ISN GO Research & Prevention Committee

Clinical Research Programs
for Developing Countries

New Guidelines for Applicants
responding to the Call for Proposals

April 2, 2012
The ISN GO Research and Prevention Committee Clinical Research Program for Developing Countries

1. **Background**

Chronic non-communicable diseases are now the major cause of morbidity and mortality worldwide, both in developed and developing world. Of these, chronic kidney disease (CKD), diabetes, hypertension and cardiovascular disease all contribute to the global burden of chronic diseases which are expected to increase rapidly in the next two decades particularly in developing countries. Here chronic diseases are replacing acute and communicable diseases as the dominant health problem, and are now the principle cause of disability and death and the use of health resources. CKD is a major risk factor for cardiovascular mortality, and kidney disease is a major complication of diabetes. Indeed, it is increasingly recognized that the burden of CKD is not only limited to its eventual requirement for renal replacement therapy but it also has major impact on public health. Patients with CKD are at risk for progression of kidney disease and development of ESRD, but also are at an even greater risk for cardiovascular disease. Moreover, traditional cardiovascular risk factors, such as diabetes and hypertension are also associated with CKD.

There is also increasing evidence that infectious diseases, still a major health problem in low-income countries, may substantially contribute to the burden of CKD. This mainly relates to poor environmental conditions, unsafe life habit, and malnutrition. Urinary tract infections, occurring in all population but with particular impact on females of all ages, especially during pregnancy, may have long-term consequences over and above the direct infectious disease morbidity and mortality these infections cause. They include chronic injury of the kidney which eventually may lead to loss of renal function, development of secondary hypertension and, for pregnant women, increased risk of maternal toxemia, neonatal prematurity and low-birth weight which usually associates to lower than normal nephron number anticipating the high risk for hypertension and chronic renal injury during the life. Moreover, in several regions worldwide tuberculosis is still endemic, with infection remaining clinically silent for years while irreversible renal destruction takes place. Glomerular involvement with parasitic diseases, including malaria, Schistosomiasis, Leishmaniasis, may also pave the way to progressive renal disease. A variety of glomerular lesions have emerged as significant clinical problems in HIV-infected patients. Therefore, kidney failure in HIV-infected patients will progressively became a major public health problem, particularly in Sub-Saharan Africa. In summary, infectious diseases in developing countries add substantial burden to non-communicable risk factors, in enhancing the global prevalence of CKD.
A more concerted, strategic and multi-sectorial approach, underpinned by solid research, is essential to help reverse the negative trends in incidence of these chronic diseases, not just for few beneficiaries but on a global health equity program. Accordingly, the International Society of Nephrology (ISN) Global Outreach (GO) Research & Prevention (R&P) Committee has developed a global program to fund kidney research that is relevant for people in developing countries.

2. **Activities supported by the Program**
The prevention program announced by the R&P Call is aimed to provide support for two main types of activities related to chronic kidney disease and its risk factors:

i. **Screening and intervention studies**
Identify the individuals at high risk for or with chronic kidney disease by screening programs. This should be complemented by activation of follow-up programs of these patients through medical management including health education, lifestyle modification and pharmacological treatment in order to reduce end stage kidney and cardiovascular disease and mortality.

ii. **Clinical research studies addressing specific local needs**
Perform small clinical research projects aimed to address specific needs at local regional/country level related to acute and chronic kidney disease.

3. **Screening and Intervention studies**
The R&P Committee of the International Society of Nephrology has developed a global early detection and intervention program for emerging countries that would be implemented according to the particular needs, organization facilities and economic imperatives of the given country. KHDC is the acronym of the program for detection and management of Chronic Kidney Disease, Hypertension, Diabetes and Cardiovascular Disease. This program has been developed as a global template which involves a screening and management phase and data assessment (available at www.theisn.org). It is, however, flexible, and acceptance will be on a competitive basis taking into account the ability of the local team to adapt the program to their local circumstances and needs. The overall aim is to encourage local capacity to enable further expansion within the country and region. ISN cannot provide funds for all prevention programs, particularly for those that require very substantial and long term commitment, which may exceed the ISN Research Committee’s financial resources. Nevertheless, within the limited resources available the ISN Research Committee is expected to provide partial financial support for a few selected applications awarded on a competitive basis. It will also help with training of personnel, developing local expertise and
with fund raising. Overall the emphasis is on a model to promote and foster autonomous prevention programs in regions where they are most needed.

The KHDC program serves as a framework for a range of broad activities aimed toward:
- Helping doctors, health care workers, institutions and governments in developing countries to establish local “prevention” programs for chronic kidney disease, hypertension, diabetes and cardiovascular disease
- Increasing public and government awareness of the pandemic chronic non-communicable diseases and their consequences.

4. Clinical research studies addressing specific local needs
Besides screening and intervention programs that address the global burden of non-communicable chronic diseases and their major risk factors, the renal community in developing countries may have specific local needs that call for targeted research. Therefore, the ISN GO R&P Committee would like to promote clinical research, at least in middle- low-income countries, where resources are potentially available. However, even developing countries that have successfully strengthened their scientific capacity have proven more adept at building their knowledge base than at applying the knowledge that their physicians/scientists acquire to address societal concerns. Therefore, the R&P Call for Proposals also encourages applications targeting clinical research projects that address specific regional needs and are relevant to the ISN GO mission. These applications must be accompanied by a letter of support from the corresponding ISN regional coordinator that explain why the chosen topic addresses a specific regional need – similar letters of support from other regional leaders would be welcome but are not required.

The Call is open to any research topics related to kidney disease dealing with local needs, i.e but not restricted to malnutrition, use of potentially toxic agents as local life style or linked to a particular work or life environment, exposure to endemic infections, and promotion of programs for mother and child health to limit low-birth weight responsible for kidney structural changes, which increase susceptibility to kidney damage from diseases such as hypertension and diabetes. To promote research in these environments, ISN R&P will help to encourage the creation of durable partnership between universities/hospitals (and possible government) and local private sector.

5. Eligibility criteria for proposals
There are several eligibility criteria for proposals. These include:
- The project must be conducted in the developing world
- Countries will be favored that are the least developed (according to World Bank ranking), but have a reasonable infrastructure to allow the implementation of the project.
- Project should be complementary to, or in alignment with, the national or institutional health strategy or mission.
- Applications should be from nationally recognized institutions.
- The project coordinator must be an ISN member.
- The project should focus on prevention and management of chronic non-communicable diseases and their risk factors or on research addressing specific local needs.
- Applications addressing specific local needs must be accompanied by a letter of support specific regional need. Prospective applicants should check with the Regional Coordinator prior to preparing their application.
- The proposal must provide detailed rationale, aims, and methodology.
- The project must be realistic in term of feasibility, with mechanism for monitoring well defined outcomes.
- A detailed budget is required.
- Sufficient evidence must be presented that the project can become self sustaining on long-term, even after the end of ISN support.
- Applications must be submitted within the established deadlines announced in this Call of Proposals.

6. **How to apply and the procedure to follow**

Proposals must be submitted by the Applicant to the Regional Coordinators of the ISN R&P Committee Prevention Program. There are eight Regional Coordinators worldwide, who are appointed to coordinate prevention activities in countries belonging to a certain ISN Regional Committee region, namely:

- **Lazlo Rosivall** (Budapest, Hungary), <rosivall@net.sote.hu>
  *(Eastern and Central Europe: Albania, Bosnia-Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Macedonia, Moldova, Poland, Romania, Serbia & Montenegro, Slovakia, Turkey)*

- **Saeed Al-Ghamdi** (Jeddah, Saudi Arabia), <Smghamdi@kfshrc.edu.sa>
  *(Middle-East, Arabic region: Bahrain, Iran, Iraq, Jordan, Israel, Kingdom of Saudi Arabia, Kuwait, Lebanon, Oman, Palestinian Authority, Qatar, Syria, United Arab Emirates, Yemen)*

- **Ricardo Correa-Rotter** (Mexico City, Mexico), <correarotter@prodigy.net.mx>
  *(Latin America: Antigua & Barbuda, Argentina, Aruba, Bahamas, Barbados, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, French Guiana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Martinique, Mexico, Nicaragua,)*
Panama, Paraguay, Peru, Puerto Rico, St. Kitts & Nevis, St. Lucia, St. Vincent and the Grenadines, Suriname, Trinidad & Tobago, Turks & Caicos Islands, Uruguay, Venezuela, Virgin Island).

- Saraladevi Naicker (Johannesburg, South Africa), <saraladevi.naicker@wits.ac.za>

- Muthu Mani (Chennai Tamil Nadu, India), <muthukrishnamani@gmail.com>
  (South Asia: Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka).

- Philip Li (Hong Kong, China), <philipli@cuhk.edu.hk>
  (East Asia: China, Mongolia, North Korea, Taiwan, South Korea, Japan)

- Peter G Kerr (Clayton, Victoria Australia), <peter.kerr@monash.edu>
  (Oceania & South East Asia: Australia, New Zealand, Pacific Islands, Papua New Guinea, Myanmar, Brunei, East Timor, Indonesia, Philippines, Singapore, Cambodia, Laos, Malaysia, Thailand, Vietnam).

- Mykola Kolesnyk (Kiev, Ukraine), <director@inephrology.kiev.ua>
  (Russia, and Community Independent States: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kirghizstan, Russia, Tajikistan, Turkmenistan, Ukraine, Uzbekistan).

Applicants are encouraged to make resubmission inquiries (to gauge the suitability of topics; or for advice on preparing a competitive application) to the Regional Coordinator assigned to his/her specific region or country. Once the application is finalized, it should be submitted to the Secretariat of the ISN R&P Committee, based at the Clinical Research Center for Rare Disease ‘Aldo e Cele Dacco’ of the Mario Negri Institute for Pharmacological Research, Bergamo, Italy (antoinette.vanengelegen@marionegri.it). The project must be prepared based on the Application template attached to these guidelines (Annex A). The applicant must apply in English. The application should be completed as carefully and as clearly as possible so that it can be assessed properly. The applicant should be precise and provide enough details to ensure the application is clear -- particularly as to how the aims of the project will be achieved; the benefit that will flow from it; whether the proposal is novel, feasible and the budget justified; and the way in which it is relevant to the program’s objectives. Hand-written applications will not be accepted. Submission of the proposal should use electronic files.

7. Evaluation and selection procedures of applications

He/she will help applicants to prepare the final project before submission to
The Secretariat registers the submitted proposals with an identification number and provides the R&P Committee with a brief comment together with the applications for evaluation. William Couser, Chairman of ISN-GO, leads the ISN Selection Committee. For each proposal, 3-4 Selection Committee members provide an individual evaluation through a scoring system that addresses specific items, namely the description of the scientific project, measurability of the objectives, the organization, the overall feasibility and the budget. At the discretion of the committee, the appropriate Regional Coordinator may be contacted for their opinion as to importance, feasibility, novelty etc. The chairman of the Selection Committee summarizes the scores and, after further evaluation with the members, identifies the awarded project to the Secretariat of ISN R&P Committee for registration. Notifications will be sent to both successful and unsuccessful applicants. Applicants not awarded will be provided with few comments that would be helpful in case the principal investigator would like to resubmit the proposal to the next available Call. There is a Board (located to the Secretariat) that will provide oversight for the overall program.
The structure of the organization for submission, evaluation and selection of the applications is shown in the following figure.

8. Application deadlines

There are two rounds each year for submission of the proposals with the following deadlines (at 10 p.m., Central Europe Time):

i. April 1st
ii. October 1st

Announcement of the awarded projects will be by the Secretariat of ISN R&P Committee on August 1st (for April submission) and January 1st (for October submission) respectively.

Announcements of successful applications will be placed on the ISN web-site (www.theisn.org).

9. Requirement of awarded projects

The Applicant of the awarded project should provide the Secretariat of the ISN R&P Committee with the brief but detailed report of ongoing activities, results and outcomes every six months. On this basis, a decision whether to continue financial support of the specific project for another year will be made. Moreover, a report of the activities related to a given project should be furnished by
the project coordinator at the annual meeting of the ISN R&P Committee. Results/outcomes of all awarded projects will be reviewed periodically by the ISN Council. The Principal Investigator should acknowledge the support of ISN-GO Research & Prevention Committee in any publications derived from the awarded project. Moreover, a copy of the published paper(s) or abstract(s) presented to national/international Meetings dealing with the project should be sent to the Secretariat of R&P Committee.

10. **Financial allocation provided in support of the Call for Proposals**

There is no specific amount of funding allocated for each request for applications. These amounts will be established every year by the ISN Council according to the global resources available. Three projects will be awarded in each of the two rounds of the Call every year. According to the ranking score of the evaluation provided by the ISN Selection Committee, the first proposal will be entitled 15,000 US $ and the second and third projects 10,000 US $ each. However, ISN reserves the right not to award all available funds, should the submitted applications be judged by the Selection Committee not scientifically sound. Moreover, if projects receive an additional year of funding, this will restrict the number of new projects that can be funded. Given the limited resources, the grant is not intended to cover all the proposed budget of a given awarded project but merely to provide significant start up support. Nevertheless, the ISN R&P Committee will work together with the Institutions receiving awards to enhance the funding by approaching local and international health providers, professional bodies, international foundations, as well as pharmaceutical companies. Since some projects are expected to be more than 1 year in duration, the ISN grant could be confirmed for the subsequent year if a second year of funding is requested, if the conditions outlined in section 8 above are fulfilled and if funding is available. However, to foster self-sustainability of each program, eventually assuring long term independence, from the second year the ISN grant will be progressively reduced. The ISN R&P Committee will be responsible for balancing the need to fund new projects every year, maintain the minimum necessary support for ongoing programs and limiting total funding to remain within available resources as approved by the Council.

10. **Budget guidelines**

The applicant should limit his/her budget request to a maximum to fit the resources available by the Call. This threshold will be established every year by the ISN-GO R&P Committee according to the annual fund assigned to the Committee by the ISN Council. In general, the budget request for each proposal should not exceed US $ 15,000. This amount is intended for reagents, equipments,
computers and internet connection, educational materials and office supplies, nurses/health care workers, laboratory technicians. It must be emphasized that the budget is not for individual salary support but only for project support. Nevertheless, the ISN R&P Committee is aware that the human resources (project coordinator, doctors, network administrators, nurses and technicians) may have to take part-time or full-time leave from their institutions to participate to the prevention project. In this case, the proposed budget may include also payment for such people just related to the time of their involvement in the project. This should be clearly specified in the budget by the applicant. However, the ISN R&P Committee encourages the applicant’s institution to consider these prevention or research programs as part of routine clinical practice and community service and to make any effort to continue the economic support of its employers (doctors, nurses, technicians, health workers) during any time period spent on the project as full time staff.

11. **Duration of proposed project**
There is no specific time limitation for projects. However, ISN advices that programs that include a clinical management component provide no less than 5 years follow-up to ensure proper evaluation of hard endpoints. For small research projects, the minimum duration is 12 months and the projected time should not exceed 36 months.

12. **Ethical committee approval and informed consent**
ISN recognizes the limitation of human study committees in developing countries. Nevertheless, the ISN R&P Committee requires that the applications - which involve human studies - be reviewed and approved by whatever the local equivalent of a human subject committee is. Should this local committee not be available, the applicant must state that the ISN and the Review Committee will work to insure that all research and data collection is conducted consistent with established guidelines for human studies, including informed consent and privacy protection. Therefore, the application must include an informed consent document in the patient language with a statement that the data collected will insure the privacy rights of individual subjects.

13. **ISN Kidney Disease Data Center**
As an integrated activity with the development of specific preventive projects, it is critical to create an ISN Data Center for Kidney Disease (KDDC) to collect and analyze data from the screening and intervention projects in developing countries. This would allow global data collection and surveillance on chronic kidney diseases, hypertension, diabetes and cardiovascular disease in emerging countries. It is emphasized that the KDDC is not intended as a registry to generate
meaningful epidemiological data about large regions or countries. Rather, it is a platform to ensure the success of current ISN-GO R&P Committee initiatives. Therefore, ISN encourages applicants responding to the present Call, whose proposal is funded, to send their screening and follow-up data to KDDC located at the Secretariat of the ISN R&P Committee. A general electronic template is already available for early detection and management programs.
ANNEX A

APPLICATION TEMPLATE
KHDC OR RESEARCH PROPOSALS

Section A:  **General Project Information (1 page)**
1. Country/region where the project takes place
2. Project title
3. Name and address of the coordinating Institution (Applicant)
   - Legal name:
   - Address:
   - Head of the Institute:
4. Name of the local coordinator of the project
   - Position:
   - Contact Address:
   - Email:
   - Phone no:
   - Fax no:
5. Duration of the project (in months)

Section B:  **Project description (maximum 10 pages)**
This section should include:
   a. Rationale of the project in the context of the need of the Applicant’s country
   b. Objectives of the program
   c. Plan of the project and methodology
   d. Expected outcomes
   e. Description of the Applicant’s Institution.
      
      *(When was your organization founded and when did it start its activities? What are the main activities of your organizations at present? Evidence of the capacity to manage and implement the present project).*
Section C: Relevant references to the project

Section D: Detailed budget for the action

Section E: Short summary of the project (maximum 1 page)

Section F: Informed consent document

(The document should be specific for the proposal and in the local language of the subject/patient who participates to the study. It must also include a statement that the data collected will insure the privacy rights of individual subject/patient. A standard form that can be translated into different languages - and adapted to local needs - is provided in Annex B).
ANNEX B

Informed consent

(Standard form)

Object:

Title of the project

I understood the purpose of the study as well as the potential benefits and risks of participating to the study. I had the opportunity to ask questions and my questions have been answered. I hereby give my Informed Consent to participate to this study. I have been given a copy of this Informed Consent Form.

I understand that, by signing this Informed Consent, I authorize access to my medical records to the monitor(s) and the auditors(s), and possibly to members of the Ethical Committees or Health Authorities, for verification of clinical study procedures and/or data.

I also realize that the information obtained from this study, including the results of all tests upon myself, will be held in both computerized and paper filing systems, although these will not identify me by name.

I understand that I am free to withdraw from the study:

- at any time
- without having to give a reason for withdrawing
- and without affecting my future medical care

Subject/Patient’s signature: ______________________________ Date: _______________
Patient’s name: _______________________________________

I, the undersigned, have fully explained the relevant details of this study to the subject/patient named above to consent

Doctor’s signature: ______________________________ Date: _______________
Doctor’s name: _______________________________________

A copy of the signed Informed Consent form must be given to the subject/patient.