ISN GO Research & Prevention Committee

Non-communicable Chronic Disease Prevention Programs in Developing Countries

New Guidelines for Applicants responding to the Call for Proposals

June 28, 2011

The ISN GO Research Committee Prevention Program

1. Background

Chronic non-communicable diseases are now of pandemic proportions and the major cause of morbidity and mortality worldwide, both in developed and developing world. Of these, chronic kidney disease, 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. Among non-communicable disease, chronic kidney disease, apparently neglected by health organizations, is actually playing a central role and represents a key element within the network of major chronic diseases. For instance, chronic kidney disease 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 chronic kidney disease is not only limited to its eventual requirement for renal replacement therapy but it also has major impact on public health. Patients with reduced kidney function represent a population not only at risk for progression of kidney disease and development of ESRD, but also at an even greater risk for cardiovascular disease. Moreover, traditional cardiovascular risk factors, such as diabetes and hypertension are also associated with chronic kidney disease.

There is also increasing evidence that infectious diseases, still a major health problem in low-income countries, may substantially contribute to the burden of chronic nephropathies. 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 an endemic infection with many cases of renal tuberculosis 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 and in particular, a unique form of glomerular damage, HIV-associated nephropathy, have emerged as significant forms of renal disease in HIV-infected patients. With the increasing rate of this viral infections, kidney failure in HIV-infected patients will progressively became a major public health problem, particularly in Sub-Saharan Africa. Therefore, in developing countries infectious diseases add substantial burden to non-communicable risk factors, in enhancing the global prevalence of chronic kidney diseases.

Medicine is developing evidence for chronic diseases, including kidney and cardiovascular diseases, but has no equity plan. 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. For that, the International Society of Nephrology (ISN) Global Outreach (GO) has developed a global program for early detection and management of chronic kidney disease and its risk factors particularly in developing countries. To this purpose, the ISN-GO Research & Prevention (R&P) Committee has prepared the present Call for Proposals to foster Applications on programs to be performed in emerging countries aimed to detect people at high risk for developing chronic renal injury or subjects already with chronic nephropathies that would benefit for early management to prevent or halt disease progression to ESRD, eventually limiting the associated great risk for cardiovascular disease.

2. The 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. <u>Screening and intervention studies</u>

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. <u>Research studies</u>

Perform small research projects aimed to address specific needs at local regional/country level related to acute and chronic kidney disease.

3. The KHDC program for Screening and Intervention projects

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.isn-online.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. The purpose of Research projects

One of the mission of R&P Committee is to promote and help to organize and perform research projects aimed to address specific needs at local/regional level linked to kidney diseases. Up to now, however, the R&P activities has largely focussed on screening and intervention programs aimed to address the global burden of non-communicable chronic diseases and their major risk factors such as diabetes and hypertension. Nevertheless, there may be specific problems related to the life style habit or the peculiar environment of a given population in developing countries that call for target research projects. Thanks to the ongoing screening programs, the R&P Committee has become aware of some of these specific local problems related to kidney disease that are looking for to be addressed. Therefore, 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. For these reasons, the R&P Committee has up-dated the present Call for Proposals by encouraging the submission of applications targeting specific small research projects that, in parallel to the conventional early detection and prevention programs would eventually enable to implement the full mission of the ISN GO for the benefit of developing countries. 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. Also for these research projects the R&P Committee is expected to provide a start-up financial support for few scientifically sound, feasible and affordable applications awarded on a competitive basis. 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
- 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 seven Regional Coordinators worldwide, who are appointed to coordinate prevention activities in countries belonging to a given ISN Regional Committee regions, namely:

- Dick de Zeeuw (Groeningen, The Netherlands), <d.de.zeeuw@med.umcg.nl>
  (Eastern and Central Europe, Russia and Community Independent States)

- Meguid El Nahas (Sheffield, UK), <M.El-Nahas@sheffield.ac.uk>
  (Middle-East, Arabic region, North Africa/Mediterranean region)

- Ricardo Correa-Rotter (Mexico City, Mexico), <correarotter@prodigy.net.mx>
  (Latin America)

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

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

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

- 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)

The applicant should send the proposal to the Regional Coordinator assigned to his/her specific region or country. The project must be prepared based on the Application template

annexed 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 and the way in which it is relevant to the program's objectives. Hand-written application will not be accepted. Submission of the proposal should be in electronic versions.

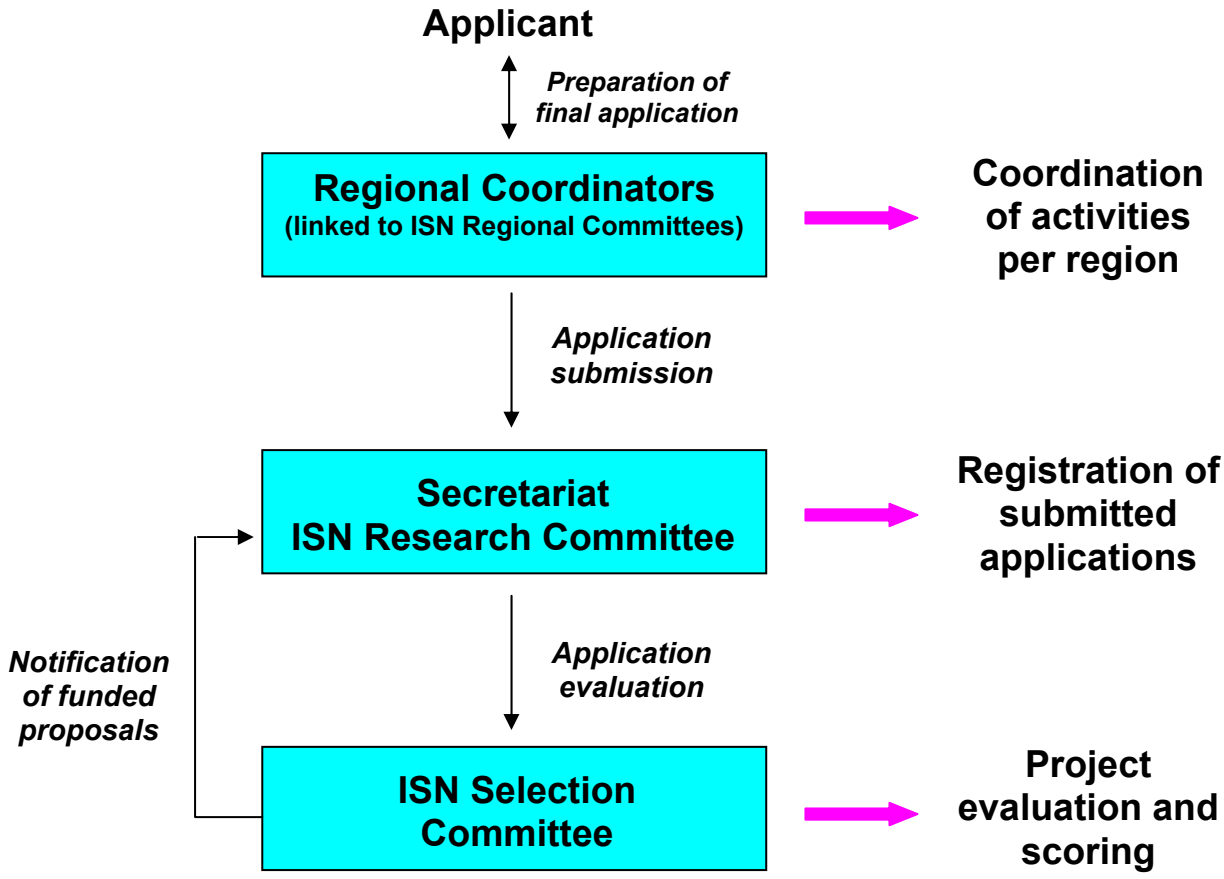
7. Evaluation and selection procedures of applications

ISN funds must be spent on programs that have clear program definition, measurable objectives and results, and a justified budget request breakdown. This has required the definition of a formal organization for ISN prevention program review and selection on a competitive basis.

According to this organization, the Regional Coordinator (which will coordinate the activities related to the prevention program at the regional level with the support of the Chair of the specific ISN Regional Committee) will be contacted by the applicant, and together they will judge whether the proposal fits the local needs and if it is feasible. He/she will help applicants to prepare the final project before submission 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 (giuseppe.remuzzi@marionegri.it).

The Secretariat registers the submitted proposals with an identification number and provides the ISN Selection Committee with a brief comment together with the applications for evaluation. The ISN Selection Committee is a group of people representative of all geographical areas where the project can potentially be established. William Couser, Chairman of ISN-GO, is leading the ISN Selection Committee. Each member of the Selection Committee provides 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. 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.isn-online.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 a 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. The ultimate mission of the KDDC is to provide the system and necessary support to improve the organization and monitoring of clinical activity (particularly the prevention program) in each center in the emerging countries. 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. Through the Data Center, the R&P Committee can better justify funding support of the projects from the ISN Council and from industry/foundation partners to receive additional funds. Moreover, with this approach, ISN will be able to clearly document the significant impact of prevention program and activities in a certain area or situation around the world.

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 from must be given to the subject/patient.