International Rare Diseases Research Consortium (IRDiRC)

Funding Member of Spain: National Institute of Health Carlos III

Spanish Call for IRDiRC Collaborative Research Joint Projects Proposals (Expressions of Interest)

Submission deadline for proposals: December 5th, 2011, 13:00h CET

Proposal submission to: irdirc.sec@isciii.es

For further information, please visit the website **http://www.isciii.es**
or contact the Joint Call Secretariat (JCS):

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Call text

1. IRDiRC MOTIVATION

a. Introduction

Unlike common diseases, a rare disease (RD) **affects a relatively small number of persons**. A disease is considered rare when it does not affect more than one person in 1500 to 2500[1]. This **low prevalence** is the common feature shared by all rare diseases, which altogether affect all biological systems, ranging for instance from nervous system diseases through vascular diseases to muscular, immunologic or metabolic disorders. It is estimated that **there exists some 6,000 to 7,000 different RD**, globally resulting in millions of patients affected with rare diseases worldwide. Most RD are of **genetic origin**, usually **life-threatening or chronically debilitating**. The severity of these diseases generally impacts heavily on the quality of life of affected patients, as well as of their family members.

Patients affected with a particular RD in a given country are scarce, as also are the specialised clinicians. The causes and natural history of RD are very often poorly understood. The rarity of patients and the high phenotypic heterogeneity of RD, combined with the lack of knowledge, information and training about these diseases result in frequent delays in correct diagnosis (see for example EurordisCare study[2]). In addition, for a significant number of RD a validated diagnostic test is still missing.

Orphan drugs (intended to treat RD) generally lead to a lower commercial return compared to treatments targeting more common diseases, due to the lower number of patients. Therefore, under normal market conditions, the pharmaceutical industry showed limited interest in developing new orphan drugs. To change these market conditions and to provide a better return on investment, several countries have adopted various pieces of legislation that provide incentives for the development of orphan drugs[3]. Nevertheless, to date, a very limited number of orphan drugs are marketed, **leaving a large majority of rare diseases without any effective treatment**. Even in the absence of a specific orphan drug, identifying best clinical/care practice amongst various existing approaches would highly benefit the patients. Often delayed diagnosis and absence of specific treatment and standards of care have a heavy weight not only on patients and families, but also on health care systems. Appropriate clinical management of rare diseases patients would hence have a positive impact for health care systems.

Increasing the number of therapeutic and care options for RD patients requires a better knowledge of pathophysiology and natural history of the RD, to help identifying potential therapeutic targets, validate biomarkers and define appropriate surrogate end-points to adequately evaluate treatments and therapies. In order to translate research results into the marketing of orphan drugs, it is important that meaningful, validated data are collected and shared internationally. Furthermore, it is essential to strengthen the links between academia and industry, so that industry better capitalises on strong academic research results to translate these into new diagnostic tools and therapies. Patients have an important role in this process.

In contrast with more common diseases, which are generally multifactorial in their causes, rare diseases often result from a dysfunction of a single pathway (like a defective gene or protein). Understanding the impact of a single defect may hence yield insights into the more complex pathways involved in common diseases. In other words, research on rare diseases may help dissecting the complex pathways underlying common diseases. Strategies for the treatment of RD, with restricted patient populations, also come close to personalised medicine: they require personalised and timely diagnostic to identify the specific RD affecting the patient, as well as a

[1] In the EU a rare disease affects not more than 5 in 10,000 people; in USA each rare disease affects less than 200,000 people; in Japan less than 50,000 people.
[2] http://archive.eurordis.org/IMG/pdf/eurordiscare1-part1.pdf; http://www.eurordis.org/sites/default/files/publications/Fact_Sheet_Eurordiscare2.pdf
[3] Regulation (EC) N° 141/2000 of the European Parliament and of the Council on Orphan Medicinal Products; USA Public Law 97-414 “Orphan Drug Act” (1983)

timely, effective and safe, personalised treatment and care. Investigating the pathophysiology and developing specific therapies for RD require new, innovative approaches, which can subsequently be applied to other diseases.

For rare disease research, coordination of efforts is key to success, in order to maximise scarce resources. Worldwide sharing of information, data and samples to boost research is currently hampered by the absence of an exhaustive RD classification, standard terms of reference and common ontologies, as well as harmonised regulatory requirements. Duplication of research efforts must also be avoided, and links between teams working on similar issues must be created.

The International Rare Diseases Research Consortium (IRDiRC) will streamline the access to relevant information, harmonised data and samples, and affected patients. It will stimulate and coordinate basic and clinical research, by promoting the links between existing resources, fostering the molecular and clinical characterisation of RD and encouraging translational/preclinical and clinical research. Priorities for such an international endeavour are the elaboration of standard terminologies and common ontologies with a view to an adequate classification of diseases, the development of predictive, validated *in vitro* and *in vivo* animal models, the identification and validation of biomarkers and surrogate end-points, and the development of new diagnostics and therapies.

b. Consortium goals

b-1. Primary goals: Developing by 2020

1) **200 new therapies for rare diseases (orphan drugs).** The consortium will develop all the necessary measures and policies to facilitate the development of new therapies for rare diseases.
    - Support top basic research for better understanding the pathophysiology of rare diseases, including the support to the development of models and resources to catalyse research in rare diseases
    - Coordinate and network patient registries: common SOPs; harmonised ethical approaches, access to patient data and samples.
    - Enhance clinical trials: identify and validate biomarkers and surrogate end-points, repurposing drugs, novel compounds (on pharma shelves).
    - Improve the regulatory framework to facilitate the development of novel therapies (involvement of EMA, FDA and patient associations is important).
2) **Diagnostics tests for all rare diseases.**
    - Use "omics" and other approaches to identify biomarkers of rare diseases (e.g. coordination of genome sequencing of patients with rare and non-classified syndromes).
    - Stimulate with industry the development of efficient, multi-purposes diagnostic tests for rare diseases.

b-2. Secondary goals

3) **Diseases classification and common ontologies**
    - Develop common ontologies for clinical description
    - Develop a new rare diseases classification (adequate definition, codification and inventorying of rare diseases)
4) The consortium will **make data accessible to the entire research community as rapidly as possible, and with minimal restriction.** The consortium will establish a common bioinformatics platform that will network all the data centres.
5) The consortium will set up an efficient structure that will coordinate this international effort so that the interests and priorities of individual participants, self-organising consortia, funding

agencies and nations are addressed. The consortium will encourage the minimal amount of redundancy between the different projects around the world**.**

6) The consortium will establish a strong dissemination and communication plan to all potential stakeholders and in particular to the patients and General Practitioners.

b.3. Foreseen Deliverables (by 2020)

- **200 new therapies for rare diseases**
- **Diagnostic tools for all know rare diseases**
- Better classification of rare diseases
- Networking (worldwide) of patient registries: build on expertise
- Commonly accepted Standard Operation Protocols (SOPs) and Ontologies
- Benchmarking of rare diseases research and funding
- Better follow up of patients
- Better understanding of Regulatory Issues: to facilitate clinical trials
- Common WEB platform: communication to patients

c. Background of the consortium

Individual researchers and consortia have been studying rare diseases for several decades. However, the rare disease research community is very fragmented mainly due to the large heterogeneity of rare diseases. Indeed, for many diseases, there are very limited amount of researchers and resources available. However, concerted efforts to organise the rare disease research community and funding are emerging in several countries but so far, international coordination is rather limited.

d. Structure of the IRDiRC consortium

The IRDiRC is a confederation of members that share the common goals and principles described in this document and have agreed to work in a coordinated and collaborative manner within a consortium.

Members consist of ***Funding Members*** and ***Research Members***, each of which is an individual or allied group that will provide a level of funding or scientific expertise to undertake a significant part of the research tasks foreseen in the International Rare Disease Research Consortium (IRDiRC). Each member will have the responsibility for financially or scientifically supporting a significant research program.

d-1. IRDiRC Funding Members

1) Single funding agency or
2) Alliance of organisations, with a representative from a single organisation within the coalition appointed to the IRDiRC Executive Committee (EXEC)

Funding agencies are encouraged to become Funding Members as they become ready to contribute financially to the IRDiRC and adopt the Consortium's policies and guidelines.

To be considered as an ***IRDiRC Funding Member***, the funding agency should provide substantial support of a minimum of $10 million US in total distributed over 5 years to a project/programme in line with the **IRDiRC** objectives. These contributions should not include overhead/indirect costs and equipment.

- National Institutes of Health (USA)

- European Commission (European Union)
- Canadian Institutes of Health Research and Genome Canada (Canada)
- National Institute of Health Carlos III (Spain)
- French National Research Agency (France)
- The Netherlands Organisation for Health Research and Development (The Netherlands)
- Telethon Foundation (Italy)

It has expressed interest to joint

- Federal Ministry of Education and Research (Germany)
- National Institute for Health Research (United Kingdom)

There are contacts with China, Japan, Australia and New Zealand. Additional funding agencies are encouraged to become ***IRDiRC Funding Members*** in the future, as they become ready to contribute to the IRDiRC and adopt the Consortium's policies and guidelines.

d-2. IRDiRC Research Members

a) A research centre or network of national or international research groups organized to perform major research activities in line with the IRDiRC goals;

b) Other centres (data management, ethics, etc.) which contribute significantly to IRDiRC

Given that these organizations will likely have different structures, and include many investigators, scientific managers and technical staff, each organization will be asked to nominate representatives to participate in IRDiRC coordination activities, such as the working groups, workshops, and IRDiRC meetings.

Note that IRDiRC itself will not have funds to support scientific research. Rather, it is the responsibility of each research project aligned with the goals of IRDiRC to get support from IRDiRC relevant funding agency member or associated member.

d-3. Structure

IRDiRC will utilize a distributed organizational model. This model has been successfully used in other international projects, where high standards and policies have been determined at the outset, and acceptance and adherence were prerequisite for joining. This model relies on the interaction among funders (providing oversight), an international scientific steering committee (setting guidelines) and scientific groups and centres (Data Production Centres and regional- or national-level Data Analysis and Coordination Centres involved in data production, quality assessment and data management). The strength of the Consortium's structure relies not only with its component parts but also in the bilateral flow of information between the groups.
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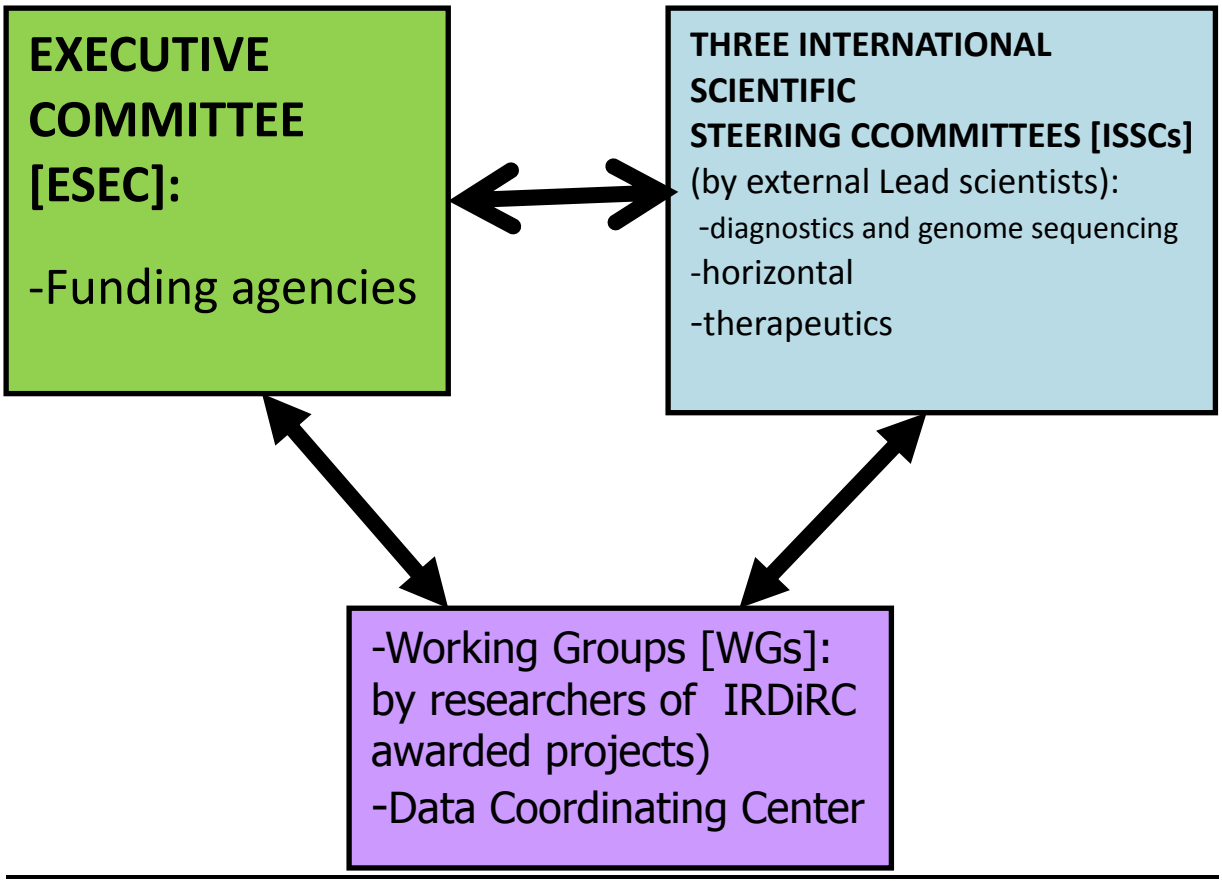

d-4. Governance

- **IRDiRC Executive Committee (EXEC)**

It is constituted of delegates nominated by the IRDiRC Funding Members and has an oversight role. The Executive Committee will:

- Review and accept nominations of new Members
- Work closely with the International Scientific Steering Committee
- Revise and adopt new recommendations related to IRDiRC policies
- Track data deposition, data quality, and data accessibility across projects
- Encourage complementarity in research funding rather than overlaps
- Periodically provide data updates to funding agencies
- Provide a forum for resolution of any conflicts, should they arise
- Provide a forum to resolve conflicting issues
- Make recommendations concerning the recruitment of consultants or establish expert committees on issues related to science, law, IPR, ethics, funding, communications, etc.
- Develop a communication strategy, with special focus on communication with the public.

A key responsibility of the Executive Committee will be to discuss IHEC policies and guidelines and revise these as issues such as technological improvements arise.

- **Three International Scientific Steering Committees (ISSCs)**

The will be composed of lead scientists in the field of rare diseases research. These committees will interact frequently through phone conferences, e-mail and regular meetings to:

- Act as scientific coordinating body
- Assess progress
- Address arising issues of scientific nature
- Encourage exchange of the best protocols and practices
- Establish temporary or permanent subcommittees to complete focused tasks
- Establish quality standards
- Facilitate data dissemination to the scientific community

There will be an **ISSC for diagnostics and genome sequencing**, other **ISCC « horizontal »** and another **ISSC for therapeutics**. Each funding agency of EXEC may nominate one candidate for each ISSC. EXEC will decide the composition of ISSCs upon nominated candidates.

- **Working Groups [WGs]**

They will be composed in a flexible manner of variable geometry by researchers of IRDiRC awarded projects.

- **Data Coordination**

A **Data Coordination Centre** will manage data flow from projects and centres to the IRDiRC database and public repositories in coordination with national or regional Data Analysis and Coordination Centres (see details in the Data Management section found later in this document). In cases where patient protection requires an access controlled database, the DCC will provide a summary of the data available and indicate how access to the data can be obtained. The Data Coordination Centre will provide regular progress reports to the EXEC and ISSCs.

The Data Coordination Centre will also coordinate data quality standards which will be required for each contributing Data Production Centre. These quality assessments will focus on evaluation of a standardized cell model which will be distributed to all centres for evaluation by epigenomic assays. The resulting data will be evaluated by the Data Coordination Centre and collaborating national or regional Data Analysis and Coordination Centres to ensure accuracy and uniformity for each production centre and across the consortium.

e. Consortium policies and guidelines

What is a consortium policy?

A consortium policy is a principle which consortium members agree to follow, during the course of the project. Although policies will likely be long-lasting, the IRDiRC will periodically review its policies. POLICIES are highlighted in grey.

What is a consortium guideline?

Consortium guidelines refer to recommendations made by IRDiRC that offer advice as to what is believed to constitute “best practices” at a given time. Given the rapid evolution in technologies or new knowledge gleaned from the data generated by IRDiRC or other groups, it is expected that guidelines will evolve. It is also expected that approaches will need to vary based on disease type, local laws, or other factors. In such cases, it is expected that IRDiRC members will be able to compare and explain differences in approaches, relative to IRDiRC guidelines. The IRDiRC has chosen to make most of its recommendations as guidelines

rather than policies to allow flexibility in approaches and promote innovation. In this document, guidelines are often written in blue-shaded boxes.

In the first document prepared by the IRDiRC, it is strived to differentiate recommendations that are policy from those that are guidelines (even if some issues are clearly a mix of both). It is up to individual projects that join the IRDiRC to declare a clear plan, e.g., samples, criteria for being a sample, exons used, quality control, etc.

Over time, the IRDiRC will generate best practices documents that will describe the current state-of-the-art, and propose modifications of the guidelines.

2. AIM OF THE SPANISH CALL FOR COLLABORATIVE RESEARCH JOINT PROJECTS PROPOSALS (Expressions of Interest)

This is not a legally binding call. The aim of the call is to enable scientists in different institution based in Spain to build an effective collaboration among them on a common multi- and inter-disciplinary research project based on complementarities and sharing of expertise, with a clear translational research approach. Project proposals shall involve a set of rare diseases or a single rare disease following the European definition i.e. a disease affecting not more than five in 10,000 persons in the European Union. **Rare infectious diseases and rare adverse drug events in treatments of common diseases are excluded from the scope of this call of expressions of interest.**

The National Institute of Health Carlos III (ISCIII) will be the funding agency for collaborative research projects awarded by IRDiRC to institutions with the facilities to carry out the project and legal and fiscal address placed in Spain.

This call is focussed in Collaborative Research Projects that should be drafted in a full Collaborative Research Joint Project Proposal.

Collaborative Research Joint Projects must clearly demonstrate the potential health (and the eventual socio-economic) impact as well as the added-value of collaboration: gathering a critical mass of patients/biological material sharing of resources (animals models, genetic characterization/correlations, diagnosis, epidemiological studies, etc.), therapeutic strategies, harmonization of data, sharing of specific know-how and/or innovative technologies.

- It must cover at least one of the topics or/and areas described below [a), b)], which are equal in relevance for this call for expression of interest on collaborative research.
- It should be used the services of -omics platforms funded by ISCIII (PROTEORED = Red de Proteómica, CNAG = Centro Nacional de Secuenciación Genómica, CGEN = Centro Nacional de Genotipado, INB = Red de Bioinformática), CAIBER = Plataforma Española de Ensayos Clínicos, RETBIOH = Red Temática de Investigación Cooperativa de Biobancos Hospitalarios, IIER = Instituto de Investigación de Enfermedades Raras, as appropriate, if necessary.
- Costs of services provided by platforms are eligible for funding request to ISCIII in this call. However, costs of equipment for platforms are not eligible.
- It may be selected up to a tentative maximum of five proposals with an overall funding up to 10.00 M€ for 5 consecutive years (excluded equipment and indirect costs).
- The selection of the proposals will be carried out by ISCIII according to its policy, standards, eligibility requirements and legal framework, following the guidelines of IRDiRC.

a) Collaborative research joint project proposals on RD Patients´ Registries, serving as core the Institute for Rare Diseases Research (IIER) and the cooperation of the Units of the Autonomous Communities of Spain.

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- It may be selected up to one proposal of duration up to 5 year that should ensure somehow its long term sustainability. It is only eligible for funding the launching phase with a cap funding up to 2.4 M€ for 3 consecutive years.

b) Translational collaborative research project proposals.

- It must cover at least one of the following topics or/and areas (b-1, b-2), which are equal in relevance for this call for collaborative research joint projects.
- It may be selected up to four proposals with an overall funding up to 7.6 M€ for 5 consecutive years.
- Up to one of the selected ones may be a high risk science proposal with a cap funding up to 4 M€ for 5 consecutive years.

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b-1) Collaborative research joint project proposals including diagnostic strategies.

- Research on development of applications for diagnosis for RD. This may include identification, characterisation and validation of (bio)-markers for diagnosis and prognosis, and therapy monitoring, development of innovative screening systems and diagnostic tools,
- Proof of concept.

b-2) Collaborative research joint project proposals on RD including therapeutic strategies.

- Definition of advanced phases in the pipeline of drug development from target validation to clinical trial,
- The generation of relevant cellular and/or animal models, and preclinical studies using pharmacological, gene or cell therapies,
- Proof of concept.

3. COLLABORATIVE RESEARCH JOINT PROJECT PROPOSAL´S ELIGIBILITY CHECK

It will be carried out by JCS at the Under-directorate General for Research Assessment and Promotion (SGEFI) of the ISCIII. **For eligibility criteria see Annex 1.**

4. COLLABORATIVE RESEARCH JOINT PROJECT PROPOSAL´S EVALUATION

Collaborative research joint project proposals on RD Patients' Registries will undergo a strategic and opportunity assessment.

The translational collaborative research joint projects proposals will undergo both a strategic and opportunity assessment and a scientific evaluation.

It will be set up a Strategic and **Opportunity Assessment Committee (SOAC) and** Scientific Evaluation Committee (SEC) external to ISCIII to carry out the evaluation process

of the proposal with the management support of the JCS at the Under-directorate General for Research Assessment and Promotion (SGEFI).

- **The Strategic and Opportunity Assessment Committee (SOAC)** is a panel of experts, appointed by ISCIII. **The Scientific Evaluation Committee (SEC)** is a panel of internationally recognised experts, appointed by ISCIII.
- SOAC and SEC members will not submit or participate in any proposal within this call, and must sign a confidentiality form and a statement to confirm that they do not have any conflicts of interest.
- The SOAC and SEC may also nominate external peer reviewers (not participating in any proposal) for them to be assisted, as appropriate

5. APPLICATION

a. Eligibility of applicant institutions (please see Annex 1)

Collaborative research project proposals may be submitted by applicants belonging to one of the following categories of non for profit institutions whose facilities to carry out the project and the fiscal and legal address is placed in Spain:

- Academia, Public Research Performing Organisations (OPIs) (research teams working in universities, other higher education performing institutions or research performing bodies).
- Clinical (research teams working in hospitals and/or other health care settings, health organizations and managing entities of health research such as Foundations).
- Public Health (research teams working in public health and/or other health care settings, health organizations and managing entities of health such as Foundations).

Participation of small and medium-size enterprises (SMEs) and other industrial participation is encouraged but should be ensured in advance with their own funding. Evidence/ Proof of it should be provided to the JCS. Eligible institutions of awarded project proposals could subcontract SMEs services through a call for public tender if it is conveniently justified for reaching the project objectives. Subcontracting cannot overpass 50% of the awarded funds by ISCIII.

- Please note that the inclusion of a non-eligible project partner requesting ISCIII´s funding in a proposal may **lead to the rejection of the entire proposal without further review**.
- Whilst applications will be submitted jointly by research groups, each one is therefore subjected to meet the **eligibility criteria of the ISCIII as funding agency**.
- Applicants are strongly advised to self-check to ensure eligibility in advance of submitting an application.

Only collaborative research joint project proposals will be selected. Each joint project consortium submitting a proposal must involve a **minimum of three research groups** from **at least three eligible institutions** to be funded by ISCIII. Research groups from non-eligible organisations for funding may participate in projects proposals if they are able to secure their respective own funding on time the concerned project full proposals are submitted. This must be stated in the proposal. Subcontracting cannot overpass 50% of the awarded funds by ISCIII.

The number of participants and their research contribution should be appropriate for the aims of the joint collaborative research project and reasonably balanced in terms of scientific contribution and workload.

CIBER and CAIBER are eligible as project consortium partners. A researcher can only participate in one project proposal, except in case of services providers. CNAG, CGEN, PROTEORED, INB and RETBIOH could be eligible if a relevant mother organisation with legal personality is the beneficiary of the grant

Each collaborative research joint project should represent the critical mass to achieve ambitious scientific goals to meet IRDiRC aims and should clearly demonstrate an added value from consortium working together.

Each joint collaborative research project proposal must nominate a project consortium coordinator among the project proposal partner principal investigators (PI). The coordinator must be the principal investigator of a project proposal partner from an eligible organisation for funding. The project proposal coordinator will represent the consortium externally regarding scientific matters, towards IRDiRC and ISCIII and will be responsible for its internal scientific overall management (such as controlling, reporting, intellectual property rights issues and external scientific audits and contacts). Each project proposals partner will be represented by one (and only one) principal investigator. Within a proposal, each project partner principal investigator will be the contact person for ISCIII as the funding agency on administrative /financial matters.

The duration of the projects can be up to 5 consecutive years. Nevertheless, a partner can be funded or request funding for less than 5 years according to the concerned project proposal timely work programme, funding eligibility criteria and regulations.

***IRDiRC projects proposals awarded by ISCIII will be compatible or not with other ongoing projects at the time of application or at the time of the concerned IRDiRC project performance funded by other calls according to the provisions stated in the relevant calls*.**

b. Submission of collaborative research join project proposals

There will be **one stage submission procedure for joint project applications**: proposals (in English). They shall be prepared by the project partners of a collaborative research consortium, and must be submitted to the Spanish Joint Call Secretariat of IRDiRC (JCS) by one spokesperson, that must be the collaborative joint project consortia coordinator.

Collaborative research joint project **proposals** must be received by the JCS (irdirc.sec@isciii.es) in an electronic version no later than **December 5th, 2011, at 13:00h CET** (Central European Time). .

The decision on selection check of project proposal applications may be taken by December 20th. The funding decision may be tentatively communicated in the first quarter of 2012, pending on the IRDiRC policies and time frame on this matter still pending of specification.

The information given in the proposal by the applicants is binding for them. Thus, any fundamental changes, e.g. composition of the partner consortia, research team members, work plan, objectives of the project, must be communicated to the JCS with detailed justification and will only be allowed by the JCS under exceptional circumstances.

The selection of a collaborative joint project proposal will be communicated to the consortium coordinator as soon as possible and taking into account IRDiRC policies and time frame for it, still pending of specification.

The forms that have to be used for submission of joint project proposals are available on the ISCIII website (www.isciii.es).

c. Further information

If you need it, please contact the JCS.

6. Eligibility check of proposals

The JCS at SGEFI will check all proposals for compliance to ensure that they meet the call formal eligibility criteria (date of submission; number and distribution of applicant research groups; inclusion of all necessary information in English, page length of each section).

Please note that proposals not meeting the formal criteria of eligibility, requesting funding above the maximum and other rules and requirements **will be declined without further review.**

Equipment, indirect /overhead cost are not eligible for funding according to the policy of IRDiRC. Furniture and civic fabric are not eligible for funding too.

7. STRATEGIC AND OPPORTUNITY AND SCIENTIFIC EVALUATIONS

a. Evaluation criteria

Proposals will be assessed according to specific evaluation criteria (see below), using a common evaluation form. A scoring system from 0 to 5 will be used to evaluate the proposal's performance with respect to the different evaluation criteria.

a-1. Scoring system:

0: fails or missing/incomplete information;
1: poor;
2: fair;
3: good;
4: very good;
5: excellent

a-2. Evaluation criteria:

- Scientific quality of the proposal (innovative potential, adequate methodology)
- Feasibility of the project (timely work plan, adequateness of the capacities in the consortium and adjusted requested resources: Hypo- or over- budgeted proposal may be declined irrespective of other considerations).
- International competitiveness of applicant research groups in the field(s) of the proposal (previous work in the field, expertise of the research groups, proficiency of each research team project Principal Investigator and the consortium coordinator to serve as such).

- Level of collaborative interaction between the research groups, balanced partners´ composition of the project consortium and added value of it, availability of existing resource to ensure consortium coordination.
- Level of development of new treatments and biomarkers (indicated in b-2, page 9).
- Potential impact of the expected results for future clinical, public health and/or other socio-economic health relevant applications.
- Opportunity and strategic dimension.

b. Peer review of proposals

Proposals passing formal checks by JCS will be forwarded to the SOAC for assessment and SEC members for evaluation (see evaluation criteria above). The SOAC and SEC will establish a ranking of the proposals and give a recommendation for funding. Proposals will be accepted to be funded according the recommendation done by SOAC and SEC based in the ranking list.

The Joint Call Secretariat will communicate to all project coordinators the final decisions together with the external review.

8. FINANCIAL AND LEGAL ISSUES

a. Funding model

It will be used the “virtual” common pot funding model. This means that funding will be made available to each research group beneficiary organisation according to funding regulations. Prior to submitting a project proposal, applicants should verify their eligibility and the rate of financial support.

Funding may be granted by ISCIII up to five consecutive years according to IRDiRC policy. Annual pre-payments are subjected to positive assessment of the annual scientific and financial/administrative progress reports, as well as availability of funds stated in budgetary appropriations approved to ISCIII. Beneficiary Partners and research teams with financial reports concerning other project funded by ISCIII with no positive follow-up may be disqualified for funding in this call or its funding stopped after awarded.

b. Funding grant of awarded projects

Each collaborative joint project includes several research teams called collaborative research consortium partners and one project consortium coordinator. Each research partner (including the project consortium coordinator) will have a separate grant agreement subjected to national regulations according to the legal framework of Spain applied by ISCIII to grants.

Major changes in the work plan and objectives, changes to the composition of collaborative research consortia partners, on research team members, beneficiary institution of the research team or in budget distribution cannot occur during the time of validity of the grant, unless there is a specific approval by ISCIII prior to come into effect and upon good grounds. However, in case of major changes, an independent expert or experts can be consulted to help with the final decision regarding change authorization. The concerned research partner shall inform the project coordinator and the JCS on any event that might affect the implementation of the joint project.

c. Collaborative Research Joint Project Consortium Agreement and ownership of Intellectual Property Rights

The project consortium partners must sign a consortium agreement (CA) for collaborative research cooperation addressing at least consortium decision making, IPR and excluding financial matters of the grants provided by ISCIII. The project consortium should sign this CA before the official project start date. This joint project consortium agreement must be made available to JCS for check in it.

Results and new Intellectual Property Rights (IPR) resulting from projects funded by ISCIII through this IRDiRC Call will be owned by the researchers' organisations according to national rules on IPR. If several participants have jointly carried out work generating new IPR, they shall agree amongst themselves (consortium agreement) as to the allocation of ownership of IPR, taking into account their contributions to the creation of those IPR as well as the European guidelines on IPR issues.

The results of the research project and IPR created should be actively exploited and made available for use, whether for commercial gain or not, in order for public benefit to be obtained from the knowledge created.

ISCIII as funder shall have the right to use documents, information and results submitted by the research partners and/or to use the information and results for their own purposes, provided that the owner's rights are kept and taking care to specify their origin.

9. RESPONSIBILITIES, REPORTING REQUIREMENTS AND DISSEMINATION

The consortium coordinators of all the funded joint projects must submit **concise annual scientific joint project progress reports (except the last year) and a final scientific project report** (within three months after the end of the joint project) to the JCS. All reports must be in English and use a common report form that will be provided. The research partners are jointly responsible for delivering on time the progress reports, and the JCS will only accept reports delivered on behalf of the joint project, thorough the consortium coordinator. Each concise scientific progress report should address at least relevant outcomes and deviations from the timely work programme and why and corrective measures adopted.

Each project partner should submit annual financial reports to the JCS, according to national regulations and ISCIII requirements that may be followed-up as appropriate.

Funding recipients must ensure that all outcomes (publications, etc.) of IRDiRC collaborative joint projects include a proper acknowledgement: "**Collaborative Joint Project awarded by IRDiRC and funded by ISCIII grant nº XXX".**

The coordinators and/or partner principal investigators might be requested to present the results of their joint projects at their respective own cost in **intermediate and final status symposia/seminars** organized by the ISCIII and /or IRDiRC.

10. CONTACT AND FURTHER INFORMATION

The JCS manages the implementation of this IRDiRC call for research collaborative joint projects and the follow-up phase until the awarded joint research projects have ended. It will be the primary contact point referring to the joint call procedures between the project

research consortia, the peer reviewers the funded organisations (beneficiaries). The project coordinator will be the spoke person contacted by the JCS during the application procedure, so he/she must forward this information to the other participants in the joint collaborative project.

Further information on this Call for IRDiRC collaborative research joint project proposals and the follow-up of awarded joint projects is available at the ISCIII website (www.isciii.es). The contact persons in the JCS for any questions regarding this Call for IRDiRC collaborative research joint project proposals are:

- Ignacio Baanante. Tel.: (++34) 918222576; Email: ibaanante@isciii.es
- María Druet. Tel.: (++34) 918222530; Email: mdruet@isciii.es

Annex 1 – FUNDING COMMITMENT AND ELIGIBILITY CRITERIA

Country	Spain
Funding organisation	National Institute of Health Carlos III (ISCIII) through the Fund for Health Research (FIS/SGEFI). Web site: http://www.isciii.es
National contact persons	1) Mr. **Ignacio Baanante** Tel.: [++34] 91 82 22576, email: ibaanante@isciii.es 2) Ms**. Maria Druet** Tel.: [++34] 91 82 22530, email: mdruet@isciii.es Subdirección General de Evaluación y Fomento de la Investigación Instituto de Salud Carlos III (ISCIII) Monforte de Lemos, 5 E-28029 Madrid – Spain/España
Eligibility of a partner as a beneficiary institution	**Public R&D centres:** • Hospitals, other health care settings as well as other public organisations with a health mission. [Any of them within the National Health System that manages Research through a Foundation (according to the Act 50/ 2002, of December 26th) must also present the foundation's statutes] • A CIBER, CAIBER • Universities • The ones recognized as such according to the Act 13/1986, of April 14th, as well as the other ones hold by Public Administrations **Other Private R&D centres**, **non for profit:** • Hospitals or other health care settings, as well as other private organisations with a health mission and with own legal personality and proof of capacity or activity in relation to R&D actions [They must submit their statutes in which it must be stated a mission and aims in relation to a capacity and activities in R&D actions on a non for profit basis]. • Universities
Eligibility of principal investigator or other research team member	- Each researcher can only participate in a proposal, except in the case –omics platforms funded by ISCIII, IER, CAIBER and RETBIOH as service providers and not as project partners. - Compatibility regarding to alive projects or parallel applications within the R+D+I National Plan of Spain, European Union or international frameworks, is subjected to the specification stated in the corresponding calls for proposals. - The violation of this principles implies the ineligibility of the concerned pre-proposals - Private R&D centres must present a proof of the legal link between it as a project consortium Spanish partner and every respective researcher included as research team. - Each researcher of the core research team of a project consortium Spanish partner (other than the Principal Investigator) must have a job contract with or a fellowship with such a Spanish project partner or a documented relationship with a CIBER, lasting until the end of the project or beyond. - The Principal Investigator (PI) of the research team of a project consortium Spanish partner must be a senior researcher having a job contract with such a project partner or a documented relationship with a CIBER, lasting until the end of the granted project or beyond.

	- Excluded personnel as PI: • Those on training as Health Specialist • Those on research training (e.g. PhD students, or on contracts “Rio Hortega”) • Research personnel contracted by a RETICS or a CONSOLIDER • Those on post-doctoral improving training (e.g. contracts “Sara Borrel“ or contracts “Juan de la Cierva”)
Eligibility of costs, types and their caps	• Expenses can only be committed and invoices charged with dates within the time the Spanish grant is alive. • Consumables. • Commissions [Subcontracts]: up to 50% of the Spanish funds awarded by ISCIII per project Spanish partner grant. • Travel and allowance just only for the partner research team members, if for presenting results and for field studies and coordination. • Hiring technical manpower (other than core research team members, excluded: Students or fellowships). Prefixed bulk cost (salary + taxes + socials security, etc.) per contract up to 5 years: ○ Technical expert, higher degree: 27,550.00 € ○ Technical expert, medium degree: 22,800.00 € ○ Technical expert, FP II: 19,000.00 € • Equipment, furniture, civil fabric indirect /overhead costs are not eligible for funding
National phase	• Submission of the proposal must be carried out by the coordinator (by using an on-line application)
Grant delivery of awarded funds by ISCIII to projects partners and its requirement	• Every year pre-financing, to each beneficiary consortium partner of a collaborative research joint project awarded by IRDiRC after joint project scientific progress report sent by the consortium coordinator and financial report of justification of expenses charged to this grant from each legal partner sent by it, as well as to other previous grant pre-financing and scientific reports, their checks and follow- up, evaluations and assessments.
Further guidance	http://www.isciii.es - *Legal frame* [mandatory to fulfil as other applicable legal requirements, as appropriate]: • Act 14/2007 of July 3rd, 2007, of Biomedical Research. • Organic Act 3/2007, of March 22nd, for Effective equality of Men and Women [of Spain]. • Act 40/2002, of December 26th, on Foundations • Act 30/1992, 26 November 1992, on the Legal System of the Public Administrations and Common Administrative Procedure • Act 30/2007 of 30th October, for Public Sector Contracts • Annual General Budgetary Acts. • General Act 47/2007, of November 26, for Budgeting. • General Act 38/2003, of November 17th, 2007, of Grants. Among other issues: to be up to date in payments of taxes and social security contributions: This requirements must be fulfilled just before paying. • Legal requirements to obtain the beneficiary status of collaborative institution: according to articles 12, 13.2, 15 and 16. • Subcontracting: according to articles 29.2 and 29.7. • Community Framework for State Aid for Research and Development and Innovation (2006/C 323/01).