief overview of the structure of MaGiCAD is shown in the Figure 1.



3. POLICY ON THE CORE MAGICAD STUDY

3.1 Responsibilities of persons involved

Each of the groups in the organisation chart above have certain responsibilities with respect to the MaGiCAD study. These are outlined below. The current and past members of each of the groups are given in Appendix 3.

All current and past members of the MaGiCAD team are responsible for ensuring that their valid contact details are lodged with the MaGiCAD Study Co-ordinator. Failure to do so, may lead to loss of rights under section 3.5.

3.1.1 Commercial Sponsor.

The commercial sponsor owns all of the intellectual property generated using the MaGiCAD samples or data, and has full responsibility for all non-academic use of the MaGiCAD samples and data. However, academic rights to the use of the MaGiCAD samples and data have been deferred to the MaGiCAD Management Committee.

3.1.2. Management Committee.

The management committee will decide on all academic uses of the MaGiCAD samples and data. They are responsible for the scientific conduct of the study and for ensuring that MaGiCAD is run in accordance with the ethical guidelines.

The Lead Clinician will always be a member of the management committee. He or she will have overall responsibility for the clinical conduct of the study.

3.1.3. Medical panel

The Medical Panel is responsible for generating the independent angiogram reads, and for all other medical issues related to MaGiCAD.

3.1.4. Clinical research associates (CRAs)

The CRAs are responsible for the day-to-day running of MaGiCAD. One CRA will be designated the Study Co-ordinator and is the designated contact point for the MaGiCAD Study.

3.1.5. Papworth Hospital Research and Development Department

Papworth Hospital R & D department is responsible for facilitating the running of MaGiCAD at Papworth Hospital, and ensuring that MaGiCAD is run within the current Governance framework.

3.1.6. Public Advisory Panel

In accordance with national guidelines on clinical research, all large clinical studies should have an advisory body consisting of members of the general public to advise

on questions that such studies might address. The Public Advisory Panel for MaGiCAD will be responsible for providing advice and feedback on the public view of the study.

3.2 Composition of the Management Committee

The Management Committee shall be composed of between three and six individuals, one of whom shall always be the Lead Clinician.

Current members of the Management Committee may resign, giving a minimum of three months notice in writing, whereupon they will lose their rights as member of the management committee except under sections X, Y and Z which remain in perpetuity unless explicitly forfeited. Resigning members of the Management Committee need not be replaced unless the size of the Committee would fall below three members.

At any time, an individual may be co-opted onto the Management Committee by unanimous agreement of the current Management Committee.

3.3 Alterations to the MaGiCAD Constitution

Alterations to the MaGiCAD constitution may be made by unanimous decision of the MaGiCAD Management Committee. The Management Committee will endeavour to ensure that any changes that are made are not effective retrospectively, except where required by law. Changes will then be circulated to all involved.

3.4 Use of MaGiCAD samples and data

Prior to any use of any sample from the MaGiCAD study (including serum, plasma, urine or DNA) approval must be sought. For commercial studies, permission must be sought from the Commercial Sponsor. For non-commercial and academic studies permission must be sought from the MaGiCAD Management Committee.

For non-commercial and academic studies, there are three ways in which samples may be used: (A) as part of the Core Study; (B) as part of a Peripheral Study or (C) as part of an Auxiliary Study. All requests for samples from current members of the Management Committee shall be considered as part of the Core Study. All applications for samples from scientists outside the MaGiCAD team shall be considered as Auxiliary Studies. Requests for samples from members of the MaGiCAD team other than members of the Management Committee shall be considered as either part of the Core Study or as Auxiliary Studies at the discretion of the Management Committee.

3.4.1. As part of the Core Study.

Such requests should generally be approved. Only when a substantial quantity of sample is to be used or when the use of sample requires the thawing of the final previously unthawed sample should the request be considered by the Management Committee in the same way as applications under section 3.2.3.

Data collected as part of the MaGiCAD study may be used freely by all members of the MaGiCAD management committee, subject only to the conditions in sections X, Y and Z.

3.4.2. As part of a Peripheral Study

The Principal Investigator of a Peripheral Study shall have full access to all of the additional data and samples. Access to the additional data and samples by any other scientists, including current members of the Management Committee will be at the discretion of the Principal Investigator.

Any use of the core MaGiCAD data and samples as part of a Peripheral Study is governed as if it were part of the Core Study, in accordance with section 3.2.1 above.

3.4.3 As part of an Auxiliary Study

Applications for use of the MaGiCAD samples or data in an Auxiliary Study must be made in accordance with the conditions set down in Section 5.

Briefly, following a successful application by a principal investigator the required amount of sample will be provided to the principal investigator. On completion of the Auxiliary Study, any unused sample will be returned to the MaGiCAD team. Provision of the MaGiCAD samples or data to Principal Investigators is on the explicit understanding that it will be used solely for the purpose outlined in their application, and that the proposed Auxiliary Study will be completed in a timeframe approved by the Management Committee. Any proposed use of MaGiCAD samples or data outside or beyond that previously approved for the Auxiliary Study must be the subject of a further application to the Management Committee.

3.5 Publication

The Management Committee strongly supports the publication of results from the MaGiCAD study in the peer-reviewed literature. However, there may be occasions when material contained in a proposed manuscript may be of commercial value. Therefore, prior to submission for publication, any manuscript describing MaGiCAD samples or data must be submitted to both the Management Committee and the Commercial Sponsor for approval. The Commercial Sponsor may delay submission of the manuscript for a maximum of three months from the date of receipt only in the case where the manuscripts contains data over which the Commercial Sponsor intends to seek patent protection. The Management Committee may delay or prevent submission of any manuscript deemed to misrepresent any aspect of the MaGiCAD study, or which is deemed to scientifically invalid, misleading or fraudulent indefinitely, until such concerns have been addressed. In all other cases, both the Commercial Sponsor and the management committee will endeavour to authorise submission of the manuscript within four weeks, and usually considerably earlier.

3.5.1 Authorship

For every publication describing the use of MaGiCAD samples or data the current and all past members of the Management Committee may elect to be authors.

Current members of the Medical Panel may elect to be authors on all publications describing the use of MaGiCAD samples or data, together with past members of the Medical Panel who provided independent readings of at least 50 angiograms (listed in Appendix 3). Past members of the Medical Panel who provided independent readings of less than 50 angiograms may elect to be acknowledged on all manuscripts.

The current Commercial Sponsor and any past Commercial Sponsor(s) that contributed to the funding of MaGiCAD may elect to be acknowledged on all publications.

Current CRAs, as well as all past CRAs that were involved in the recruitment and/or preparation of blood samples of at least 50 patients, may elect to be acknowledged on all publications describing the use of MaGiCAD samples or data. In addition, for the first publication(s) describing the characteristics of the MaGiCAD Core Study these individuals may elect to be authors on the manuscript. On this initial manuscript(s) the appropriate members of the R & D Department at Papworth Hospital may elect to be acknowledged.

The Management Committee stresses that the above is a minimum requirement for acknowledging the input of the various groups to the MaGiCAD study. It may be that for some publications certain members of staff will have invested considerably more time into the work described than would be credited by the above policies. In these cases, further recognition may be necessary and is encouraged.

It is the responsibility of the corresponding author to ensure that all appropriate parties have been contacted and given the option to exercise their right to accreditation in accordance with these conditions. If no valid contact details for an individual are lodged with the Study Co-ordinator, this responsibility of the corresponding author is waived with respect of that individual.

4. PROCEDURE FOR INITIATING AUXILIARY STUDIES

The significant amount of time and money invested in collection of the background data and samples of the MaGiCAD cohort should be used in as many ways as possible to further scientific progress. Therefore, we welcome all applications for use of the data and samples by members of the wider scientific community. However, as samples are limited, there will be a review process before any Auxiliary Study is begun.

Although collaboration with one of the scientists involved in the MaGiCAD study is not a condition of receiving either data or samples, we anticipate that the majority of Auxiliary Studies will be done on a collaborative basis with one or more members of the MaGiCAD team.

An Auxiliary Study is defined as one that derives support from other than MaGiCAD funds. Examples include studies funded by academic institutions, grant-giving bodies, commercial sources or those performed at no cost.

4.1 What can be provided

There is a considerable amount of background information available on each of the MaGiCAD patients. For full information on the questionnaire that has been administered to the patients and the information taken from the medical notes please see our web-site at http://www.magicad.org.uk/.

For measurement of coronary artery disease status, we have the details of the angiogram read by the patient's own clinician during their treatment. In addition, each patient's angiogram has been re-read by two senior cardiologists.

For each patient arterial blood was taken, and both serum and platelet-poor plasma prepared. A single spot urine sample was also aliquoted and frozen. DNA will also be prepared from the majority of the MaGiCAD patients. Each of these samples are precious, and supplies are very limited. Therefore, samples will not necessarily be available for each proposed Auxiliary Study.

4.2 Applications for use of MaGiCAD data and/or samples

4.2.1 Factors to be considered prior to application

The Principal Investigator of a proposed Auxiliary Study will be responsible for all additional costs that are incurred by the MaGiCAD team in complying with their request. This includes both the obvious and the hidden costs, such as:

a) any administration expenses involved, including removal of identifying data so that patients' confidentiality will be protected
b) any costs for notification of alert values.
c) any costs for coordinating the provision of data and/or samples

It is also imperative that confidentiality of the patients is maintained. The recipient of data agrees not to use any of the data or samples in any effort whatsoever to establish the individual identities of the MaGiCAD patients. Partly to protect the confidentiality of the patients, investigators granted access to data must adhere to the data and materials distribution agreement outlined below (Appendix 4).

Note that any application from a for-profit entity, or from any individual using funds that derive from a for-profit entity, requires the approval of the Commercial Sponsor.

4.2.2 The application process

In order to gain access either to the MaGiCAD database or to samples collected within MaGiCAD (serum, platelet-poor plasma, spot urine or DNA) the application form provided on the web-site (http://www.magicad.org.uk) must be completed and submitted to the Study Co-ordinator. This form consists of various background information, including:

a) A description of the samples and/or data requested.
b) Whether collaboration with members of the MaGiCAD study is planned, and to what extent the MaGiCAD team members will be involved in the Auxiliary Study.
c) A description of any additional work that would have to be undertaken by members of the MaGiCAD team (other than collation of the standard dataset and postage etc.).
d) A summary of how the study will be funded.

This electronic form must be accompanied by a Research Proposal. The Research Proposal should contain the following information:

a) A description of the aims and methods of the study
b) Proposed study design, including power calculations to justify sample size
b) Proposed timetable of the study, including proposed date of return of data to MaGiCAD
d) Experience of the laboratory in performing the appropriate assays.

A brief curriculum vitae of the Principal Investigator must also be supplied, including a list of recent publications. Further supporting documentation may also be provided if absolutely necessary, although we would strongly prefer that this be kept to a minimum.

Applications will be evaluated by the MaGiCAD Management Committee using the criteria given below. The result of the evaluation will then be passed on to the applicant as soon as possible.

4.2.3 Evaluation of Auxiliary Study proposals

The MaGiCAD Management Committee will review the proposals as rapidly as possible following submission. This review process should usually take no more than 8 weeks. The following criteria will be used to evaluate the proposal:

a) Scientific merit. This includes justification of the rationale for doing the study, study design, power and preliminary data
b) Amount of samples requested. Requests for larger quantities of sample are less likely to be approved
c) Resources. The Auxiliary Study must have the resources, including funds and staff, to complete the project.

Furthermore, it is a prerequisite that proposed Auxiliary Studies do not interfere with, nor significantly overlap with, the MaGiCAD Core Study or currently approved Peripheral or Auxiliary Studies.

Following the review process, the applicant will be notified of the result of the application. If the application is approved, the applicant must then complete and return the Data and Materials Distribution Agreement (DMDA) prior to postage of the samples and data to the applicant (see Section 4.3 below). If the Management Committee reject the application, the reasons for a negative outcome will usually be

passed on to the applicant. If these issues can be suitably addressed by the applicant the application may be re-submitted, at the discretion of Management Committee.

4.3 The Data and Materials Distribution Agreement

Prior to distribution of any data or samples, the Principal Investigator must sign a DMDA governing the use of the data and samples (see Appendix 1). A summary of the Data and Materials Distribution Agreement is given below.

The researcher(s) participating the Auxiliary Study agree:

1. that the DMDA (together with the data and samples) is non-transferable;
2. to acknowledge the ownership by the Commercial Sponsor of all MaGiCAD data and samples, including any intellectual property developed using the MaGiCAD data or samples during the performance of the Auxiliary Study;
3. to retain control over all data and samples and to return unused samples;
4. to use MaGiCAD data or samples for the sole purpose of the described research project;
5. not to attempt to identify or contact study participants;
6. not to use biological materials in human experimentation;
7. comply with subjects' informed consent;
8. to complete the Auxiliary Study within the timeframe agreed with the Management Committee;
9. to comply with the requirements of section 3.5 with regard to submission of manuscripts for publication; and
10. to provide a copy of all data generated in the Auxiliary Study to the MaGiCAD Study Co-ordinator, subject to the provisions of section 4.4.2

A hard copy of the completed and signed DMDA must be received before any data or samples will be released. On receipt of the signed DMDA, samples and/or a CD-ROM with the appropriate data will be mailed to the Principal Investigator, typically within four weeks.

4.4 Running of the Auxiliary Study

After approval of an Auxiliary Study, adherence to the Research Protocol as submitted in the application is imperative. If changes in the structure or concept of the Auxiliary Study, or extensions to the Study, are proposed or unavoidable, the MaGiCAD Study Co-ordinator must be contacted. Depending on circumstances, a further application to the Management Committee may have to be made.

4.4.1 Policy on publications

All publications, presentations and abstracts arising from use of MaGiCAD data and/or samples must be reviewed and approved by the MaGiCAD management committee prior to submission or presentation in accordance with Section 3.5.

4.4.2 Collation of data into the MaGiCAD database

Copies of all data collected during the Auxiliary Study must be provided to the MaGiCAD Study Co-ordinator. This data should be supplied in both a raw (completely unmodified in any way) format as well as in the format(s) used for any analyses. Both electronic and hard copies must be provided, within the timeframe agreed with the Management Committee.

The Principal Investigator of the Auxiliary Study shall have the first and exclusive opportunity to analyse, present and publish all aspects of the data collected from within the Auxiliary Study. The data shall not be made available to other researchers (including members of the MaGiCAD team) for analysis until a period of 12 months after receipt of the data by the Study Co-ordinator. From this time onwards, all data from the Auxiliary Study will be incorporated into the MaGiCAD database distributed to the Principal Investigators of future Auxiliary Studies.

5. General Considerations

5.1 Derivation of priority

Where any of the provisions of this constitution are in conflict with the provisions of earlier legal agreements, the provisions of the earlier agreement shall be deemed to have priority.

5.2 Nature of contacts

All formal contacts between parties required by this constitution may be made by electronic mail (provided that an acknowledgement from the other party is received) or in writing.

The Principal Investigator of each Auxiliary Study shall be considered the sole point of contact with the MaGiCAD team. Communication with this individual shall be deemed to discharge all responsibilities of the MaGiCAD team required by this constitution.

The current MaGiCAD Study Co-ordinator (whose up-to-date contact details are available on the website at http://www.magicad.org.uk) shall be deemed the sole point of contact with the MaGiCAD team. Communication with this individual shall be deemed to discharge all responsibilities of the external researchers for contacting the MaGiCAD team (including the Management Committee) that are required by this constitution.

5.3 Reservation of Rights

The Management Committee reserves the right, by unanimous decision, to undertake additional agreements related to MaGiCAD, provided only that they are not in conflict with the provisions of this constitution. For example, the Management Committee may agree to distribute data from the MaGiCAD database through a mechanism other than an Auxiliary Study.

5.4 Violations and Remedies

Violation of any one of the provisions of this constitution does not invalidate the requirements of any other provision. Any such violation should be reported as soon as possible to the Management Committee, who reserve the right to seek any appropriate remedy.

5.5 Arbitration

In the event of disagreement over the interpretation of any part of this constitution, or over any issue not covered by the provisions of this constitution, the general principle set out herein shall form the basis for resolution. Where agreement cannot be reached, a final decision, binding on all parties, shall be sought from an Arbitration Panel consisting of three senior academics from Cambridge University selected by the R&D Department at Papworth Hospital.

APPENDIX 1. PERIPHERAL STUDIES

A1.1 MaGiCAD: Heparin

Principal Investigator: Dr David Grainger
The aims of this study are:

- To collect a samples of arterial and venous blood from a group of patients
- To investigate the effect of administering heparin to patients on the levels of circulating chemokine concentrations.

Patients were recruited between: April and July 2002 (17 patients in total)

A1.2 MaGiCAD: Out-patients (Dr. David Grainger)

Principal Investigator: Dr David Grainger
The aims of this study are:

- To collect information about patients arriving at Out-patients Clinics at secondary referal centres throughout East Anglia
- To determine the best strategy for introducing a metabonomics-based test for coronary artery disease into the existing clinical management paradigm

Patients were recruited between: Not yet begun

Last updated: 21st March 2003

APPENDIX 2. AUXILIARY STUDIES

None

Last updated: 21st March 2003

APPENDIX 3. THE MAGICAD TEAM

A3.1 Commercial Sponsor

TCP Innovations Ltd
UK registered company 4333576 (England & Wales)
9 St. John's Street, Duxford, Cambridge, CB2 4RA, UK.

A3.2 Management Committee

Current Members:
Dr. Peter Schofield (Lead Clinician)
Dr. David Grainger
Dr. David Mosedale

Past members:
Prof. Jim Metcalfe

A3.3 Medical Panel

Current members:
Dr. Peter Schofield
Dr. Sarah Clarke
Dr. Sadia Khan

Past members:
Dr. Duncan McNab

A3.4 Clinical Research Assistants

Current members
Ms Annik Panicker (Study Co-ordinator)
Translational Research Unit, Papworth Hospital NHS Trust, Papworth Everard, Cambridge CB3 8RE
Mrs. Caryl Barnard
Dr. Claire Nugent

Past members
Mrs. Sarah Hayns
Rebecca Schofield (less than 50 patients)

A3.5 Public Advisory Panel

Current members
None

Last updated: 17th December 2004