LEONARDO da VINCI PRIZE FOR THE MOST EFFICIENT SOLUTION IN PARTICLE DETECTION FOR EARLY CANCER DIAGNOSIS

Rules and Request For Application (RFA)

(Dedicated to Valentina Vigna and All Victims from premature cancer death)

Open to authors, Principal Investigators, persons responsible for cancer research projects or to anyone who would like to nominate a project for which he is willing to provide all necessary material and is willing to answer questions based on scientific arguments that will support his or the author's claims.

In order to reach all possible projects that could offer the highest reduction in premature cancer deaths, this PRIZE will be given the maximum publicity through press releases and by sending the material relative to this competition to the leaders of the major research centers in the world, in particular to the major research centers in particle physics (CERN, FERMIIab and BNL).

The prize (initial fund of \$10,000 that will increase until the date of the award of the prize) will be awarded to the most efficient solution in particle detection targeted to early cancer diagnosis. This will stimulate a competition in the particle detection technique of tracking tumor markers which indicates to be the most promising in early cancer detection. This technique allows the acquisition of data from signals that provides as early as possible information on the mutation of normal cells to cancerous cells at the morphological and functional level. However, if anyone knows of a solution in another field that he believes (and can support with scientific arguments) could have a higher impact on premature cancer death reduction, he is invited to submit his solution to this SCIENTIFIC PROCEDURE so that by being public, if such a project emerges, it will be given visibility during the analysis of the documents that were submitted to justify in such an event the creation of another competition targeted to compare projects with experts in the project's specific field.

WHEREAS, during the past 50 years the reduction in cancer deaths has been recorded as a mere 5%, (even by showing an increase from 1975 to 2007 as reported by The National Institute of Health -NIHand by The National Cancer Institute -NCI in 2010) while for heart disease the reduction was 64%, although fewer investments were allocated. Raw data confirming these data are published by NIH-NCI-SEER (Surveillance Epidemiology and End Results), while their graphic representation was published by *FORTUNE* Magazine in 2004, by *WIRED* Magazine in 2008 and by <u>The New York Times in April 24, 2009</u>;

WHEREAS, according to June 2, 2010 report from the World Health Organization (WHO), it has been predicted that by 2030 there will be more than 13 million deaths from cancer worldwide and nearly 21 million cases diagnosed annually. (Compared to 12.7 million new cancer cases and 7.6 million cancer deaths occurring in 2008);

WHEREAS, the cancer costs increased during the past 50 years by **100 fold**. In fact, direct medical expenditures for cancer in the U.S. were \$1.2 billion in 1963 and jumped to \$93.2 billion in 2008. (In comparison the increase in cost of primary food in the U.S. was **only 4 fold**. For example: bacon went from \$0.79/lb to \$2.99/lb; eggs \$0.55 dz. to \$1.29/dz.; bananas \$0.10/lb to \$0.39/lb, etc.);

WHEREAS, it has been demonstrated that cancer research failed during the past 50 years: Reduction of the cancer death rate in the world's most industrialized countries that have a cancer cost of \$741 billion/year (that is \$750/per-capita annually) is approximately the same as in less developed countries

(These data have been gathered by the World Health Organization, adapted by the American Cancer Society and published by the National Institute of Health and the National Cancer Institute. The cost of \$750/per capita annually has been calculated based on the total cost of cancer in the U.S. in 2008 at \$228.1 billion divided by the population of 304 million. This equals \$750/per-capita annually);

WHEREAS, while experimental data show that early cancer detection saves lives, innovations providing higher efficiency in early cancer detection are surprisingly not funded;

WHEREAS, it is necessary instead to focus on technologies targeted to early cancer detection;

WHEREAS, it is known that cancerous cells differentiate from normal cells through different signals that provide information about their mutation (Such signals are related to changes in: odor, temperature, tissue density, fluorescence, metabolism, perfusion, etc.);

WHEREAS, among all these signals, the ones most reliable and useful for early cancer detection are those which show an abnormal biological process even before a morphological change occurs. For example when there is an increase in nutrient requirement (abnormal metabolism) which is typical for the development of a tumor and other signals which provide less reliable information when taken alone, but which become more useful when they are associated with information relative to the abnormal metabolism or other biological process;

WHEREAS, Positron Emission Technology captures and counts in the unit of time signals arriving from the tumor markers (e.g. molecule, protein, etc.), such as tumor markers placed on the molecules of the nutrient to the body cells. However, the over 5,000 current PET (Positron Emission Tomography) devices are not suitable for early cancer detection because they capture only one signal of every 10,000 arriving from the tumor markers and the examination is very expensive;

WHEREAS, both signals, those arriving from the tumor markers and measured with the technique of the Positron Emission Technology which provides dynamic information within the unit of time (consumption of nutrient by the tumor), and those signals measured with the technique of Computed Tomography (CT) which provide static information (tumor dimension) are both based on particle detection (photons) and both sets of information, when detected and measured accurately at a low cost are useful for early cancer detection reducing the radiation to the patient and reducing costs;

WHEREAS, for both applications efficiency is defined as the ratio, during a unit of time, between the number of signals captured by the medical imaging device and the number of signals "emitted" (for PET) by the tracer (radiation) administered to the patient or by the radiation "transmitted" through the patient's body (for CT);

WHEREAS, Steve Fluckiger from the firm Jones Day, who works with other consultants to satisfy requests from philanthropists such as Bill Gates, to find (following "a disciplined process") the best and most reliable technologies which will have the biggest impact for humanitarian causes;

WHEREAS, <u>CANCER DEATHS are INCREASING</u> and that, in order to address the problem we need to support the implementation of an Open Public SCIENTIFIC PROCEDURE that funds only projects with a real potential to reduce premature cancer deaths by implementing the <u>Cancer Research Project</u> <u>Comparison Table</u> where authors must provide their estimate of the reduction in cancer deaths and costs they expect to attain with their projects upon receiving the funding requested;

WHEREAS, people who have at heart the problem of reducing premature cancer deaths (and trust that through a public competition, authors of the best projects will engage in a scientific discussion on the essence of their claims to the goal of making emerge the project with the highest potential to reduce premature cancer death), have already created an endowment of \$10,000 for the Leonardo da Vinci Prize, a fund that can increase until June 18, 2011;

Because of all of the above, because of the request by over 7,000 people who signed the petition targeted to identify the most efficient solution in particle detection for early cancer diagnosis, because of the will of those who want to create a fund of over \$10,060 (Bank account for the Leonardo da Vinci Prize: cc. 960022454, ABA 114000093, SWIFT FRSTUS44).

The Leonardo da Vinci Prize has been created for the most efficient solution in particle physics for early cancer detection.

The Prize is open to authors, Principal Investigators, persons responsible for cancer research projects or anyone who would like to nominate a project for which he is willing to provide all necessary material and is willing to answer questions based on scientific arguments that will support his or the author's claims.

In order to participate to this competition it is necessary to submit to the email address: insiemecontroilcancro2@gmail.com and to Dr. Vincenzo Vigna, Chairman of the Leonardo da Vinci competition at: Direzione Scientifica del Policlinico I.R.C.C.S. San Matteo, Piazzale Golgi, 27100, Pavia (Italy) (v.vigna@smatteo.pv.it, info@pec.vincenzovigna.it), by May 30, 2011 a description of the proposed cancer research project not to exceed 15 pages (with no limit to links of related referenced bibliographical material). Because the competition deals with arguments related to particle physics, the scrutiny of the proposals as well as the public debate to identify the most efficient project that will satisfy the requirements of the rules of this competition will take place in an open forum at the Department of Physics with experts in this subject. It is required that the applicant provide documentation comparing the proposed project to each project it is believed to be superior to. The comparison description of each compared project should not exceed 5 pages. In addition the author of the proposal should answer the <u>questionnaire</u> relative to the Cancer Project Comparison table.

Authors who intend to participate to this competition should comply with the following requirements:

- a) Submit a cancer research project
- b) Demonstrate the project has potential to reduce premature cancer deaths
- c) Provide an estimate of the percentage of lives saved from premature cancer deaths
- d) Provide an estimate of cost reduction for each life saved compared to current costs
- e) Provide scientific arguments to support estimates at c) and d)
- f) Provide a plan to measure experimental results
- g) Provide a date when an estimate of the first results may be obtained after funding is assigned

CRITERIA THAT MUST BE FOLLOWED TO ASSIGN THE LEONARDO DA VINCI PRIZE

1. The scientific procedure must be Public and Open to all projects from any country in the world.

2. On June 8, 2011, connected via web from the University of Pavia (through the Caltec, EVO system and via web streaming), all proposals received via email or on paper will be analyzed publicly so that every participant will be able to verify directly that no one has been left out. Authors and Principal Investigators who submitted a proposal will be invited to participate in person (or via EVO Caltec system connection) to support with scientific arguments the superiority of their system compared to the others.

3. Participants who cannot attend the meeting in person or via web EVO Caltec system will be informed about the other projects, and within 5 working days they should discuss (through exchange of emails and documentation that should also be made public) with the authors and/or Principal Investigators who claim their project to be superior in efficiency (as described in items 8 and 9 below) with respect to their project.

- 4. A panel of scientists and people who have an interest in the reduction of premature cancer deaths who guarantee a scientific review will evaluate the consistency of each author's claim in a public meeting on June 8, 2011 to be held at the University of Pavia. At this meeting the authors will have to defend the superiority of their project over claims of superiority presented by other projects during the competition. Reviewers knowledgeable in the specific field will be able to point out possible errors in calculations and provide the correct ones.
- 5. In the event of a disagreement among the members of the review panel and/or authors of different projects, an agreement should be found by proposing an experiment where results will prove who was correct among the two parties. In order not to waste time and money on experiments to reach results that could have been demonstrated using calculations and logical reasoning, before building the experiment, authors and P.I.s responsible of the projects in disagreement should provide three letters signed by leaders in the field from the most important research laboratories in the world who state clearly that in their opinion the disagreement cannot be solved with calculations and logical reasoning, essentially proposing that an experiment is the only way to solve the controversy at the minimum cost in money and time to expedite benefits to the bed of the patient. In the event this intermediate test will generate a delay in the progress of transferring benefits to the bed of the patient, the person who insisted on conducting the experiment and who is shown by the results to be wrong, should recognize his incompetence and should refrain to be a reviewer in the future in the evaluation of research projects.
- 6. Funding such an experiment considered essential as indicated above should be submitted to the Decision Makers who handle taxpayer's public funding for cancer research. Because of the power of the public who will have the possibility to follow the scientific procedure, together with the power of the over 7,000 people who signed the petition mentioned before, because of the importance to identify the project with the highest potential to reduce premature cancer death (the key objective for this competition) and because of the fair approach of this SCIENTIFIC PROCEDURE, guaranteed by leaders of the most important research laboratories in the world (who after confirm that calculations and/or logical reasoning cannot provide a definitive answer to the controversy will approve an experiment to resolve the issue), in the absence of any indication from Decision Makers of the existence of projects that offer higher efficiency in the same field, funding for this experiment should take priority over other projects that did not follow such a procedure based on comparison among different projects.
- 7. As an additional guarantee to identify the best innovation or project, and to stress that the reviewer's task is to evaluate the superiority of one project with respect to another based on the soundness of logical reasoning and calculations, a reviewer or P.I of another project who claims superiority in efficiency (as detailed in items 8 and 9) of his project or innovation should provide letters and emails written by leaders in the field with responsible positions in the most important research laboratories in the world. This is to ensure that reviewers will not use the tactic of requiring results only from some authors and not from others (so that two different weights and measurements will not be used) before providing funding that was requested in the first place to reach such results,
- 8. The first phase of determining the winner of the Leonardo da Vinci prize will be to select projects which claim a superiority in efficiency in particle detection with respect to the innovations described in the <u>letter dated March 23, 2011</u> (this letter from nine scientists and professionals to the U.S. President, Barack Obama and to the leaders of the Major U.S. Research Laboratories describes, provides scientific references and supports with scientific arguments and testimonials those innovations) in terms of capturing in real-time as many signals as possible satisfying a specific selective criteria (algorithm) designed to discover a specific particle but adaptable to identify several different particles. It should also have the capability to accurately measure all parameters of the characteristic of the signals generated by the particles at the minimum cost for each signal captured.

9. FROM AMONG THE PROJECTS SELECTED IN ITEM 8, THE PRIZE WILL BE AWARDED TO THE ONE TARGETED TO EARLY CANCER DETECTION THAT SHOWS SUPERIORITY IN EFFICIENCY TO ALL OTHER PROJECTS, WHERE EFFICIENCY IS DEFINED AS THE RATIO, WITHIN THE UNIT OF TIME, BETWEEN THE TOTAL NUMBER OF PAIRS OF 511 KeV PHOTONS CAPTURED (from the radioisotope administered to a 70 kg. human considered the standard, or from a phantom equivalent to a 70 Kg. human) and accurately measured AND THE TOTAL NUMBER OF PAIRS OF 511 KeV PHOTONS EMITTED. Total number of 511 KeV pairs of photons in time coincidence detected by the instrument EFFICIENCY = Total number of 511 KeV pairs of photons emitted by the radioisotope injected to the patient a. In the event two projects show the same superior efficiency, the prize will be awarded to the one having the lower cost per photon captured, b. In the event the project "Y" superior in efficiency has a cost per valid photon captured higher than the result obtained by the following formula $(C_{\gamma} > \{[1+(E_{\gamma} - E_x)/E_x]^{1.3} * C_x\})$, with respect to the cost of capturing a valid photon for a project "X" with efficiency " E_{x} " *immediately below in superiority, than the prize will go to project "X".* (In the formula " E_{y} " represent the efficiency of project "Y", and " E_X " represents the efficiency of project "X" immediately below in superiority. For example, looking along the fourth row of the table below, project "Y" has been found to be 4.5 times superior in efficiency to project "X", therefore, applying the formula, the cost for each photon captured by project "Y" should not exceed 7.06 times the cost of each photon captured by project "X"). For example: increase efficiency: " E_{y} " cost per photon captured: "C_y" $\begin{array}{l} C_{Y} \leq [1+(~E_{Y}-E_{x})/~E_{x}]^{1.3} * C_{x} \leq 1.27 * C_{x} \\ C_{Y} \leq [1+(~E_{Y}-E_{x})/~E_{x}]^{1.3} * C_{x} \leq 2.46 * C_{x} \\ C_{Y} \leq [1+(~E_{Y}-E_{x})/~E_{x}]^{1.3} * C_{x} \leq 5.09 * C_{x} \end{array}$ $E_{Y} = 1.2 * E_{x}$ $[1+(E_Y - E_x)/E_x] = 1.2$ $E_{Y} = 2.0 * E_{x}$ $[1+(E_{Y} - E_{x})/E_{x}] = 2.0$ $E_{Y} = 3.5 * E_{x}$ $[1+(E_Y - E_x)/E_x] = 3.5$ $C_{Y} < [1+(E_{Y} - E_{x})/E_{x}]^{1.3} * C_{x} < 7.06 * C_{x}$ $[1+(E_{Y} - E_{x})/E_{x}] = 4.5$ $E_{Y} = 4.5 * E_{x}$ COST PER VALID PHOTON CAPTURED IS DEFINED AS THE RATIO BETWEEN THE COST OF THE DEVICE AND THE NUMBER OF PAIRS OF 511 KEV PHOTONS CAPTURED IN ONE SECOND received from the radioisotope administered to a 70 Kg. human (or from a phantom equivalent to a 70 Kg. human), that has been injected with a 10 mCi dose of radioisotope. Cost per \$802 Direction of photon \$70 Research should captured CHANGE toward Current-PET \$60 Example: Higher Efficiency and Lower Cost \$50 Current PET device costs \$2 million. Dividing this cost by 37,000 (which is the number of \$40 photons captured per second when injecting 10 \$30 mCi of radioisotope) we arrive at the cost per valid photon captured of \$54. \$20 This competition is a stimulus to develop more \$10 efficient and lower cost projects (see green arrow in the blue area at right), however, no projects are rejected even if they fall outside of 005 .01 .015 .02 .025 .03 .035 .04 .045 .05 the blue area. Efficiency THE TOTAL COST OF THE DEVICE SHOULD NOT EXCEED \$10 MILLION THE INCREASE IN EFFICIENCY NOT ONLY REDUCES THE RADIATION TO THE PATIENT BUT ENABLES CANCER TO BE DETECTED EARLIER, WHICH WILL SAVE LIVES.

THE FORMULA OF THE EFFICIENCY IS THE JUDGE (and ultimately the experiment will confirm the

result of the formula) WHICH IS APPLIED OBJECTIVELY AND EQUALLY TO ALL PROJECTS TO THE BENEFIT OF CANCER PATIENTS AND TAXPAYERS. IN THIS WAY FAVORITISM IS ELIMINATED.

Current item 9 which deals with capturing signals (pair of photons at 511 KeV) received from tumor markers with increased efficiency is the key element, the conclusion of the logical reasoning presented in the previous list of "WHEREAS" (which starts from analyzing the problem from the big picture of no results versus high costs, down to the very details of the signals generated when there is a mutation from normal cells to cancerous cells, to the technology that allows the latter to be detected at an early stage which is what finally will provide a substantial reduction in cancer death) which will allow a change in direction to cancer research that to date has shown a failure. This improvement in efficiency (and cost reduction) is the key element that should be achieved and what is now missing. If implemented it will provide results in premature cancer death reduction. The assignment of the award ultimately should focus on choosing the project that has the **highest potential in premature cancer death reduction**. A plan to measure results will therefore be evaluated that should verify an effective reduction in premature cancer death. For example by planning a test safe for the patient performed on a representative sample of 10,000 people ages 50-75, selected in a location with a constant cancer death rate of 50 deaths per year recorded over the previous 20 years (which is the average worldwide).

- 10. After the first phase verifies that there are no authors or reviewers who have scientific arguments claiming superiority of their projects, then on June 18, 2011, at the Room Ugo Foscolo at the University of Pavia (Italy) at noon (time in Italy), the Leonardo da Vinci Prize will be awarded to the project (or innovation) which has passed all tests and therefore can demonstrate its superiority in efficiency over others.
- 11. The guarantee of the correctness and transparency of this procedure of assignment of the prize will be supported by the participation of the public because the entire procedure will be made public (documents, debates, discussions and controversies).
- 12. Furthermore the realization of this scientific procedure, or "disciplined process" as called by Steve Fluckiger that will end with the assignment of the Leonardo da Vinci prize will be the tool that will allow to all those who, with their donation, want to create a better world for future generations (as for example the members of the <u>Giving Pledge</u>).
- 13. Ultimately the Department of Nuclear and Theoretical Physics of the University of Pavia will not be held responsible in assigning erroneously a prize, because by having pursued the interest of the University to facilitate a scientific Procedure it can continue its role of being the most prestigious University open to the development of new ideas from innovators such as Leonardo da Vinci, Alessandro Volta, etc.

N.B.

Summary of deadlines and project presentations that clarifies and overwrites previous statements:

Details about the May 30, 2011 deadline:

 For projects submitted directly by the author, a description of the project limited to 15 pages (with no limit to bibliographical references), must be sent to: <u>insiemecontroilcancro2@gmail.com</u>, <u>v.vigna@smatteo.pv.it</u>, <u>info@pec.vincenzovigna.it</u>.

Authors are also requested to answer the questionnaire relative to the Cancer Project Comparison table. For practicality these questions are reported here:

- a) Cancer research title:
- b) Principal Investigator P.I. (Researcher proposing the research)
- c) Category
 - I. Category 1 __fundamental research (long term results available more than ten years from now) or
 - II. Category 2 __immediate application (results in reduction in cancer deaths and cost in less than 10 years)
- d) Estimated percentage of lives saved annually from premature (< 75 years of age) cancer death __%
- e) Scientific arguments supporting estimate (provide website or email address)_
- f) Cost per life saved compared to the current costs _____
- g) Total cost of the project _____
- h) Estimated date of results from the time full funding is provided_____
- Results Measurement Plan showing how estimates can be verified experimentally. (For example: a safe test on a representative sample of 10,000 people ages 50-75, selected from a population in a location with a constant cancer death rate of 50 deaths per year recorded over the previous 20 years). (provide website or email address).
- 2. For projects submitted by a third party, only a description of the project limited to 15 pages is required (with no limit to bibliographical references).

On May 31, 2011, the Chairman of the Leonardo da Vinci competition will communicate to all authors of the projects (those submitted directly by the authors and those submitted by third parties) the complete list of every project received so that each author who claims superiority may prepare supporting documentation (limited to 5 pages per project) using scientific arguments demonstrating the superiority in efficiency for his/her project with respect to the other projects (according the specifications in the rules of the competition).

Details about the June 8, 2011 deadline:

Authors may submit their comparison of superiority in efficiency (limited to 5 pages) of their project with respect to the other projects as follows:

- In writing, to the addresses <u>insiemecontroilcancro2@gmail.com</u>, <u>v.vigna@smatteo.pv.it</u>, <u>info@pec.vincenzovigna.it</u>, by 2:00 p.m. (Italian time) on June 8, 2011
- Directly in person at the meeting at the University of Pavia on June 8, 2011
- Via web connection at the meeting on June 8, 2011

All claims will be discussed and evaluated publicly in a transparent manner through the scrutiny of all projects via web that will begin at 2:00 PM on June 8, 2011 at the University of Pavia.

Organizers should allow sufficient time for all parties to present their claims and defend the superiority of their project with respect to the others. In the event it is impossible to demonstrate the superiority in efficiency of one project over another, the areas of disagreement should be clearly defined and an experimental test at the minimum cost should be identified that will resolve the ambiguity.

Furthermore, in the event of a disagreement that becomes an animated debate, any party can request equal time to present all his/her claims or to rebut the claims from other parties.

REQUEST FOR PUBLIC COMMENTS TO THE LEONARDO DA VINCI PROPOSED RULES FOR THE COMPETITION

SHOULD BE SENT BEFORE APRIL 20, 2011, WHEN IT WILL BE MADE FINAL

The proposed rules for the competition Leonardo da Vinci will be published on the web sites <u>www.vincenzovigna.it</u>, <u>www.insiemecontroilcancro.org</u>, <u>www.unitedtoendcancer.org</u>, <u>www.mce-aifavin.it</u> and will be sent to the leaders of the most important research laboratories in this field in the world with the request to send public comments so that all parameters can be identified that could contribute to reach the objective to select the most efficient project in particle detection targeted to early cancer detection with highest potential to reduce premature cancer deaths and costs.

If the proposed rules present barriers to identifying and awarding groundbreaking science with high impact in the reduction of premature cancer death and costs, please point out the provisions and recommend changes. To the extent possible, address comments to specific rule provisions. Such comments should be sent before 8:00 PM (time in Italy) on April 20, 2011 to: insiemecontroilcancro2@gmail.com, info@pec.vincenzovigna.it, v.vigna@smatteo.pv.it or to the address: Vanna Sereno, Viale Martiri, 6 – 12045 Fossano (Italy).

Deadline comments to the rules: April 20, 2011.

Final version of the rules (comments accepted/rejected will be justified and published) April 22, 2011

Deadline for project submission: May 30, 2011.

Project evaluations: Public event with web connection via EVO system, held at the Department of Physics,

University of Pavia (Italy), via U. Bassi, 6: Wednesday, June 8, 2011, from 2:00 p.m. to 7:00 p.m. (time in Italy).

If necessary the scrutiny of the projects will continue each day thereafter from 2 p.m. to 7 p.m. until complete.

Prize awarded: June 18, 2011, Room Ugo Foscolo, University of Pavia, at noon (local time)

Organizing committee: ws@insiemecontroilcancro.org www.mce-aifavin.it – www.unitedtoendcancer.org

Chairman: Dr. Vincenzo Vigna: info@pec.vincenzovigna.it