ERA-NET on Translational Cancer Research (TRANSCAN)
Joint Transnational Call for Proposals 2012 (JTC 2012) on:

"Translational research on primary and secondary prevention of cancer"

Call Text

Submission deadline for pre-proposals: 15 February 2013 at 17:00 (CET)

Link to guidelines for applicants

Link to pre-proposal application form

Link to electronic proposal submission **(available from 14 January 2013)**

For further information, please visit www.transcanfp7.eu

or contact the **Joint Call Secretariat (JCS)** at:

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"Translational research on primary and secondary prevention of cancer"

1. MOTIVATION

Cancer is the most important cause of death and morbidity in Europe after cardiovascular diseases. Although the rate of people dying from the disease is declining, recent estimates predict nearly 1.3 million deaths from cancer in the European Union in 2012 (http://www.eurekalert.org/pub_releases/2012-02/esfm-nep022712.php). The burden of cancer will continue to increase as a result of the demographic change promoted in Europe by the population stagnation and ageing.

Facing this scenario, it is mandatory to identify and implement at both the national and European level supportive initiatives aiming at cancer control. By definition, cancer control aims to reduce the incidence, morbidity and mortality of cancer and to improve the quality of life of cancer patients. These ambitious ultimate objectives can be only achieved through the implementation of evidence-based interventions for prevention, early detection, diagnosis, treatment, and palliative care. Thanks to the enormous progress in the understanding of the causes of cancer and of the mechanisms underlying the tumourigenic and metastatic processes, approximately one third of all cancers can now be prevented and some of the most common types – including breast, colorectal and cervical cancer – can be cured if detected early.

Prevention of cancer, especially when integrated with the prevention of other chronic diseases, likely represents the most cost-effective long-term method of cancer control with the highest potential impact on public health. Recent statistics of the American Cancer Society have estimated that in the past two decades more than a million cancer deaths have been avoided and the overall cancer death rates have decreased by about 15-20% in the USA, largely as a result of improved prevention programmes, early diagnosis/detection, and advances in treatment.

Prevention of cancer and of cancer progression can be achieved through i) interventions to decrease the rate of incidence, ii) early detection to increase the efficacy of therapy, and iii) interventions to prevent disease recurrence or to improve cancer patients' care and quality of life. Operational definitions to categorise these approaches are: i) primary cancer prevention, aiming at preventing the start of the carcinogenic process through reduction of the risk factors (physical, chemical or biological) or of the exposure to risk factors or of their impact, e.g. through chemoprevention; ii) secondary cancer prevention, aiming at the detection of precancerous molecular changes or lesions before the development of malignancy, when the disease has a high potential for cure, through screening and early detection methods or treatment of precancerous lesions to attempt causing their regression; iii) tertiary cancer prevention, aiming at preventing

disease recurrence, or reducing disease morbidity and related complications, through a variety of interventions such as adjuvant therapies, surgical interventions and palliative care.

The TRANSCAN network of national and regional funding organisations, established under the ERA-NET scheme of the European Commission, has the goal of coordinating the activities of the partners in translational cancer research at the European level through the funding of multinational collaborative projects. The projects funded within the frame of the TRANSCAN calls are expected to have a concrete impact on the control of neoplastic diseases, through the development and rapid implementation of interventions aimed to benefit not only the cancer patients, but also the individuals at high risk of developing cancer, as well as the healthy population.

The TRANSCAN partners have agreed to focus their Joint Transnational Call 2012, or JTC 2012, on “Translational research on primary and secondary prevention of cancer”, based on the above mentioned considerations.

The following partner funding organisations have agreed to participate in the JTC 2012:

- Austrian Science Fund (FWF), Austria
- Research Foundation Flanders (FWO), Belgium
- French National Cancer Institute (INCa), France
- ARC French Foundation for Cancer Research (ARC Foundation), France
- Federal Ministry of Education and Research (BMBF), Germany
- The Chief Scientist Office of the Ministry of Health (CSO-MOH), Israel
- Ministry of Health (MOH), Italy
- Latvian Academy of Sciences (LAS), Latvia
- National Research Fund (FNR), Luxembourg
- Dutch Cancer Society (DCS), The Netherlands
- The Research Council Norway (RCN), Norway
- Norwegian Cancer Society (NCS), Norway
- National Centre for Research and Development (NCBiR), Poland
- Foundation for Science and Technology (FCT), Portugal
- Institute of Oncology Prof. Dr. Alexandru Trestioreanu (IOB), Romania
- Slovak Academy of Sciences (SAS), Slovakia

- The Scientific and Technological Research Council of Turkey (TÜBITAK), Turkey

2. AIM OF THE CALL

2.1 Scientific project

The risk of cancer can be reduced, generally speaking, by acting across the entire population or by focusing interventions on subgroup populations at higher risk, who could most likely benefit from prevention plans, approaches and tools. Ideally, comprehensive cancer prevention addresses the entire population, while trying at the same time to respond to the needs of the different subgroups at risk.

During the last decade, the knowledge on the cancer etiology and pathogenesis at the molecular level as well as on the heterogeneity of neoplastic diseases has gained enormous progress from the application of high-throughput technologies including genomics, epigenomics, transcriptomics and proteomics. These technological advances are indeed considered as promising tools for risk assessment, early detection, and targeted therapies. In this context, epidemiologic studies are needed to characterize and critically evaluate the “omics” discoveries in well-defined populations for their potential for cancer prediction, prevention and response to treatment. Moreover, in the era of personalised medicine, an increasing need exists for identifying and validating genetic and metabolic pathways as well as molecular signalling pathway alterations representing specific risk factors or predictors of cancer outcomes. This knowledge is expected to lead to the design of approaches better tailored to disease targets, patient sub-groups or, in some cases, to individual patients.

JTC 2012 aims at developing transnational innovative projects in cancer prevention, focused on the research of the mechanisms responsible for maintaining a healthy status *vs*. those underlying cancer development, and clearly oriented towards a rapid translation of the existing and newly acquired knowledge into individual- or patient-tailored interventions at highest potential for cancer control.

Transnational research proposals must address the following topic:

“Translational research on primary and secondary prevention of cancer”

and must cover at least one of the areas specified below, which are equal in relevance for this call and which should comprise the specific aspects as indicated.

Primary cancer prevention.

A) Identification and validation of cancer etiology drivers, based on molecular epidemiology-derived evidences:

i) identification and validation, in biological samples derived from well-defined populations of cancer patients, of new genes and/or genetic polymorphisms and/or molecular pathways involved in the etiology of neoplastic diseases, including familial cancers.

B) Identification and validation of cancer preventive or predisposing factors, based on molecular epidemiology-derived evidences:

i) identification and validation, in biological samples derived from well-defined populations of healthy individuals or cancer patients, of molecular determinants (genes and/or genetic polymorphisms and/or molecular pathways) of behavioural risk factors, including but not limited to diet, physical activity, sun exposure and tobacco use;

ii) development of approaches to cancer prevention based on the knowledge of the molecular mechanisms associated to behavioural risk factors; these studies are expected to lead to a rapid implementation of novel and more effective practices of cancer prevention.

C) Investigation, prompted by clinical trials results, of molecular mechanisms of action of potentially cancer preventive drugs and of their combination, with a particular focus on the identification of modalities for inducing synergistic effects:

i) validation of molecular targets for chemo-preventive agents, in terms of their potential of preventing the emergence of pre-cancerous lesions;

ii) evaluation in early phase clinical trials of screening techniques and methodologies to identify synergistic effects of known or novel chemo-preventive agents;

iii) use of existing animal models for evaluation and rapid screening of new cancer preventive drugs and of combinations of known cancer preventive drugs;

iv) prevention studies in pre-clinical settings and model systems, for the evaluation of efficacy, safety, pharmacokinetics and pharmacodynamics of novel chemo-preventive agents; these studies are expected to be instrumental to the implementation, at the beginning of the second year of the project, of Phase I or Phase II clinical trials.

D) Clinical prevention trials of cancer-preventive agents:

i) Phase I or Phase II clinical trials focused on testing or tailoring interventions based on specific biological mechanisms underlying the action of new cancer-preventive agents;

ii) testing in Phase I or Phase II clinical trials of combinations of known cancer-preventive agents, based on previous laboratory or early phase clinical results.

E) Development of strategies and tools for immune prevention of cancer:

i) identification and validation, in biological samples from cancer patients, of genetic and molecular determinants of cancers associated to infectious agents, with the aim of developing tools and approaches for immune-mediated prevention of infections by agents proven or suspected to be associated with the initiation and development of neoplastic diseases;

ii) development of novel vaccines or vaccination strategies against cancer-associated viral infections, by pre-clinical testing in model systems and clinical testing in Phase I or Phase II clinical trials, to be initiated at the beginning of the second year of the project.

Secondary cancer prevention.

A) Validation of biomarkers and development of technologies and methodologies for early detection and cancer screening:

i) validation in model systems or in Phase II clinical trials of genetic and molecular determinants of use in cancer detection, early diagnosis and staging, and/or early prediction of prognosis, including biomarkers for imaging;

ii) preliminary clinical validation in Phase II clinical trials of techniques, including “omics”-based ones, and methodologies for early cancer detection, comprising but not limited to novel imaging technologies, fluorescence and immunohistochemical assays, endowed with a potentially higher sensitivity, specificity, and reproducibility.

B) Research on integration of age and co-morbidity, in terms of underlying mechanisms:

i) identification and validation, in biological samples from cancer patients, of genes and/or genetic polymorphisms and/or molecular pathways responsible for the impact of ageing and co-morbidity on cancer progression and prognosis.

The research projects submitted within this call must be based on novel ideas stemming from consolidated previous results and must be clearly endowed with a strong translational research orientation, i.e. i) bench to bed studies allowing a rapid implementation into public health-related decisions or into the clinics, or ii) bed to bench studies, based on previous sound clinical results and aiming at their mechanistic understanding. The research proposals should be built on an effective, multidisciplinary and multi-professional collaboration between academic, clinical, epidemiological, public health research teams and industry. The research teams within a consortium should include investigators of all scientific disciplines, research areas and expertise necessary to achieve the proposed objectives. The sharing of relevant results, data sets and/or resources within international research consortia will be a prerequisite for funding.

The research proposals must demonstrate complementary and synergistic interactions among the partner teams. There should be clear added value in the transnational collaboration over the individual projects, in terms of:

i) gathering a critical mass of subjects/patients and/or subjects/patients databases and corresponding biological materials that would not be possible at a national scale;

ii) sharing of resources (biobanks, models, databases, diagnostic tools, etc.), of specific know-how and/or innovative technologies, and of expertise [data management and harmonisation, ethical, legal, and social issues (ELSI), early phase clinical trials design, conduct, management and follow-up, etc.]. It is highly recommended, whenever applicable, to build on existing repositories of biological and bio-molecular resources in order to increasing the respective feasibility and enabling the collaborative studies and related exchange of samples. In all cases, the projects should address the issues of potential efficacy and cost-effectiveness of the proposed interventions and also clearly demonstrate the potential health impact.

The following types of projects are excluded from funding:

- Primary cancer prevention studies on the impact of environmental, occupational, socio-economic, or psychosocial risk factors.
- Genome-Wide Association Studies.
- Phase III or phase IV clinical trials.
- Projects close to marketing their products (e.g. drugs, biomarkers, technologies, assays).
- Comparative studies based on investigation of other applications of established diagnostics or therapeutics.
- "De novo" construction of research resources and infrastructure, particularly new assembly of material collections.

2.2 Capacity building and training activities (optional)

Translational research has the ambition to remove barriers to multidisciplinary and multi-professional collaboration. It is envisioned that clinicians, researchers and the various operational staff from various sectors (academia, industry, regulatory bodies) will effectively work together to expedite the translation of scientific discoveries to clinical application and to more rapidly fuel research directions with observational or clinical findings. In fact, the complexity of the process requires, at the individual and collective levels, the creation of translational medicine research interfaces/infrastructures. To reach that goal, TRANSCAN has defined in its objectives to support capacity building and training programmes for multidisciplinary teams, through the combination of training and mobility in an integrated process: i) training of individual researchers/professionals in order to bring new expertise to an existing multidisciplinary translational team, and/or ii) recruitment of individual researchers/professionals by a translational research team in order to cover disciplines unavailable in the existing team. This type of activities, when present, will be supported within the projects which will be selected for funding under the JTC 2012.

Thus, applicants may add to the proposal, an additional part for training activities (with an associated separate budget, in compliance with the rules of the respective national/regional funding organisations concerning the funding of the training activities). The training activities should be coherent with the objectives of the research project, and aimed to strengthening the ability of participating team(s) to perform the work detailed in the project plan in addition to the long-term improvement of its (their) overall scientific capacity. For example, these activities could

be (the following list is just indicative but not exclusive) 1) students exchanges, 2) short term training of scientists, operational staff, etc., 3) training workshop to a specific technique or procedure, 4) short training (1 or few weeks) in several partner teams by one expert, etc. However activities related to project management should be included in the scientific project, it cannot be optional for a successful project and activities related to the results dissemination such as symposium, conferences are out of the scope of this capacity building and training activities component. The training component will be evaluated independently and will not have an impact on the overall assessment of the proposal.

3. CALL IMPLEMENTATION BOARDS

The Call Steering Committee (CSC) and the Scientific Evaluation Committee (SEC) will manage the evaluation procedure of pre-proposals and full proposals and the final selection of research projects, with support of the Joint Call Secretariat (JCS).

The CSC is composed of a single representative from each national/regional funding organisation participating in JTC 2012. The CSC will supervise the preparation and the implementation of the call and will take all decisions concerning the call. Based on the ranking list of the full proposals compiled by the SEC and on available funding, the CSC will make its recommendations for the projects to be funded. The CSC recommendations will be sent to the national/regional funding organisations for their final decisions. Members of the CSC are not allowed to submit proposals to this call.

The SEC is a panel of internationally recognised scientific experts responsible for the evaluation of submitted pre- and full proposals. SEC members are not allowed to submit or participate in proposals within this call, and must sign declarations on conflicts of interest and confidentiality.

4. APPLICATION

4.1 Funding recipients and eligibility

Joint transnational research proposals may be submitted by applicants belonging to one of the following categories depending on national/regional eligibility rules as specified in Annex 3:

- Academic research groups (from universities or other higher education or research institutions).
- Clinical/public health sector research groups (from hospitals/public health and/or other health care settings and health organisations).
- Enterprises (depending on national/regional eligibility rules), with particular emphasis on small and medium-sized enterprises.

Please note that the inclusion of a non-eligible partner in a proposal leads to the rejection of the entire proposal without further review.

Only transnational projects will be funded. Each consortium must involve a minimum of three (3) and a maximum of seven (7) research groups from at least three (3) different countries participating in the call. In addition, a research consortium must not involve more than two (2) research groups from one country. The majority of research groups in a consortium as well as the coordinator of a consortium must be from a JTC 2012 funding partners country/region (see above). A consortium may include one (1) research group (included in the maximum number of 7) from a country/region not partner in this call if, at the stage of the pre-proposal submission, this group can provide a written confirmation that their funding is already secured.

Each transnational consortium must nominate a coordinator from one of the countries/regions funding the JTC 2012. The coordinator will be responsible for the internal scientific management (such as controlling, reporting, intellectual property rights issues, etc.) and for the external representation towards the JCS and the CSC. Each consortium partner will be represented by one principal investigator, who will be the contact person for the respective national/regional funding organisation.

A research consortium must involve at least one basic or pre-clinical research team and one clinical team. A consortium may also involve other teams with specialised skills and know-how that will make the project feasible (biobanks, model systems, technological platforms, biostatistics, bio-informatics, data management etc.) or expertise (epidemiology and molecular epidemiology, early phase clinical trials, public health, ELSI etc.). A collaborative research consortium should have sufficient critical mass to achieve ambitious scientific, technological and medical goals and, along with the particular contribution of each research team, should clearly demonstrate the added value of the transnational consortium. The translational nature of the research results is the key goal of TRANSCAN and, therefore, the research consortium should also clearly demonstrate a knowledge transfer towards clinical, public health and/or industrial applications.

While applications of researchers or research groups from several countries will be submitted jointly by the coordinators of these groups, individual groups will be funded by the funding organisation from their country/region that is participating in the TRANSCAN JTC 2012. The applications are therefore subjected to eligibility criteria of national/regional funding organisations.

Applicants should refer to the annexes of the document "Guidelines for Applicants" containing all the specific national/regional eligibility criteria and should contact their respective national/regional funding organisation contact points for additional clarification (see Annex 1. Contact information of the national/regional funding organisations).

NOTE: *An eligibility check before the pre-proposal submission is mandatory for the following funding organisations: The Ministry of Health (MOH), Italy and The Dutch Cancer Society (DCS), The Netherlands.*

The duration of the projects can be up to three (3) years. According to the eligibility criteria of the funding organisations contributing to TRANSCAN JTC 2012, a research group may receive funding for less than three years.

4.2. Submission of joint proposals

There will be a two-stage submission procedure for joint applications: pre-proposals and full proposals. Both types of proposals must be written in English and must be submitted to the JCS by the coordinator.

The proposals should strictly follow the rules described in the document "*Guidelines for applicants*", and use the forms available through the TRANSCAN website (http://www.transcanfp7.eu/). Applicants should take note of individual national/regional rules, and contact their national/regional contact points for any questions.

The pre-proposals must be submitted to the electronic submission system of the JCS no later than 15 February 2013, at 17:00 (Central European Time). The decision on the results of the pre-proposal evaluation meeting will be communicated to the coordinators on the second week of May 2013.

The information given in the pre-proposal is binding. Thus, any fundamental changes between the pre-proposal and the full proposal (e.g. composition of the consortia, objectives of the project, etc.) must be communicated to the JCS with detailed justification and will be allowed by the CSC only under exceptional circumstances.

The full proposals will have to be submitted to the electronic submission system of the JCS not later than 24 June 2013 at 17:00 (Central European Summer Time). Please note that full proposals will only be accepted from applicants explicitly invited by the JCS to submit them.

The decision on the results of the full-proposals' evaluation meeting will be communicated to all the (successful and unsuccessful) coordinators in October. Proposals' coordinators will receive a summary of the evaluation conclusions in due time.

5. EVALUATION

5.1 Evaluation criteria

Pre-proposals and full proposals will be assessed according to defined evaluation criteria. A scoring system from 0 to 5 will be used to evaluate the proposals performance with respect to the different evaluation criteria:

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

Pre-proposal evaluation criteria:

- Relevance of the project regarding the topic (primary and secondary prevention of cancer) and the overall objectives of the call (translational research).
- Scientific excellence: soundness of the rationale and of the research hypothesis(es); innovative approach, originality and feasibility of the project; expected progress beyond the state-of-the-art.
- Quality of the implementation plan and of the project management: appropriateness of the methodology and associated work plan, with particular regard to the study design, the study population(s), and the statistical and biostatistical analysis and power calculations; appropriateness of the planned management structure; appropriateness of the resources to be committed (personnel, equipment, etc.) and of the estimated budget.
- Quality of the transnational research consortium: experience of the research consortium partners in the field(s) (for young teams, appropriateness of their current work and training of their members should be considered); quality of the consortium as a whole (including complementarity and added value of the multinational collaboration).
- Potential impact with reference to the development, dissemination and use of project results: potential impact of the expected results on cancer prevention and control, in terms of translation into public health or clinical practices and/or into pharmaceutical/industrial applications; appropriateness of measures for the dissemination and/or exploitation of project results including socio-economic aspects and anticipation of intellectual property issues (patenting, industrial exploitation, marketing, etc.).

Please note that in the case that the implementation of a clinical trial is comprised in the proposal, the following evaluation criteria will be applied:

- Clinical aspects of the clinical trial:
  - Soundness of the evidence presented in support of the medical need and of the trial rationale;
  - Adequateness and feasibility of the clinical trial design to verify the hypothesis(es) and to respond to the medical need;
  - Clarity of concept for further clinical and/or epidemiological and/or research actions/steps;
  - Innovation and relevance of the trial in terms of potential clinical and public health impact;
  - Soundness of the clinical trial design, with special regard to the estimated size effect;
  - Adequateness of the controls and/or comparators;
  - Relevance of the outcome measures/endpoints;
  - Compliance with the regulatory requirements and adequateness of the consideration of the ELSI issues;

- Qualification of the teams involved in the implementation and monitoring of the clinical trial;
- Adequateness of the trial management;
- Adequateness of the infrastructural support to the clinical trial;
- Adequateness of the financial plan.

- Statistical and biostatistical aspects of the clinical trial:
  - Precision of the hypothesis at the base of the study and coherence of the trial design with said hypothesis;
  - Adequateness of the clinical trial design to verify the hypothesis(es);
  - Adequateness of the outcome measures/endpoints with respect to the overall objectives of the trial;
  - Adequateness of the target and study population;
  - Adequateness of the consideration of the potential clinical and epidemiological consequences of the trial results;
  - Adequateness of the randomisation criteria, if applicable;
  - Adequateness of the assumptions underlying the sample size calculations, as substantiated by the literature;
  - Adequateness of the proposed strategy for statistical and biostatistical analysis.

Full proposal evaluation criteria:

- Relevance and clarity of the objectives with respect to the specific medical need and aims of the call.
- Scientific quality of the proposal: scientific excellence of the proposal, in terms of innovative approach, originality and expected progress beyond the state-of-the-art; availability and quality of preliminary data; international competitiveness.
- Quality of the transnational research consortium: level of expertise of the individual teams partners in the research consortium in the field(s) of the proposal (team scientific track record, publications, patents, etc.; for young teams, appropriateness of their current work and training of their members should be considered); quality of the collaboration between the research teams and added value of the research consortium with respect to the individual teams; quality of the consortium governance and management (planning, meeting, etc.).
- Methodology and feasibility of the proposal: relevance, originality and soundness of the methodology, with particular regard to the study design, the study population(s), and the statistical and biostatistical analysis and power calculations; adequacy of the planned work plan implementation: work packages management and schedules), appropriateness of the resources to be committed and of the estimated budget; proposal feasibility [e.g. human resources; access to individuals/patients cohorts, and/or individuals/patients databases

and/or corresponding repositories of high quality biological and bio-molecular resources associated with epidemiological or clinical data; access to model systems, technological platforms and relevant infrastructures (OMICS, Next Generation Sequencing, bioinformatics, diagnostics and/or drug development, cancer screening techniques and methodologies, data management); availability of the necessary specific expertise (epidemiology and molecular epidemiology, cancer etiology, cancer genetics, cancer screening, pharmacology, early phase clinical trials design, conduct, management and follow-up, public health, ELSI etc.).

- Impact: potential impact of the expected results on cancer prevention and control, in terms of translation into public health or clinical practices and/or into pharmaceutical/industrial applications; appropriateness of measures for the dissemination and/or exploitation of project results including socio-economic aspects and anticipation of intellectual property issues (patenting, industrial exploitation, marketing, etc.).
- Capacity building and training activities: (*If the scientific proposal is selected for funding within the JTC 2012, the optional component of capacity building and training activities will be evaluated for an additional separate budget. For this reason, this component will be evaluated independently and will not have an impact on the scientific assessment of the proposal. A proposal could be recommended for funding without the part related to capacity building and training activities if the evaluation of this part is poor*):
    - Content: relevance and coherence of the capacity building and training activities with the proposal objectives.
    - Candidate: background (scientific, medical, etc), coherence with the CV, scientific production.
    - Host team: expertise of the host team in the field, qualification in research of the responsible person).

Please note that in the case that the implementation of a clinical trial is comprised in the proposal, the following evaluation criteria will be applied:

- Clinical aspects of the clinical trial
    - Soundness of the evidence presented in support of the medical need and of the trial rationale;
    - Adequateness and feasibility of the clinical trial design to verify the hypothesis(es) and to respond to the medical need;
    - Clarity of concept for further clinical and/or epidemiological and/or research actions/steps;
    - Innovation and relevance of the trial in terms of potential clinical and public health impact;
    - Soundness of the clinical trial design, with special regard to the estimated size effect;
    - Adequateness of the controls and/or comparators;
    - Relevance of the outcome measures/endpoints;
    - Compliance with the regulatory requirements and adequateness of the consideration of the ELSI issues;

- Qualification of the teams involved in the implementation and monitoring of the clinical trial;
- Adequateness of the trial management;
- Adequateness of the infrastructural support to the clinical trial;
- Adequateness of the financial plan;
- Potential of commercial exploitation.

- Statistical and biostatistical aspects of the clinical trial:
  - Precision of the hypothesis(es) at the base of the study and coherence of the trial design with said hypothesis(es);
  - Adequateness of the clinical trial design to verify the hypothesis(es);
  - Adequateness of the outcome measures/endpoints with respect to the overall objectives of the trial;
  - Adequateness of the target and study population;
  - Adequateness of the consideration of the potential clinical and epidemiological consequences of the trial results;
  - Adequateness of the randomisation criteria, if applicable;
  - Adequateness of the assumptions underlying the sample size calculations, as substantiated by the literature;
  - Adequateness of the proposed strategy for statistical and biostatistical analysis;
  - Impact of non-compliance and missing values on the sample size.

5.2 Eligibility check of pre-proposals and first step of evaluation

5.2.1 Eligibility check

The JCS will examine all pre-proposals to ensure that they meet the call's formal criteria (date of submission, number of participating countries and groups, inclusion of all necessary information in English, adherence to the proposal template). The JCS will forward the pre-proposals to the national/regional funding organisations, which will perform a formal check of compliance with their respective regulations.

After completion of the eligibility check, the CSC will take the final decision and the pre-proposals not considered eligible will be rejected without further review. The coordinators of the non eligible pre-proposals will be informed by the JCS.

5.2.2 Evaluation of pre-proposals

Pre-proposals passing the formal eligibility checks will be forwarded to the SEC members for their evaluation according to the evaluation criteria for pre-proposals described above.

All necessary steps will be taken by the CSC to ensure that the SEC members have no conflict of interest for those proposals that they have to evaluate. SEC members must also formally declare that no such conflict of interest exists at any time of their evaluation duty and will sign a confidentiality agreement concerning all documents and the entire process.

Each pre-proposal will be allocated to two (2) SEC members, who fit the profile of the application. The SEC will meet, discuss the pre-proposals and establish a ranking of the pre-proposals. The CSC will meet in order to decide, based on the SEC recommendations, which pre-proposals will be invited for the full proposal submission.

The JCS will communicate to all project coordinators the final decision with respect to their pre-proposals.

5.3 Eligibility check of full proposals and second step of evaluation

The JCS will check the full proposals to ensure that they meet the formal criteria of the call and have not changed substantially from the respective pre-proposals before sending them to the external reviewers.

A full proposal may be excluded from further review, if the proposal objectives or the composition of the consortium deviate substantially from the previously submitted pre-proposal. In any case, major changes must be communicated to the JCS, which will contact the concerned national/regional funding organisation for a discussion of this issue; a formal decision on whether such an exceptional change may be justified will be taken by the CSC.

Each full proposal will be sent to at least two (2) external reviewers who fit the profile of the application and to the two (2) SEC members who had reviewed the corresponding pre-proposal. The external reviewers and the SEC members will independently assess the full proposal according to the evaluation criteria above mentioned, and will deliver their evaluation reports to the JCS. The JCS will send the external reviewers' evaluation reports to the SEC members in preparation of the second SEC meeting. During the second SEC meeting, the SEC member selected as rapporteur for each full proposal will present a summary of all the corresponding individual evaluation reports. The SEC members, after consideration of the individual evaluation results, will compile a ranking list of the full proposals recommended for funding.

5.4 Funding decision

Based on the ranking list of the full proposals compiled by the SEC and on available funding, the CSC will make its recommendations for the projects to be funded. The CSC recommendations will be sent to the national/regional funding organisations for their final decisions.

The JCS will communicate to all project coordinators the final decision. Proposals' coordinators will receive a summary of the evaluation conclusions in due time.

6. FINANCIAL AND LEGAL ISSUES

6.1. Funding model and funding details

The TRANSCAN JTC 2012 funding organisations have agreed to launch a joint call using the "virtual common pot" funding model. This means that funding will be made available by each national/regional funding organisation according to their specific regulations, for research groups in their country/region.

The funding rate within the call will be variable up to a maximum of 100% of the funds requested, according to national/regional rules. Funding is granted for a maximum of three years according to national regulations.

Prior to submitting a proposal, applicants should take note of individual national/regional rules described in the annexes of the document "Guidelines for applicants" in order to verify their eligibility, the eligible costs and potential budget available. Applicants are strongly encouraged to contact their national/regional funding organisations (see Annex 1. Contact information of the national/regional funding organisations) for any clarification.

Depending on the time needed for the administration of granting funds to the respective national/regional research groups, individual projects of a research consortium are expected to start in April 2014.

6.2 Research consortium agreement and ownership of intellectual property rights

It is mandatory for a funded research project consortium to sign a consortium agreement (CA) for cooperation, addressing the issues indicated in the document "*Guidelines for Applicants*" on consortium agreements, including the issues involving Intellectual Property Rights (IPR). The research consortium is strongly encouraged to sign this CA before the official project start date. Upon request, this consortium agreement must be made available to the concerned TRANSCAN JTC 2012 funding organisations.

Results and new IPR resulting from projects funded through the TRANSCAN JTC 2012 will be owned by the researchers' organisations according to national/regional rules on IPR. If several participants have jointly carried out work generating new IPR, they shall agree amongst themselves (CA) as to the allocation of ownership of IPR, taking into account their contributions to the creation of those IPR as well as the European Commission´s guidelines on IPR issues.

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

The JTC 2012 funding organisations 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 owners´ rights are kept.

6.3 Confidentiality of proposals

Proposals and any information relating to them shall be kept confidential within the external reviewers, the SEC and the CSC. Proposals shall not be used for any purpose other than the evaluation and subsequent monitoring of the funded projects.

Full proposals will be required to include a publishable summary, which will clearly identify the main goals of the project. If a proposal will be funded, this information will be published on the TRANSCAN website. All other project details shall be kept strictly confidential.

7. REPORTING AND DISSEMINATION

The coordinator of a funded transnational research consortium must submit annual scientific project reports (within 2 months), and a final scientific project report (within 3 months after the end of the project) to the JCS. All reports must be in English and use reporting forms, one for the annual reports and one for the final report, that will be provided to the coordinators of the funded projects in due time.

In addition to these centrally-administered TRANSCAN reports, it may also be required that principal investigators of individual research projects submit financial and scientific reports to their national/regional funding organisations. The progress and final results of each individual contract/letter of grant will be monitored by the respective national/regional funding organisations.

In case of serious difficulties in the conduct of the research project, the coordinator shall inform the JCS and the involved funding organisations. The relevant funding organisations will decide upon the proper actions to be taken.

Funding recipients must ensure that all results (publications, etc.) of their research projects consortium activities include a proper acknowledgement that the projects were supported in part by the respective funding organisations under the framework of the TRANSCAN initiative.

The coordinators and/or principal investigators may be asked to present the results of their projects at an intermediate and/or a final TRANSCAN status symposium.

8. CONTACT AND FURTHER INFORMATION

The JCS is set up at the French National Cancer Institute (INCa), Department of Cancer Biology - Research and Innovation division, 52, avenue André Morizet 92513 Boulogne-Billancourt Cedex, FRANCE. The JCS will assist the CSC during the implementation of JTC 2012 as well as during the monitoring phase (until 3 months after the funded research projects have ended). The JCS will be responsible for the central management of the call evaluation and monitoring. The JCS will be the primary contact referring to the JTC 2012 procedures between the research consortia, the funding organisations (CSC) and the peer reviewers (SEC + external experts).

Further information on TRANSCAN, the JTC 2012 and the monitoring is available at the TRANSCAN website: http://www.transcanfp7.eu/.

ANNEX 1. CONTACT INFORMATION OF THE NATIONAL/REGIONAL FUNDING ORGANISATIONS PARTICIPATING IN TRANSCAN JTC 2012

Country/Region	Participating funding organisations	Website	National contact points
Austria	Austrian Science Fund (FWF)	http://www.fwf.ac.at/	**Dr. Stephanie RESCH** Austrian Science Fund Haus der Forschung, Sensengasse 1 1090 Vienna, Austria Tel: +43-1-505 67 40-8201 E-mail: stephanie.resch@fwf.ac.at
Belgium: Flemish region	Research Foundation - Flanders (FWO)	http://www.fwo.be/	**Dr. Olivier BOEHME** Senior Science Administrator Research Foundation - Flanders Egmonstraat 5 B-1000 Brussels, Belgium Tel. +32 2 550 15 45 E-mail: olivier.boehme@fwo.be
France	French National Cancer Institute (INCa)	http://www.e-cancer.fr/	**Estelle GERBAUD, PharmD** Cancer Biology Department / Research and Innovation Division 52 avenue André Morizet 92513 Boulogne Billancourt Cedex, France Tel: +33 (0)1 41 10 14 16 E-mail: egerbaud@institutcancer.fr
	ARC French Foundation for Cancer Research (ARC Foundation)	http://www.arc-cancer.net	**Ms. Christelle DAVID-BASEI, PhD** Scientific Director Fondation ARC pour la recherche sur le cancer Direction de l'Action Scientifique 9 Rue Guy Moquet – BP 90003 94803 Villejuif Cedex, France Tel: +33 (0)1 45 59 59 44 E-mail: cdavid-basei@arc-cancer.net **Ms. Nancy ABOU-ZEID, PhD** Scientific Officer – Partnerships Fondation ARC pour la recherche sur le cancer Direction de l'Action Scientifique 9 Rue Guy Moquet – BP 90003 94803 Villejuif Cedex, France Tel: +33 (0)1 45 59 58 44 E-mail: nabou-zeid@arc-cancer.net
Germany	Federal Ministry of Education and Research (BMBF) / PT-DLR	http://www.gesundheitsforschung-bmbf.de http://www.gesundheitsforschung-bmbf.de/de/4639.php	**Project Management Agency of the German Aerospace Centre** (PT-DLR) - Health Research-Heinrich-Konen-Str. 1 53227 Bonn, Germany Tel: +49 (0)228/3821-1210 Fax: +49 (0)228/3821-1257 E-mail:

			gesundheitsforschung@dlr.de
Israel	The Chief Scientist Office of the Ministry of Health (CSO-MOH)	http://www.health.gov.il	**Dr. Benny LESHEM** The Medical Research Administration Chief Scientist Office Israeli Ministry of Health 2, Ben Tabai St. Jerusalem 91010, Israel Tel: +972-2-568-1208 E-mail: benny.leshem@moh.health.gov.il
Italy	Ministry of Health (MoH)	http://www.salute.gov.it	**Dr. Maria FERRANTINI** Directorate General for Health and Biomedical Research and Supervision of National Health Bodies and Institutions Ministry of Health – Ministero della Salute Viale Giorgio Ribotta, 5 00144 Rome, Italy Tel: +39 065994.2684 E-mail: transcan@sanita.it **Dr. Tiziana CATENA** Directorate General for Health and Biomedical Research and Supervision of National Health Bodies and Institutions Ministry of Health – Ministero della Salute Viale Giorgio Ribotta, 5 00144 Rome, Italy Tel: +39 065994.3528 E-mail: transcan@sanita.it **Dr. Silvia PARADISI** Directorate General for Health and Biomedical Research and Supervision of National Health Bodies and Institutions Ministry of Health – Ministero della Salute Viale Giorgio Ribotta, 5 00144 Rome, Italy Tel: +39 065994.2684 E-mail: transcan@sanita.it
Latvia	Latvian Academy of Sciences (LAS)	http://www.lza.lv	**Dr. Maija BUNDULE** Centre of European Programs Latvian Academy of Sciences 1 Akademijas laukums, Riga, 1050 Latvia Tel: +371 67227790 E-mail: maija.bundule@lza.lv **Dr. Uldis BERKIS** Centre of European Programs Latvian Academy of Sciences 1 Akademijas laukums, Riga, 1050

			Latvia Tel: +371 67409242 E-mail: uberkis@latnet.lv
Luxembourg	National Research Fund (FNR)	http://www.fnr.lu	**Frank GLOD** Tel: +352 26192533 E-mail: frank.glod@fnr.lu
The Netherlands	Dutch Cancer Society (DCS)	http://www.kwfkankerbestrijding.nl/	**Ms. Wia TIMMERMAN** KWF Kankerbestrijding Delflandlaan 17/ Postbus 75508 1070 AM Amsterdam The Netherlands Tel: + 31 20 5700520 E-mail: wtimmerman@kwfkankerbestrijding.nl **Ms. Merel HOOZEMANS** KWF Kankerbestrijding Delflandlaan 17/ Postbus 75508 1070 AM Amsterdam The Netherlands Tel: + 31 20 5700520 E-mail: mhoozemans@kwfkankerbestrijding.nl
Norway	The Research Council of Norway (RCN)	http://www.rcn.no	**Henrietta BLANKSON** The Research Council of Norway, Division for Society and Health, Department for Health Boks 2700 St. Hanshaugen N-0131 Oslo E-mail: hbl@rcn.no Tel: + 47 22 03 71 76 **Karianne SOLAAS** The Research Council of Norway, Division for Society and Health, Department for Health Boks 2700 St. Hanshaugen N-0131 Oslo E-mail: kso@rcn.no Tel: +47 22 03 70 84
Norway	Norwegian Cancer Society (NCS)	www.kreftforeningen.no	**Dr. Nina ANENSEN** Kreftforeningen Postboks 4, Sentrum 0101 Oslo Norway Tel: +47 93 00 74 07 E-mail: nina.anensen@kreftforeningen.no
Poland	National Centre for Research and Development (NCBiR)	http://www.ncbr.gov.pl	**Mr. Marcin CHMIELEWSKI** National Centre for Research and Development (NCBR) Section for Research Projects BIOMED Nowogrodzka Str. 47a, 00-695 Warsaw, Poland Tel: +48 22 39 07 109 E-mail: marcin.chmielewski@ncbr.gov.pl

			Ms. Malgorzata ZIEMINSKA National Centre for Research and Development (NCBR) Section for Research Projects BIOMED Nowogrodzka Str. 47a, 00-695 Warsaw, Poland +48 22 39 07 140 E-mail: malgorzata.zieminska@ncbr.gov.pl
Portugal	Foundation for Science and Technology (FCT)	www.fct.pt	**Cristiana LEANDRO** Departamento de Relações Internacionais (DRI) Fundação para a Ciência e Tecnologia Av. D. Carlos I, 126 1249-074 Lisboa Portugal Tel.: +351 213 924 381 cristiana.leandro@fct.pt
Romania	Institute of Oncology Prof. Dr. Alexandru Trestioreanu (IOB)	http://www.iob.ro	**Prof. Dr. Rodica ANGHEL, PhD MD** Institute of Oncology "Prof Dr Al Trestioreanu" Bucharest 252 Fundeni street, Sector 2, Bucharest, Romania Tel: +40 212271400 E-mail: rodicamanghel@gmail.com **Mr. Sabin CINCA, PhD** Institute of Oncology "Prof Dr Al Trestioreanu" Bucharest 252 Fundeni street, Sector 2, Bucharest, Romania Tel. +40.213183561 E-mail: sabincinca@yahoo.com
Slovakia	Slovak Academy of Sciences (SAS)	http://www.sav.sk	**Mr. Jan BARANCIK, PhD** Department for International Cooperation of SAS, Slovak Academy of Sciences, Štefánikova 49 814 38 - Bratislava, Slovak Republic Tel: +421 2 5751 0137 E-mail: barancik@up.upsav.sk **Ms. Anna GÁBELOVÁ, PhD** Cancer Research Institute Slovak Academy of Sciences Vlarska 7833 91 - Bratislava, Slovak Republic Tel: +421 2 59327-512, 202, 502, 526 E-mail: exongaba@savba.sk **Ms. Iveta HERMANOVSKÁ** Department for International

			Cooperation of SAS, Slovak Academy of Sciences, Štefánikova 49 814 38 - Bratislava, Slovak Republic Tel: +421 2 5751 0136 E-mail: hermanovska@up.upsav.sk
Turkey	The Scientific and Technological Research Council of Turkey (TÜBITAK)	http://www.tubitak.gov.tr/	**Ms. Nihan ERYILMAZ** TÜBİTAK Tunus Caddesi No:80 06100 Kavaklıdere / Ankara, Turkey Tel: + 90 312 468 53 00 / 1007 E-mail: nihan.eryilmaz@tubitak.gov.tr

ANNEX 2. INDICATIVE FUNDING COMMITMENT OF THE FUNDING ORGANISATIONS PARTICIPATING IN TRANSCAN JTC 2012

Country/ Region	Participating funding organisation	Envisioned amount of funding (M€ for 3 years)	Anticipated number of fundable research groups
Austria	Austrian Science Fund (FWF)	1 M €	4
Belgium: Flemish region	Research Foundation Flanders, Fonds Wetenschappelijk Onderzoek Vlaanderen (FWO)	0.2 M €	1
France	French National Cancer Institute (INCa)	1.5 M €	5-10
	ARC French Foundation for Cancer Research (ARC Foundation)	0.3 – 0.5 M €	1 - 3
Germany	Federal Ministry of Education and Research (BMBF)	3 M €	10-12
Israel	The Chief Scientist Office of the Ministry of Health (CSO-MOH)	Up to 0.24 M €, Depending on budget availability	Up to 4
Italy	Ministry of Health (MoH)	2 M €	6-7
Latvia	Latvian Academy of Science (LAS)	0.25 M €	2
Luxembourg	National Research Fund (FNR)	0.25 M €	1-3
The Netherlands	Dutch Cancer Society (DCS)	1 M €	4
Norway	The Research Council of Norway (RCN)	0.5 M €	1 - 4
Norway	Norwegian Cancer Society (NCS)	0.5 M €	1 - 4
Poland	National Centre for Research and Development (NCBiR)	1.5 M €	3 - 6
Portugal	Foundation for Science and Technology (FCT)	0.4 M €	2

Romania	Institute of Oncology Prof.Dr. Alexandru Trestioreanu (IOB)	0.25 M €	1 - 2
Slovakia	Slovak Academy of Sciences (SAS)	0.210 M €	2
Turkey	The Scientific and Technological Research Council of Turkey (TÜBITAK)	0.6 M €	3 - 4

ANNEX 3. ELIGIBILITY OF BENEFICIARY INSTITUTIONS FOR THE FUNDING ORGANISATIONS PARTICIPATING IN TRANSCAN JTC 2012

Country/ Region	Participating funding organisation	Eligible beneficiary institution [1]		
		Academia	Clinical/ public health	Enterprise
Austria	Austrian Science Fund (FWF)	Applications for projects from Austria may only be submitted by single natural persons. Affirmation of the research institution (academia, clinical/public health, enterprise) of the applicant is mandatory.	Applications for projects from Austria may only be submitted by single natural persons. Affirmation of the research institution (academia, clinical/public health, enterprise) of the applicant is mandatory.	Applications for projects from Austria may only be submitted by single natural persons. Affirmation of the research institution (academia, clinical/public health, enterprise) of the applicant is mandatory.
Belgium: Flemish region	Research Foundation Flanders, Fonds Wetenschappelijk Onderzoek – Vlaanderen (FWO)	Yes [2]	Only officially research institutions and university hospitals, and always in cooperation with a Flemish university (Cf. art. 9 of the Regulations on New Research Projects of FWO)	No
France	French National Cancer Institute (INCa) ARC French Foundation for Cancer Research (ARC Foundation)	Yes	Yes	No. Industrial companies could participate if they are able to secure their own funding
Germany	Federal Ministry of Education and Research (BMBF)	Yes	Yes	Yes
Israel	The Chief Scientist Office of the Ministry of Health (CSO-MOH)	Yes	Yes	Only on their own budget
Italy	Ministry of Health (MoH)	No	Yes	No
Latvia	Latvian Academy of Sciences (LAS)	Yes	Yes	Yes

Luxembourg	National Research Fund (FNR)	Yes, according to the legal rules of the FNR	Yes, according to the legal rules of the FNR	No
The Netherlands	Dutch Cancer Society (DCS)	Yes, according to grant conditions KWF Kankerbestrijding	Yes, research institutes and university hospitals according to grant conditions KWF Kankerbestrijding	No. Industrial companies could participate if they are able to secure their own funding
Norway	The Research Council of Norway (RCN)	Yes	Yes	No
Norway	Norwegian Cancer Society (NCS)	Yes	Yes	No
Poland	National Centre for Research and Development (NCBiR)	Yes, according to the national legal rules	Yes, according to the national legal rules	Yes, according to the national legal rules
Portugal	Foundation for Science and Technology (FCT)	Yes, according to the national rules	Yes, according to the national rules	Yes, according to the national rules (max. of 50% of the total budget)
Romania	Institute of Oncology Prof. Dr. Alexandru Trestioreanu (IOB)	No	Yes	No
Slovakia	Slovak Academy of Sciences (SAS)	Yes	Yes	Yes
Turkey	The Scientific and Technological Research Council of Turkey (TÜBITAK)	Yes	Yes	Yes

Please note that the information on this table is only indicative. Applicants are encouraged to contact their national/regional contact points for further information.

(1) The eligibility of companies and institutions is subjected to different conditions in each country/region. Further details regarding the eligible beneficiaries and other national eligibility criteria and requirements are available on the “guidelines for applicants” and the TRANSCAN website (http://www.transcanfp7.eu/).

(2) Only clinics associated with universities are eligible for the FWO.