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FINANCING OF TRANSLATIONAL RESEARCH PROJECTS in the **CARDIOVASCULAR field**

Third Round of Grants

CNIC-TRANSLATIONAL 2009

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1.- Introduction

The CNIC faces the great challenge of establishing a new translational research model, approached from two directions, which enables both the translation of basic knowledge to the diagnosis, treatment, prognosis or prevention of cardiovascular diseases and which contributes to answering scientific questions that arise from daily clinical practice at the patient's bedside.

For this purpose, the CNIC, through the Translational Research Department, has decided to set up a specific program of grants to finance translational research projects in the field of cardiovascular diseases.

This initiative is set within the framework of the general objectives of the Translational Cardiovascular Research Department, whose main mission is to facilitate the conversion of knowledge generated in basic research laboratories into clinical practice, as well as to encourage the research process through the questions generated in healthcare centres. As such, the Department aims to contribute to the creation of bidirectional links between the CNIC's basic researchers and the researchers of the National Health System.

2.-Objectives

Specifically, the objectives of the present round of grants are as follows:

- To encourage the carrying out of projects that facilitate the conversion of knowledge generated through research into improvements in clinical practice.
- To promote collaboration between the CNIC and leading cardiovascular research groups in Spain and abroad.
- To attract the best researchers in order to establish future collaborations with the CNIC.

3.- Requirements of the funding recipients

The research groups that participate in the applications must be led by a principal investigator. The healthcare institutions and/or public or private centres to which the principal investigators of the projects belong may be beneficiaries of the financing encompassed in this round of grants, under the terms and conditions set forth in subsection 3 of section 11 of the *Ley General de Subvenciones* 38/2003, of 17th November.

In the case of centres within the National Health System that manage their research activities through foundations governed by private law under the provisions of Ley de Fundaciones 50/2002 of 26th December, or other bodies governed by private or public law, and which choose to apply for funding through these bodies, the PI coordinator of the project must have a formal link with the Centre within the National Health System, the foundation governed by private law or the body governed by public or private law.

In any event, the beneficiaries must fulfil the requirements established in section 13 of the *Ley General de Subvenciones* and must not be in breach of the circumstances set forth in point 2 of the aforementioned section. The justification of not being in breach of the aforementioned circumstances may be carried out through the means set forth in point 7 of section 13 of the *Ley General de Subvenciones*.

It will not be necessary to set up the guarantees referred to in subsections j) and k) of point 3 of section 17 of the *Ley General de Subvenciones*.

The main beneficiary of the financial assistance will be the body that acts as coordinator and manager of the financing, to which the principal researcher-coordinator of the project is linked. The said body will be considered the ***Principal Funding Recipient***.

The Funding Recipients will assume the obligations and responsibilities regulated in *Ley General de Subvenciones* 38/2003, of 17th November, as well as those established in the regulatory bases of the round of grants established in the present document.

4.- Requirements and structure of the studies

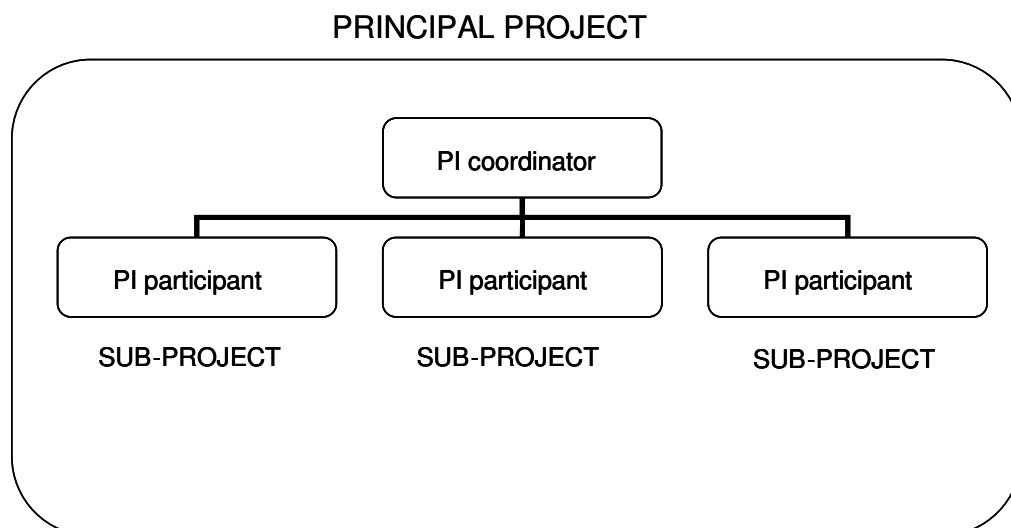
The structure of the studies for the carrying out of the research project will be flexible. Nevertheless, a common nomenclature is established in order to facilitate the management and processing of the rounds of grants.

The study must be structured as an overall **Principal Project**, which may or may not be made up of different **Sub-projects**.

Where the studies within a Principal Project are distinguished only by being undertaken in different centres, and share the same goals and methodology (i.e. multicentre clinical trials), they will not be considered as Sub-projects. In such cases, the proposal will be considered as a Principal Project not composed of Sub-projects.

The Principal Project will have a single Principal Investigator, entitled Principal Investigator-Coordinator, **PI-coordinator**.

The Sub-projects, if there are any, must have their respective principal investigator, entitled **PI-participants**.



The studies must always be led by a PI-coordinator who in terms of functions, statutes and work is attached to the CNIC or a public healthcare centre that belongs to the National Health System. The said link must be formalised by the PI at least during the period encompassed between applying for the project and the completion of the research project for which financial assistance is applied through this round of grants.

The PI-coordinator must be able to prove at all times that the express consent of the body to which he/she is attached has been given, as end beneficiary of the financing encompassed in this round of grants.

The PI-coordinator must hold the qualification of Doctor and must have accredited experience in research, proven by his/her publication of scientific articles and the obtainment of funds, as a principal researcher, for the carrying out of research projects.

The PI-coordinator will fulfil the role of scientific manager of the project and also be in charge of the scientific-technical and administrative management of the programme and the set of activities necessary for the proper implementation of the financed research project. Furthermore, he/she will also act as PI-participant, leading one of the sub-projects in those cases in which the Principal Project is coordinated.

Part of the grant obtained in this round will be allocated to the Principal Funding Recipient to enable the PI-coordinator to apply a percentage of his/her dedication to execution of the project and to collaboration with the CNIC, as provided in the agreement between the Principal Beneficiary Institution and the CNIC.

No principal investigator (PI-coordinator or PI-participant) may appear as such in more than one project or sub-project application in the same round of grants.

PI-coordinators or PI-participants of projects provisionally selected for funding in a previous grants round can apply again in the current round.

Private companies may participate in the round of grants through collaborations in sub-projects providing that they contribute resources for the carrying out of the principal project.

The research project must be mostly carried out in Spanish centres. However, coordinated multi-centre projects may include sub-projects that are carried out in centres or institutions whose

registered address is not in Spain (foreign collaborator centres), providing that they respect section 20 of the *Ley General de Subvenciones* and 13.2.f) of the said Law.

The financing allocated to sub-projects carried out as a whole in foreign centres may not exceed in total 15% of the overall budget allocated to the carrying out of the so-called Principal Project.

5.- Priorities

The CNIC has a series of priorities regarding the characteristics, type and design of the studies, as well as of the research fields or subjects that it considers of greatest interest and which are listed in this subsection. Nonetheless, it must be pointed out that the said priorities or preferences serve as a guide and are not exclusive.

5.1. Characteristics of the study

- The research must be carried out exclusively in humans, including laboratory research in samples or specimens from human beings. In coordinated projects (participation of more than one centre) it may be acceptable for one sub-project to include animal research, providing that it is directly related to the subject of the principal project.
- Priority will be given to those projects that involve the participation and coordination of several centres (multi-centre projects) or groups that are organised within a principal project with several sub-projects. Nevertheless, individual work groups that show sufficient quality will not be ruled out.
- Projects that involve cooperation between clinical and basic researchers will be looked upon favourably.
- Projects that involve collaboration with researchers and groups of the CNIC will also be looked upon favourably.

5.2. Research subjects or fields

The round of grants is aimed at clinical and translational research projects, including studies on the molecular and genetic bases of diseases, the effectiveness of new diagnostic or therapeutic techniques, or effectiveness studies in prevalent diseases, all within the cardiovascular field.

In **ANNEX I** there is a **non-exclusive** list that serves as a guideline of the research areas considered by the CNIC to be of greatest interest.

6.- Basic principles and Ethics Committees

Research projects must observe the fundamental principles established in the Declaration of Helsinki, in the Convention of the Council of Europe relative to human rights and biomedicine, in the UNESCO Universal Declaration on the human genome and human rights, and must also fulfil the conditions laid down in Spanish legislation on the sphere of biomedical investigation, personal data protection and bioethics.

Projects that involve research on humans or the use of biological samples with a human origin will be governed by the provisions of Act 14/2007, of 3 July, on Biomedical Investigation, and the necessary authorisation issued by the Ethics Committee of the centre where the study is to be conducted will be presented, pursuant to legal regulations in force. The authorisation will be issued by Chairman or the Secretary of that committee and will contain a reference to the minutes of the meeting at which the agreement was adopted.

Research projects that specifically involve the use of cells or tissue originating from human embryos or stem cells deriving therefrom must comply with the provisions of Act 14/2007, of 3 July, on Biomedical Research.

Projects that entail clinical trials will comply with the provisions of Royal Decree 223/2004, of 6 February.

Projects that involve animal experimentation must observe the provisions of regulations in force and, in particular, Royal Decree 1201/2005, of 10 October, on the protection of animals used for experimentation and other scientific purposes, and Act 32/2007, of 7 November, on the care of animals during their exploitation, transport, experimentation and sacrifice.

Projects that involve the use of genetically modified organisms must observe the provisions of Act 9/2003, of 25 April, on the confined use, voluntary release and commercialisation of genetically modified organisms, and Royal Decree 178/2004, of 31 January, which approves the general regulation on its application.

Projects that involve the use of biological agents will observe the provisions of Act 31/1995, of 8 November, on Occupational Hazard Prevention, and Royal Decrees on its application with regard to the hazards associated with exposure to biological agents.

Projects that involve the acquisition or exchange of genetic material will observe the provisions of the Convention of Biological Diversity and the International Treaty on Phytogenetic Resources for Food and Agriculture, and the provisions of Act 30/2006, of 26 July, on Nursery Seeds and Phytogenetic Resources.

7.- Conditions, duration and maximum amount per project

The **maximum award for a Principal Project**, whether or not composed of Sub-projects, **will be 1 million euro**, including indirect costs.

The total funding to be awarded in the 2008 round of grants is 3 million euro.

The scheduled duration for the execution of the Principal Project may be from 3 to 5 years.

The assistance awarded through the present round of grants will be released to the Principal Funding Recipient to which the PI-coordinator is attached and to each of the beneficiary bodies associated with the programme, through the Principal Funding Recipient.

The Principal Funding Recipient of each project will be obliged to sign the corresponding agreement with each of the bodies to which the various principal investigators who make up the research team are attached. These agreements will guarantee the transfer of the funds necessary for the execution of the activities by the beneficiary groups, in accordance with the activities plan for the carrying out of the research project.

The financing encompassed in this round of grants will be allocated in order to cover the following costs that are directly related to the carrying out and execution of the proposed project:

DIRECT COSTS:

- Personnel costs: Part of the subsidy must be allocated to covering the payment or hiring of whatever staff may be necessary in order to free the PI-coordinator from ancillary tasks. The hiring of personnel (doctors, advanced degree holders, bachelor's degree holders and research support technical personnel) through the financing provided through this round of grants, under whatever type of work contract, in accordance with the legislation in force, will not involve any commitment in respect of their subsequent hiring by the applicant bodies. As such, when applicable, it is also necessary to take into account the *Real Decreto* 63/2006, of 27th January, which approves the *Estatuto del Personal Investigador en Formación*.
- Consumables necessary for the execution of the project.
- The costs of investment in scientific-technological equipment, whose cost per piece of equipment must always be below 60,000 euros. Large scientific-technological pieces of equipment or infrastructures will not be financed.
- Travel expenses and subsistence allowances in order to attend meetings or conferences related to the carrying out of the project.
- The coordination costs necessary for the execution of the project, such as those derived from economic management (transfers of the financing obtained from the other centres that participate in the project, gathering of economic reports, etc.) or those linked to the scientific management of the project (start-up and follow-up meetings, gathering of scientific reports, etc.).

This chapter will include a section dedicated to the Principal Funding Recipient to enable the PI-coordinator to apply a percentage of his/her dedication to execution of the project and to collaboration with the CNIC, as provided in the agreement between the Principal Funding Recipient and the CNIC.

INDIRECT COSTS

- The funding granted will include 15 percent of direct costs, as indirect costs, to be applied to this type of expenses in centres to which the PIs belong (PI-coordinator and PI-participants). When preparing the budgets for each of the sub-projects and the principal project, a budget item will be included to cover these indirect expenses (15% of direct costs), as provided in the budget form.

The cost deriving from audits that may be necessary for follow-up of the economic execution of the project will be included in these indirect expenses.

When the amount of costs exceeds the amounts set forth in section 31.3 of the *Ley General de Subvenciones* 38/2003, of 17th November, the formalities and obligations concerning the mode of acquisition of goods, established in the aforementioned section, must be observed.

The structure of needs (budget items) of the research groups presented in the application will be approved at the time of the awarding of the grant and will be binding. However, if over the course of the project it is considered necessary to make changes to this structure (budget items), they may be requested and will be considered for approval and application for the following annual period.

At least 80% of the expense budgeted for each of the chapters of Financing for each year will be executed. In the event that the execution percentage is lower than 80%, detailed justification will be presented which will be assessed to determine whether to carry forward the remainder to the following year. At completion of the project, the total budget will have been executed or it will be returned.

8.- Compatibility of the financing

The financing awarded through this round of grants will be compatible with other financial assistance or subsidies, whatever its nature and whatever body awards them.

It will not be possible to renounce projects already under execution derived from other rounds of grants with the aim of obtaining new financing for the same project through the present round of grants.

9.- General instructions, required documentation and deadline for the presentation of applications

The application and all **the required documentation must be presented in English**. The documents must be sent by post and e-mail.

The application form and other standardised forms will be available on the Internet at the following address: www.cnic.es.

An example of the application form together with the required documentation, with the corresponding signatures, must be sent by post to the following address:

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Departamento de Gestión Científica
Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III
Melchor Fernández Almagro, 3
28029 Madrid – Spain

The documentation must also be sent by e-mail in PDF format, indicating CNIC-TRANSLATIONAL in the subject field, to the following address:

proyectostraslacional@cnic.es

All the documentation required in order to participate in this round of grants must be sent by the PI-coordinator who will be responsible for its presentation.

In order to request the financing regulated in the present round of grants, an example of the following documentation must be provided:

PRINCIPAL PROJECT

-Document A: Standardised application model signed by the PI-coordinator of the Principal Project and by the legal representative of the centre to which it is attached.

The signature of the legal representative of the body in the application implies the commitment of the body to support the proper execution of the project should the subsidy applied for be awarded and having checked the data presented in the application.

-Document B: Report of the principal research project, in a standardised model, which must include:

- A project summary
- A general introduction to the research subject
- General objectives
- Work plan and general schedule

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-Document C: Overall budget, in a standardised model, which must include the budgets of the various sub-projects that make up the principal project, broken down according to each need or budget item. The said budget must be broken down into annual periods.

Furthermore, this document must also include the Coordination Costs and their justification.

SUB-PROJECTS

-Document 1: Standardised application model signed by the PI-participant of the sub-project and by the legal representative of the centre to which it is attached.

The signature of the legal representative of the body in the application implies the commitment of the body to support the proper execution of the project should the subsidy applied for be awarded and having checked the data presented in the application.

Furthermore, the said application must be signed by all the members of the research team that are going to participate in the sub-project as proof of agreement.

-Document 2: Scientific report of the sub-project, in a standardised model, which must include:

- A sub-project summary
- Background
- Work hypothesis
- Specific objectives
- Methodology
- Infrastructures and resources
- Work plan and schedule

-Document 3: Budget of the sub-project, in a standardised model, which must be broken down according to each need (budget item) and into annual periods.

If the Principal Project is made up of sub-projects, the PI-coordinator must present the general documents of the Principal Project (Documents A, B and C), the corresponding sub-project that is going to be led by the PI-coordinator with his/her research group (Documents 1, 2 and 3) and the remaining documentation derived from the other sub-projects.

If the Principal Project is not made up of sub-projects (non-coordinated project), for the purposes of presenting the documentation it will be treated as a sub-project (Documents 1, 2 and 3) and it will not be necessary to provide additionally the general documents of the Principal Project.

The following must be added to the above documentation:

- a) The statutes or founding or governing rules of the applicant body to which the PI-coordinator is attached.
- b) The CVs of the PIs (coordinator and participants) that must expressly include at least the following epigraphs: professional experience, projects financed as principal investigators, scientific publications and patents awarded.

Investigators can only participate in a single Principal Project for the purposes of this round of grants.

The **deadline for the presentation of completed application forms** and all additional required documentation **is 10 July 2008**.

Once the application presentation deadline has passed and applications have been revised, the CNIC management will approve the provisional list of accepted and non-accepted applicants by means of a resolution that will be published on the CNIC's website (www.cnic.es). If applicants are not accepted the reasons for non-acceptance will be stated.

Non-accepted and omitted candidates will have 10 days starting from the day after the publication of the resolution in order to put right the deficiencies that have led to their exclusion or omission. If the said deficiencies are not put right, it will be considered that the interested party has given up on the application.

Applicants who are not accepted in the provisional list who, within the aforementioned period, do not put right the deficiencies observed in the presented documentation, or who do not appeal against the aforementioned omission, will be definitely excluded from participating in the process.

Once the deadline for putting right deficiencies has passed, the final list of accepted and non-accepted applicants will also be published on the CNIC's website.

The non-fulfilment of the terms of the round of grants, the breach of the requirements established therein, as well as the hiding or altering of data, or any other kind of interference with the information, will constitute cause for the throwing out of the application, notwithstanding that set forth in sections 56 to 58 of the *Ley General de Subvenciones* 38/2003, of 17th November.

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10.- Assessment and selection of the applications

The assessment and selection of the applications will be carried out by means of a competitive awarding procedure, in accordance with the advertising, transparency and non-discrimination principles, which will consist of two stages: a scientific-technical assessment process and a selection process.

The first stage of scientific-technical assessment will be carried out by the *Comisión Técnica de Evaluación de Enfermedades Cardiovasculares del Fondo de Investigación Sanitaria (FIS) del Instituto de Salud Carlos III* and International Expert Board.

The scientific-technical assessment will be carried out in accordance with the following criteria:

- a) Scientific quality and originality of the project
- b) Degree of compliance with the methodology, the design of the study and the work plan in relation to the objectives of the project.
- c) Scientific and socio-health relevance.
- d) Feasibility of the proposal.
- e) Experience and capacity of the principal researchers and their research teams to fulfil the planned activities.
- f) Degree of compliance of the requested budget in respect of the proposed objectives.

The FIS Technical Committee and each of the international experts will assess the projects, as well as the sub-projects in the case of coordinated projects, and will award a score of 1 to 10 for each of the criteria, where 10 is the maximum score. The average score for each project will be determined and a list of projects assessed will be drawn up showing the scores obtained from highest to lowest.

In the second stage and once the scientific assessment has been carried out, the selection process will be carried out by the Selection Committee of the CNIC, made up of the Centre's Research and Management Committee, taking into account the score of each project from the first stage

assessment. This process will be coordinated by Dr. Ginés Sanz, Head of the Translational Cardiovascular Research Department of the CNIC.

The selection process will be carried out in accordance with the following criteria:

- a) Technical assessment of the feasibility of the project.
- b) Degree of compliance of the projects with the objectives and priorities established by the CNIC.
- c) Ethical aspects of the proposed research.
- d) Multidisciplinary participation of basic and clinical research teams.
- e) Coordination of the research activity. Participation of different centres, as well as the degree of compliance of the size, composition and dedication of the research team with the objectives proposed in the project.

The CNIC Selection Committee will decide the projects considered fundable within the top scoring projects of the first scientific-technical assessment phase that fulfil those selection criteria. The number of fundable projects will be determined by their quality and based on budget availability of the CNIC for this round of grants.

The proposal resulting from the application of the said criteria will include:

- a) A prioritized list of fundable projects, including a budget proposal for them and a list of the projects considered to be non-fundable.
- b) An individual report with the most relevant aspects of the final scientific-technical assessment.

According to the scientific-technical assessment carried out and considering all the criteria set forth above, the Selection Committee, following the approval of the Management, will issue a **provisional resolution** listing the projects considered to be fundable and including the budget allocated to each of them. The said list will be published on the CNIC website (www.cnic.es). Following publication, applicants will have a period of 10 calendar days to make representations. Once these have been examined, the provisional resolution final proposal will be formulated and will once again be published on the centre's website.

At any time during the assessment process, prior to the final awarding resolution, the CNIC may ask for whatever reports or clarifications it considers necessary, both from the applicant body and from the researcher in charge, as well as from any other body it considers opportune.

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The provisional resolution proposal will include the following information:

- a) The funding recipients of the financial assistance and the principal participating investigators.
- b) The overall amount of each financial assistance package and its item breakdown

The provisional resolution proposals do not create any right in favour of the proposed beneficiary in respect of the CNIC, until such time that it has been notified of the final awarding resolution.

11.- Final resolution and awarding

The following additional documentation will be necessary for the final awarding resolution:

a) Collaboration agreement - MULTILATERAL, signed by all the legal representatives of the public or private institutions or centres to which the principal investigators (coordinators and participants) of the Principal Projects and sub-projects belong, in accordance with the model established in **Annex II** of these regulations.

The number of signed original copies (not photocopies) of this agreement to be presented is equal to the number of participating entities in the Project plus one additional copy for the CNIC's files.

The date on which the agreement comes into force shall be that of the official concession of the award, and the termination of the agreement shall coincide with the final date of the award period.

b) A copy (not original) of the agreements established between the Principal Funding Recipient and the various funding participating recipients (Collaboration agreement – BILATERAL), which ensure and guarantee the necessary transfer of funds for the proper execution of the financed project.

Annex III to these regulations provides a suggested model for this type of agreement. Nonetheless, the Principal Funding Recipient may adopt a different model in accordance with its internal regulations.

c) Report by the Research Committee of the centre (or similar body of the centre, or failing this, its Management Commission) to which the PI-coordinator is attached, which states the feasibility of the research project in all respects.

d) Set of reports and authorisations from the Clinical Research Ethics Committee and other collective bodies responsible for overseeing the fulfilment of the agreements and rules in place concerning research, which may be considered necessary, in accordance with that set forth in subsection 6 "*Basic principles and Ethics Committees*". In all cases, the authorisation will be issued by the President or corresponding collective body and must include the reference to the minutes of the session in which the agreement was reached.

e) Authorisation of the *Agencia Española de Medicamentos y Productos Sanitarios del Ministerio de Sanidad y Consumo* if clinical trials are involved.

f) Details of the Principal Funding Recipient's bank account to which funds should be transferred in the event of official concession of an award. Name of bank and bank account number (20 digits).

g) Supporting documentation confirming compliance by the Principal Funding Recipient with its tax and social security obligations.

The deadline for the final resolution of the procedure will be 70 calendar days from the publication of the provisional resolution final proposal on the CNIC's website (www.cnic.es).

In accordance with section 25.3 of Law 38/2003, the PI-coordinator will be informed in writing of the final resolution, whether assistance is awarded or refused, in order to guarantee that all the interested parties are informed.

In the case of a final resolution awarding assistance, the notification will include the following information:

- a) The funding recipient of the financial assistance and the principal participating investigators.
- b) The overall amount of each financial assistance package and its item breakdown.
- c) The deadlines for presenting the annual follow-up and final reports.

The final resolution, both in the case of awarding and refusing assistance, will also be published on the CNIC's webpage (www.cnic.es).

12.- Follow-up

The scientific-technical and economic follow-up of the awarded financial assistance will be carried out in accordance with the procedures and forms that will be published on the CNIC's website (www.cnic.es). Furthermore, the CNIC may assign the bodies, commissions and/or experts that are deemed necessary in order to carry out the opportune actions for the follow-up and checking of the application of the received financial assistance and may ask for the presentation of any additional information deemed necessary or may audit the beneficiaries of the financial assistance.

The PI-coordinator of the project will agree to present a scientific report and an economic report to the CNIC each year. The first annual reports shall be presented ten months after the official concession of the award by the CNIC, and subsequent reports will be due every twelve months after this date. Reports shall be sent by post and e-mail, in the same way as stipulated for the presentation of the application forms for participation in this round of grants.

At the same time, the CNIC may ask the PI-coordinator to prepare an oral presentation of results obtained, at a special session of the CNIC, for follow-up of the project financed. That presentation, if made, will be communicated beforehand to the PI-coordinator.

Reports, along with the oral presentation, if any, will be assessed and the renewal of financing for successive years will depend on that assessment. Nevertheless, the CNIC may collate complementary information at any time to conduct a follow-up of development of the project funded.

Each research project, and all sub-projects that form a part thereof, will be assessed annually by the CNIC through the corresponding committees. External assessors who are experts in the area of development of the project may form part of those committees.

The results of the said assessments will be sent to the PI-coordinator of the project who in turn will inform the other PI-participants.

The first annual payment will be transferred to the Principal Funding Recipient, centre or institution to which the PI-coordinator is attached, in accordance with the approved budget and as set forth in

the awarding resolution. The Principal Funding Recipient will also be responsible for distributing the funds amongst the other beneficiary bodies, to which the PI-participants belong, in accordance with the agreements signed with them.

The remaining payments, corresponding to the following annual periods, will depend upon the fulfilment of the requirements established for this purpose in the round of grants. These annual payments will be released upon positive evaluation of the corresponding scientific and economic reports.

The beneficiary will be obliged to provide the checks geared towards guaranteeing the proper execution of the activity financed through this round of grants. It will also be subject to the financial control activities that correspond to the General Intervention of the *Intervención General de la Administración del Estado* and to those set forth in the legislation of the *Tribunal de Cuentas*.

Throughout the term of the project, the CNIC reserves the right to audit the bodies that form part of the project, having given notice to the legal representatives of the bodies, as a quality control measure of the procedure. The cost of the audit will be borne by the fundable indirect costs of the project.

If, as a result of the assessment and revision by the CNIC Follow-up Committee for this type of financing, it can be inferred from the audit report that the expenses funded were not adequately justified or that the regulatory bases of this round of grants and the purposes for which funding was granted were totally or partially breached, that circumstance will be notified to the beneficiary along with the results of the verification made and the procedure will commence for total or partial refund of the assistance granted. The refund procedure, including the amount and payment term, will be determined by the CNIC Follow-up Committee, based on the circumstances of the breach, and notified to the beneficiary of the assistance.

Two months before the completion of the term of the project, the PI-coordinator will be obliged to present a final scientific, economic and management report on the activities carried out, and will also be obliged to make the annual oral presentation in the special session scheduled at the CNIC.

The breach of any of the terms and conditions of the round of grants, as well as the hiding or altering of data, or any interference with the requested information, will result in the application being thrown out.

13.- Procedure

Final resolutions on granting will be approved by the Delegate Committee of the Board of Trustees of the CNIC Foundation.

Subsequently, both the regulatory bases of round of grants and definitive resolutions on granting will be ratified by the Board of Trustees of the CNIC Foundation.



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ANNEX I.- Priority Research Areas

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Priority Research Areas

Annex I provides a **non-exclusive** list that serves as a guideline of the cardiovascular research areas considered by the CNIC to be of greatest interest.

1.- Atherosclerosis and vascular biology

- Progression and regression mechanisms and indicators of atherosclerosis, including studies on the molecular and genetic bases of the disease, biomarkers and new imaging techniques.
- Endothelial dysfunction, including its relationship with inflammation, ageing and risk factors. Endothelial repair.
- Genetics and risk factors: interaction between genes and between genes and environmental factors.
- Acute coronary syndromes.
- Development and validation of new diagnostic and therapeutic approaches.

2.- Myocardium, heart failure and valves

- Ischemia-reperfusion, including studies on myocardial protection and new ischemia markers.
- Molecular bases of hypertrophy and ventricular remodelling.
- New approaches to the early diagnosis, treatment and prevention of cardiac insufficiency.
- Adult valvular disease, including degeneration mechanisms and valvular calcification.

3.- Arrhythmias

- Genetic bases of arrhythmias.
- Assessment of new therapies and technology in their treatment.
- Effectiveness of the treatment in prevalent arrhythmias, particularly atrial fibrillation.



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ANNEX II.- Model Collaboration Agreement - MULTILATERAL

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COLLABORATION AGREEMENT

FOR THE CARRYING OUT OF THE RESEARCH PROJECT (*Project title*) FINANCED BY THE "CNIC TRANSLATIONAL 2009" ROUND OF GRANTS

In (place), on (date)

BY AND BETWEEN

On one side the legal representatives of each of the institutions to which the Principal Investigators involved in the carrying out of the research project belong,

1. Name and surnames of the legal representative, with ID number, as (*position that he/she holds*), and on behalf of and representing the *Centre/Institution* (henceforth "..."), whose registered address is at, in accordance with the powers awarded

2. Name and surnames of the legal representative, with ID number, as (*position that he/she holds*), and on behalf of and representing the *Centre/Institution* (henceforth "..."), whose registered address is at, in accordance with the powers awarded

3.

4.

And on the other side,

Mr. Alberto Sanz Belmar, Managing Director of the FUNDACIÓN CENTRO NACIONAL DE INVESTIGACIONES CARDIOVASCULARES CARLOS III (henceforth "CNIC"), in accordance with powers that he has been granted for the purpose of entering into Agreements by the Board of the CNIC Foundation, and recorded in public deed before the Notary Public of Madrid Mr. Joaquín Corell Corell, on 24th October 2008 and with protocol number 2987.

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Both parties mutually acknowledge their sufficient legal capacity to enter into the following Agreement and for this purpose,

THEY HEREBY DECLARE

First.- That, on 3rd March 2008, the CNIC Foundation, through the Translational Cardiovascular Research Department of the CNIC, published on the centre's webpage (www.cnic.es) the Round of Grants for the financing of translational research projects in the cardiovascular area (henceforth "CNIC-TRANSLATIONAL"), in accordance with its founding purpose of fostering research related to cardiovascular diseases, their prevention and the promotion of scientific and healthcare progress in this field.

Second.- That the Translational Cardiovascular Research Department's main mission is to facilitate the conversion of knowledge generated in basic research laboratories into clinical practice, as well as to encourage the research process through the questions generated in healthcare centres.

Third.- That one of the noteworthy aims of the CNIC-TRANSLATIONAL Round of Grants is fostering the carrying out of projects that facilitate the conversion of the knowledge generated through research into improvements in clinical practice and the promotion of collaboration between groups of the CNIC and Spanish research groups of excellence, in particular those that belong to the National Health System.

Fourth.- That, as is set forth in the text of the said round of grants, subsequent to participation therein and having obtained the favourable provisional resolution for the application presented, in order to obtain the final resolution it will be necessary and obligatory to establish a Collaboration Agreement for the formal setting up of the research team as well as the acquisition of the commitment to carry out the research project (*include Research Project Title*), in accordance with the budget set forth in the provisional resolution, according to Annex A of the present Agreement.

As the round of grants also sets forth, in order to obtain the favourable final resolution, the research team must always be led by a Principal Investigator – coordinator attached to the CNIC or a public healthcare centre that belongs to the National Health System, which may be made up of several research groups belonging to different public or private centres that may be Spanish or foreign, which work together in a coordinated fashion in the carrying out and execution of the translational research project.

For the purpose of formalising the setting up of this research team, the present Collaboration Agreement must contain the signatures of the Principal Investigators (coordinator and participants) of the research groups, as well as the signature of the legal representative of the institution to which each of them belongs.

The aforementioned round of grants establishes that the research team, once set up, must carry out the translational research project in accordance with the activities plan and budget that have been favourably assessed, as set forth in the notification of the provisional resolution.

The notification of the provisional resolution, the project report and the budget are attached in Annex A of the present collaboration agreement.

Fifth.- That the following Principal Investigators, linked to the signatory institutions of the present Collaboration Agreement, form the research team that will carry out the research project set forth in Annex A:

- representing the *Centre/Institution*: Name and surnames of the Principal Investigator, position and ID number.
- representing the *Centre/Institution*: Name and surnames of the Principal Investigator, position and ID number.
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Sixth.- That Dr., with ID number, who belongs to the *institution/centre*, has been selected and named as PRINCIPAL INVESTIGATOR – COORDINATOR for the carrying out of the research project (*Include Project Title*), the *institution/centre* being considered as the FUNDING RECIPIENT of the financial assistance.

THEY HEREBY AGREE

First. - Purpose

The purpose of this Agreement is the formal setting up of the research team, within the framework put in place by the provisional resolution of the CNIC- TRANSLATIONAL 2009 round of grants, for the carrying out of the Project (*include Project title*).

Second.- Objectives

The general objectives of the research team will be those described in the Project Report, which is included in Annex A.

Third.- Research field

These general objectives will be pursued through the research activities plan described in the Project Report, included in Annex A.

Fourth.- Variations

1. Once the Round of Grants has been resolved, should there be any variations in the composition of the research team formalised in this agreement, due to the addition or pulling out of researchers, the Principal Funding Recipient will request the authorisation of the CNIC Foundation. In any event, the institutions agree to maintain the critical mass of the research team and the scientific excellence of the financed project.
2. For the purpose of the CNIC-TRANSLATIONAL 2009 round of grants, the team will be kept together until the end of the prescription period set forth in sections 39 and 65 of the General Subsidies Law.

Fifth.- Collaboration with the CNIC

As provided in the bases of this round of grants, the Principal Investigator Coordinator will collaborate with the CNIC with regard to development of the project by acquiring the following undertakings:

- a) In coordination with the Head of the Translational Cardiovascular Research Department of the CNIC (hereinafter, "the Department"), to connect the project with the strategic lines of the centre.
- b) To conduct the scientific follow-up of the project and report periodically to the Head of the CNIC Department on progress made.

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- c) To collaborate in training activities and scientific events sponsored by the Department in which their participation is requested.
- d) To collaborate and advise on dissemination activities relative to the results deriving from development of the project funded by the CNIC.

Sixth.- Dedication of the Principal Investigator Coordinator

The activities performed by the Principal Investigator Coordinator by virtue of his/her association with public and private institutions shall not interfere with optimum execution of the project, nor with accomplishment of the aims of this agreement, nor with commitments acquired by virtue hereof

The Principal Investigator Coordinator shall dedicate at least% of his/her time in the institution of origin to the joint project and to the commitments deriving therefrom in relation to the CNIC.

Seventh.- Publications

Publications of results obtained from the work of the Principal Investigator Coordinator in development of the project will acknowledge and set forth his/her affiliation with the CNIC Foundation as well as his/her membership of the institution of origin, without prejudice to acknowledgement corresponding to other investigators who have participated in those works.

Eighth.- Intellectual and Industrial Property

The intellectual property rights (author's rights) derived from the activities carried out thanks to the financing provided by the CNIC according to the present agreement will correspond to the author(s) of the said results. Nevertheless, in all the communications that refer to the said results, express mention must be made of the financial sponsorship of the CNIC.

The ownership of the intellectual property rights (patents, models of use or other industrial property titles) derived from the activities carried out thanks to the financing provided by the CNIC through the present agreement will correspond in equal parts to the CNIC and to the signatory institution of the present agreement where the said activities have been carried out. In the case of industrial property rights derived from activities carried out in more than one institution, the CNIC will retain 50% of the ownership of the industrial property rights of each of the institutions involved.

Notwithstanding the above, the CNIC and the institution(s) involved must sign the corresponding specific agreements that regulate the obligations and rights of the various owners in respect of each of the industrial property titles. These agreements must be signed prior to lodging the application for industrial property ownership rights with the proper administrative body, which under no circumstances will be the responsibility of the CNIC.

The signatory institutions of this agreement must notify the CNIC immediately and in writing of any research result derived from the activities carried out with the financing provided by the CNIC through the present agreement that may be likely to lead to a request for industrial property ownership rights, in order to undertake the opportune steps for making the said application.

Ninth.- Confidentiality-Advertising of results

The signatory institutions of the present agreement agree that any data, information, results, etc. (for the purposes of this agreement "the information") with which they are provided by the remaining institutions, or which has been generated over the course of the carrying out of the activities financed through the present agreement, will be kept confidential and will not be revealed to any third party without the prior written authorisation of the remaining institutions, unless:

- I. The information was already known to a third party prior to the signing of this agreement.
- II. It was revealed by a third party with a right to do so.
- III. It was in the public domain or entered the public domain through acts not attributable to any of the parties.
- IV. It was required out of legal necessity.

The signatory institutions of the present agreement will safeguard the restricted circulation of the said Information, being responsible for ensuring that this obligation is met by all the people who have access to it, as set forth in this Agreement.

The Information that is exchanged by institutions through the present agreement may only be used by them exclusively for the purpose of the present agreement.

The signatory institutions of this agreement and the CNIC must agree on scientific-medical and any other kind of publications, as well as on the public presentations of results generated by the carrying out of the activities executed with the financing provided by the CNIC through the present agreement. In any event, the CNIC will be acknowledged as sponsor in all the publications.

The signatory institutions of this agreement must provide the CNIC with a copy of any article, manuscript, presentation or document of a non-confidential nature distributed on the results of the activities carried out with the financing provided by the CNIC through the present agreement, at least 30 days before its presentation, delivery or notification to a third party. The CNIC will be granted a maximum period of 30 days from the date on which it receives the document in order to object to the publication due to it containing information liable to some kind of industrial property protection, or information liable to be commercially sensitive. It must set forth its reasons for objecting by identifying the passages of the manuscript where the said information can be found.

If the CNIC makes objections in accordance with that set forth above, the institution that aims to publish will proceed (i) to remove from the manuscript the information identified as being liable to some kind of industrial property protection and will send the modified manuscript to be subjected to and approved by the procedure of the above paragraph, or (ii) it will not publish until the request for industrial property rights ownership has been processed before the proper administrative body.

Notwithstanding the above, the CNIC may demand the non-publication of the information for a maximum period of one year when publication may involve the loss of additional business opportunities that cannot be the object of protection at this time and whose future commercial exploitation therefore depends directly on the time at which publication goes ahead.

Tenth.- Follow-up Commission

The CNIC Foundation will set up a Follow-up Commission in order to follow-up the execution of the research project (*include Project title*), in accordance with the financing awarded. The said commission will be made up of the Principal Investigators (coordinator and participants) and two CNIC representatives.

The Follow-up Commission's functions will include that of clearing up any doubts that may arise as regards the interpretation and fulfilment of the agreement, as well as that of establishing whatever formulas may be necessary in order to deal with and reach agreements and consequences regarding the possible patentability of the result of the project, application, registration, exploitation, defence, actions, transmission, licences and any other disposition concerning the patent.

Eleventh.- Start and Duration

The duration of the present agreement will coincide with the execution period of the awarded project, as set forth in the provisional awarding resolution, starting from the date of the final awarding resolution.

Twelfth.- Notice of Termination

Any of the parties involved may give notice of the termination of the present Agreement by providing written notice to the management body of the project and the CNIC Foundation six months before the date of termination. In this case, the Follow-up Commission must determine the way in which to conclude the actions underway that are affected by the notice of termination.

Thirteenth.- Solution of disputes

The parties involved agree to seek an amicable solution to whatever differences may arise in the interpretation or execution of the present Agreement. Failing this, any disputes will be resolved before the courts and tribunals of the city of Madrid, Spain.

Fourteenth.- Legislation

The signatories agree to abide by the legislation in force and that set forth in the CNIC-TRANSLATIONAL 2009 round of grants.

In witness whereof, the signatories hereby sign the present Collaboration Agreement, with the express approval of the Principal Investigators of the groups that make up the research team, in the place and on the date shown, in numbered copies (letters and figure).

NAME OF THE BODY

Signature and stamp of the Legal Representative	Signature of the Principal Investigator - Coordinator
Signed:	Signed:

NAME OF THE BODY

Signature and stamp of the Legal Representative	Signature of the Principal Investigator - Participant
Signed:	Signed:

NAME OF THE BODY

Signature and stamp of the Legal Representative	Signature of the Principal Investigator - Participant
Signed:	Signed:

CARLOS III NATIONAL CARDIOVASCULAR RESEARCH
CENTRE FOUNDATION (CNIC)

Signed: Mr. Alberto Sanz Belmar

CNIC-TRANSLATIONAL 2009



**FINANCING OF TRANSLATIONAL RESEARCH PROJECTS
in the CARDIOVASCULAR field**

Third Round of Grants

CNIC-TRANSLATIONAL 2009

ANNEX III.- Model Collaboration Agreement - BILATERAL

CNIC-TRANSLATIONAL 2009

COLLABORATION AGREEMENT (BILATERAL)

BETWEEN (*Name of the Main Beneficiary Body*) AND (*Name of the other Participating Body*)

In [*place*], on [*date*]

BY AND BETWEEN

Party of the first part,

Forename and surname(s) of the legal representative of the Main Beneficiary Body, holder of tax ID number, in his/her capacity as (position held) and in name and representation of the *Centre/Institution* (hereinafter referred to as "..."), with right of abode at, in accordance with the powers of attorney granted

And party of the second part,

Forename and surname(s) of the legal representative of the Participating Body, holder of tax ID number, in his/her capacity as (position held) and in name and representation of the *Centre/Institution* (hereinafter referred to as "..."), with right of abode at, in accordance with the powers of attorney granted

Both parties, mutually recognise the other's sufficient legal standing and representative powers to the bound by this Agreement.

RECITALS

1. Whereas (*name of the Main Beneficiary Body*) is to receive the corresponding funding in order to carry out the "*Name of Main Project*" project (File Number,), coordinated by (*name of researcher*), of the Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), under the auspices of the "CNIC-TRANSLATIONAL 2009" official notice, published on the Centre's web page. This research project has been considered fundable by the CNIC as shown in the ruling issued on, notified to the Coordinating Head Researcher of the project and made public through the centre's web page.

2. Whereas in accordance with the planned development of the project, the parties deem it appropriate to have participation in the aforementioned project by (*name of Main Participating Researcher*) from (*name of participating body*), which expressly authorises his/her participation, to carry out the study entitled: "*Title of the Sub-project*", in accordance with the report and budget for the study, attached to this agreement (Annex I).

In view of the foregoing, the parties hereto agree to sign this Agreement, which shall be governed by the following:

CLAUSES

One. The party of the research project concerning Recital 1, the performance of which is commissioned to the researcher (*name of researcher*) from (*name of the Main Beneficiary Body*), is the Coordinating Head Researcher of the project.

Two. The term of this agreement shall run from the date of obtaining the Definitive Concession Ruling to the project finalisation date (*end year of the project*).

Three. For the purpose of contributing to the expenses stemming from the part of the study within the project that falls to the researcher(s) of the Participating Body (*name of the aforementioned Body*) the Main Beneficiary Body (*name of the aforementioned Body*) shall deposit into account number (20 digits) at (*name of the Bank*), held in the name of (*full name of the Participating Body*) holder of Corporate Tax Code, the sum of (*in letters and figures*) euros the first year, the sum of (*in letters and figures*) euros the second year, the sum of (*in letters and figures*) euros the third year, the sum of (*in letters and figures*) euros the fourth year and the sum of (*in letters and figures*) euros the fifth year.

Payment shall be made in accordance with the following calendar: Annual payment following receipt of annual funding from the Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), in accordance with the rules of the official notice, once the corresponding positive evaluations of the annual scientific and economic report of the project have been received from the CNIC.

Four. The publications or results that stem from the development of the foregoing research must recognise and place on record the participation of all researchers that have taken part, as well as the institutions to which they belong.

The parties hereby undertake to respect the rules of this official funding agreement of CNIC projects with regard to intellectual and industrial property and nondisclosure and dissemination of results.

Five. This Collaboration Agreement is of a Private Contract nature and the parties hereby agree to submit any litigation concerning interpretation of this agreement to the courts of Madrid.

In witness whereof, they sign this Agreement in two counterparts, on each of the pages, in the place and on the date *ut supra*.

For the Main Beneficiary Body

For the Participating Body

Signature and stamp of the Legal Representative

Signature and stamp of the Legal Representative

Signed:

Signed:

ANNEX I of Model Collaboration Agreement - BILATERAL

Registration Number of Principal Project:

Principal Project Title:

Name of the Coordinator Centre:

Name and surname of the Principal Investigator - Coordinator:

Title of the Sub-project:

Name and surname of the Principal Investigator - Participant:

Please attached Document 2 (Sub-project Report) and Document 3 (Sub-project Budget).