



# Brochure

# Invitational Call

# Congenital Heart Disease

A joint approach of the Dutch Heart Foundation and Hartekind Foundation to enhance the survival and quality of life for patients with congenital heart diseases



## Content

1	Background.....	2
2	Purpose and subject of this Grant.....	3
3	Principles and conditions .....	4
	3.1 Theme and ambitions (the consortium contributes to) .....	5
	3.2 Scientific program .....	6
	3.3 Strategy for achieving / reaching societal impact and valorization .....	6
	3.4 Proof of effective collaboration and management .....	7
	3.5 Initiators consortium ('kwartiermakers') .....	7
	3.6 Profile Research Leaders and Workpackage Leaders .....	8
	3.7 Important general aspects.....	8
	3.8 Budget/ duration.....	9
4	Submission of proposal .....	10
5	Time schedule .....	10
6	Review process.....	11
	6.1 First check by DHF and Hartekind Foundation.....	11
	6.2 Combined role of International Scientific Advisory Committee (ISAC) and Committee Societal Quality (CSQ).....	11
	6.3 Code of Conduct on Confidentiality and Conflicts of Interest .....	12
7	Committee Advice .....	12
8	After decision/ after granting .....	12
	Complaints procedure .....	12
	After granting .....	12
	Annex 1 Checklist for the evaluation .....	14
	Clear definition of and ambitions for the theme of the consortium.....	14
	Scientific quality .....	14
	Realistic trajectory for strategy of knowledge application.....	15



## 1 Background

### **Dutch Heart Foundation and Hartekind Foundation**

The Dutch Heart Foundation (DHF) and Hartekind Foundation unite forces to battle congenital heart diseases, the most common congenital disorder. The DHF is committed to prevention, earlier recognition and detection of cardiovascular diseases, while Hartekind Foundation focusses on increasing life expectancy and quality of life of children with heart disease. Our shared long term vision is a nationwide community around the theme of congenital heart disease. This ambition starts with creating a national Congenital heart disease consortium for the next 4-5 years. The DHF and Hartekind Foundation jointly offer a maximum of € 3.000.000 for this research consortium in the area of congenital heart diseases.

### **Facts & figure**

Congenital heart diseases (CHD) are the most common congenital disorders. At the moment, more than 25.000 children and 35.000 adults live with a congenital heart disease in the Netherlands. Unfortunately, many children and adults die at an early age as a consequence of a CHD. Both children and adults with CHD suffer problems like arrhythmia, heart failure, neurocognitive and motorical backlog and consequential damage of repetitive surgical procedures. The group of adults increases due to the obtained successes of medical science.

### **Children and adults**

The DHF is committed to prevent cardiovascular disease and recognize it at an early stage. Hartekind Foundation specifically targets CHD in children. Because of the fact that more children with CHD survive, it is important to pay attention to the quality of life from childhood to maturity and beyond.

### **Use of registries**

In the Netherlands a number of patient registries are available. Two of which are targeted to register patients with CHD. DHF and Hartekind Foundation are very pleased that the steering committees of KinCor and CONCOR intend to merge their registries, accommodated by the Netherlands Heart Registration. These databases are very valuable for research. Therefore, the research should make optimal use of these registries. Also the other registries e.g. EACTS CD, should be used if necessary.

### **From CVON to DCVA**

In 2011, the DHF (together with the Netherlands Federation of University Medical Centers (NFU), the Royal Netherlands Academy of Arts and Sciences (KNAW) and the Netherlands Organization for Health Research and Development (ZonMw) started the CVON ('CardioVasculair Onderzoek Nederland') initiative aimed at creating collaborations of the best researchers at a national level in the most promising research areas in the Netherlands. Consortia, funded according to this initiative, are committed to solve important healthcare problems and are multidisciplinary and translational in nature. The emphasis is on creating



long-term support for successful consortia that provide the research community involved to efficiently attract research funds from other sources.

Since 2018 the founders of the CVON program have expanded their collaboration with the participation of the Netherlands Heart Institute (NL-HI), the Netherlands Organization for Scientific Research (NWO), Health Holland, Harteraad (the Dutch association for people with cardiovascular diseases), the Dutch Network for Cardiovascular Research (WCN), the Netherlands Society of Cardiology (NVVC), the Dutch Heart Registration (NHR) and the 4TU.Federation. They have aligned their activities in the field of cardiovascular research to form the Dutch CardioVascular Alliance (DCVA). This alliance is committed to reduce the cardiovascular disease burden by 25% in 2030 by catalyzing the translation of excellent Dutch science into health improvement. The DCVA will execute both the DHF Research Agenda and the Dutch National Research Agenda by focusing on early detection of disease. This will reduce the number of chronic patients, the recurrence of problems and counter the growth of healthcare costs by detecting cardiovascular disease before irreversible damage occurs.

The DCVA builds on the CVON strategy by encouraging and enabling well performing consortia to realize durable national collaborations to accelerate research on the most urgent and promising research themes and to bring that research towards clinical practice. In this context, the DHF has committed to invest in a nationwide theme on congenital heart disease based on the good performance of the current DHF supported consortia BAV, COBRA and Concor-genes for which financial support will end in 2019 and 2020 respectively.

In the CVON programs and in the DCVA consortia the role of the International Scientific Advisory Committee (ISAC) is pivotal. This committee was – and is - key in the selection of research proposals and is involved in the monitoring of the progress of the granted consortia.

The DHF and the Hartekind Foundation agreed that the newly formed national CHD consortium will be part of the DCVA community. Therefore, the selection procedure and the conditions/guidelines of the DCVA will be followed. In addition, it is expected of the consortium to actively contribute to the aims of the DCVA.

## **2 Purpose and subject of this Grant**

To build on the DCVA strategy, the DHF stimulates national thematic collaboration in the cardiovascular field and accelerates valorization by stimulating well performing national consortia to bring their research closer to clinical practice.

On the theme congenital heart diseases, the DHF is very pleased to join forces with Hartekind Foundation. This cooperation resulted in the current DCVA Invitational Call (called *grant* in the rest of this brochure) as outlined in this document.



The ambition of the DHF and Hartekind Foundation is to facilitate a research consortium, that contributes to the increase in survival rate and to improve the quality of life for children and adults with CHD. Therefore, the forces of both organizations are united in this grant. This grant should be seen as a starting point for organizing a broad network around the theme of congenital heart diseases. Elements of well performing consortia can be recognized as a starting point for the formation of a national consortium.

The purpose is to bring research and patient care in the CHD field to a higher (international) level. The DHF and Hartekind Foundation encourage the research leaders of the consortium to engage more researchers and parties into this consortium and develop a plan to attract additional funds to be able to further expand the research program.

The research agenda of the DHF and Hartekind Foundation are leading in setting up the purpose and development of the research proposal.

The research themes of the DHF which are relevant to this grant on congenital heart disease are:

- Earlier recognition of cardiovascular diseases
- A better treatment of heart failure and arrhythmia
- Cardiovascular disease in women

From the research agenda of the Hartekind Foundation the leading themes are:

- Arrhythmia and heart failure
- To grow up with a congenital heart disease
- The future of an operated heart

Information of the complete research agenda of Hartekind Foundation can be found on [www.hartekind.nl](http://www.hartekind.nl).

**The purpose** of the grant is to create a nationwide interdisciplinary research collaboration on congenital heart disease. Successful consortia join forces, continue their research for another 4-5 years and develop an alliance of researchers from academia, companies and other potential stakeholders around well-defined themes with high (societal/patient) impact. Promising parts of BAV, COBRA and CONCOR-genes consortia will be taken to the next step on the translational research pathway.

### 3 Principles and conditions

The following principles are important in the review process:

- There should be a clear definition of the theme the consortium contributes to, including well-defined ambitions for the short and longer term. The consortium contributes to the research agenda of DHF and Hartekind Foundation.
- Scientific Excellence: the research is innovative and international competitive.

- The scientific program for the grant is partly based on the achievements of existing well performing scientific collaborations (at least BAV, COBRA and Concor-genes) in the past period and the objectives for the next period.
- Realistic strategy including clear budget allocation for technology transfer, other valorization activities and (future) implementation. Also, collaboration with users, private partners and patient involvement will be reviewed.
- Proof of effective nationwide collaboration with added value within the consortium and other relevant consortia and partners, including the approach to attract additional funding.
- Addressing important general aspects: boys-girls, male-female differences, open access/open science and development of talent.
- The research leaders and principal investigators should represent the entire research area (see section 3.5). This means that the following fields of expertise should be represented:
  - Pediatric cardiology;
  - Congenital cardiology;
  - Pediatric cardiac surgery;
  - Fundamental research.
- The research leaders are not associated to the same University Medical Center.
- The combined registry KinCor/CONCOR is actively used by the consortium.
- Budget is allocated for the transition and maintenance of the database. The execution of the integration of the registrations is not part of this research proposal.

### Conditions

- All academic pediatric and congenital cardiology centers are involved.
- The research of the consortium should include CHD in both children and adults.
- Duration of the grant is 4 - 5 years.

The next paragraphs address these main points. In annex 1, the specific questions that will act as a checklist for the evaluation of the application are indicated.

### 3.1 Theme and ambitions (the consortium contributes to)

In order to present a clear view of how the results of the research proposal will contribute to enhance the survival and/or quality of life of patients with congenital heart diseases, the consortium has to address the scope, size and impact of the health care problem the consortium will focus on.

The ambition of the DHF and Hartekind Foundation is that cardiovascular disease, such as arrhythmia and heart failure, are recognized at an early stage. This ambition should be dealt with by the consortium.

This means that a short-term ambition (5 years) and a long-term ambition (2030-2035) should be formulated with milestones (short-term), including possible necessary non-scientific needs/actions. This in collaboration with other (CVON) consortia that work on the same healthcare problem and with stakeholders/(end-)users from for example the Dutch patient



organization on Congenital Heart Diseases (PAH) and Harteraad. The consortium has to define which parts of the formulated ambitions/milestones are the subject of the research proposal for the next five years and which parts are beyond the scope of the current timeframe or require additional funding that will be sought elsewhere by the consortium.

### **3.2 Scientific program**

The proposal should be internationally competitive, have a scientific impact and should reduce the burden of congenital heart diseases. The entire translational research pathway must be clear, but the entire pathway does not have to be executed: either fundamental - clinical or fundamental - epidemiological. This still means that the basic and clinical research parts have to be strong and synergistic. The proposed scientific program and the constitution of the consortium should be innovative and the aims and plan of work have to be feasible. Describe also how the data of at least KinCor and CONCOR registries will be used.

### **3.3 Strategy for achieving / reaching societal impact and valorization**

Based on successful findings, the consortium should indicate in this application how the next step(s) on the translational research pathway will be taken. This should result in the next Market Readiness Level towards clinical application. The envisioned end product(s) and the intended target group(s) for the product(s) should be indicated as well as the impact of the product(s) on care. What will be developed for the benefit of children and/or adults with congenital heart diseases?

The several lines of development should be illustrated in a flowchart for which a format is attached. An assessment whether this strategy for technology transfer or valorization is realistic and time- and cost-effective, will be part of the evaluation of the application. The consortium will allocate a dedicated budget for valorization activities. This includes amongst others the execution of a feasibility study, the development of a business plan, or costs necessary to secure intellectual property, that are not covered by the universities Knowledge Transfer Office or other services or funds.

In addition, the consortium is obliged to involve an HTA-expert to indicate if its strategy is realistic. The outcome of the consultation/analyses with this HTA-expert are part of the proposal as well as how HTA expertise will be continued during the project.

#### *Matching grant*

The DHF promotes the application of knowledge and stimulates the involvement of appropriate stakeholders in the consortium by making funds available to match investments from private parties up to € 500.000. With this instrument, the DHF aims to maximize the chance for appropriate and fast implementation of the research results in (clinical) care for cardiovascular patients.

The request should be done preferable for the total amount of 0,5 million euro. If this is not possible, please contact us, so we can discuss if a part of the amount can be requested. The request can be part of the current proposal and requested budget, but it can also be submitted during the term of the proposed project. If a proposal for this additional funding is



submitted in a later stage, the proposal will also be evaluated by the ISAC-CVON/Committee Societal Quality.

Please contact at all times DHF if and when this additional application will be submitted. The DHF will give you the specific requirements of this matching funding. Secondly, timely informing will allow the DHF to additionally budget the requested amount in the requested year or in light of budget constraints in the consecutive year.

#### *User committee*

Additionally, a user committee has to be installed, which has the task to monitor the use of the acquired knowledge (see the [website](#) of the DHF). The DHF and Hartekind Foundation strongly encourage to include industry/third parties, patients and other (end) users in the consortium, especially patient involvement has to be addressed. For patient participation we expect that you contact the patient organization on Congenital Heart Diseases (PAH) and Harteraad.

### **3.4 Proof of effective collaboration and management**

The sustainability of the research theme is important and should be extended beyond the duration of the present program. The further development of the research theme within the Netherlands should continue during this phase. The consortium has to show the added value of this collaboration by indicating which collaborative results were/will be achieved: (new) research angles/lines, mutual publications, mutual grant applications/ funding/matching (adding to the theme), mutual meetings, conferences, etc. How will the consortium build a nationwide (and international) community including communication plan with stakeholders. Also, the consortium has to address which steps have already been taken in the existing consortia to implement their knowledge into e.g. products, guidelines, commercial spin-offs etc.

For this next phase, the DHF and Hartekind Foundation encourage the consortium to analyze /define the composition and the specific features of the consortium and the involved research - and WP-leaders in order to optimize the quality of the consortium and to make it suitable in view of the developments within the theme. For example, are the research leaders still the most suitable leaders for the next phase? How can we foster talent from within or outside the former consortia to become a WP leader or research leader? Do we need additional expertise or a partnership with private partners do we need to be (more) successful in our next phase?

### **3.5 Initiators consortium ('kwartiermakers')**

Aligning with the research leaders of BAV and COBRA an exploration for the national consortium is performed by prof. Gerrit van der Wal with the goal to appoint initiators from the concerned fields of expertise who can start with building the consortium.

The initiators ('kwartiermakers') are:

Prof. Jeroen Bakkers (geneticist, Hubrecht Laboratory UMCU)

Prof. Mark Hazekamp (pediatric heart surgeon, LUMC and AUMC)





Prof. Wim Helbing (pediatric cardiologist, ErasmusMC and RadboudUMC)

It is possible that the initiators will be the research leaders of the final proposal, but depending on elaboration of the research program, this is not necessarily the case. The main tasks of the initiators are:

- To connect and foster cooperation
- To initiate the elaboration of a research proposal and build a consortium
- To strengthen confidence within the research field
- To be contact person both for the research field as for Stichting Hartekind and DHF

### **3.6 Profile Research Leaders and Workpackage Leaders**

The research leaders should have inspiring and binding capacities and oversee the whole field of congenital heart disease. The quality of the consortium including the research leaders will be subjected to the assessment of the ISAC. The formal criteria for research leaders and principal investigators are listed below.

#### **Criteria research leader**

- must work in a paid position at a knowledge institute throughout the entire duration of the research project. A letter must be included containing proof of a paid position for the entire duration of the research project;
- has shown leadership and is capable of leading a project of this size;
- has an excellent track record and an evident international reputation and has the potential to successfully face European competition (ERC advanced/consolidator);
- will deliver a sustainable contribution to the research area, till a minimum of three years after ending this grant;
- has the ability to attract additional funding.

#### **Criteria work package leader**

- is leading part of the project (work package);
- must be employed throughout the entire duration of the research project. If not, specific details must be supplied of what measures will be taken to deal with this;
- must be capable of making/guaranteeing agreements on behalf of the institute where she/he is employed (probably in consultation with the head of the department);
- has a proven track record and reputation (at least eligible for a Vidi grant).

The team of research leaders and work package leaders should represent the whole research area and should reflect a good balance on multiple aspects including male and female.

Research leaders are not allowed to be associated to the University Medical Center.

### **3.7 Important general aspects**

The proposal will also be reviewed on the following general aspects. These items have to be reflected in the whole proposal.



### *Differences between men and women*

Cardiovascular diseases in women is the second topic on the research agenda of the DHF. All proposals must contribute to a better understanding of and address differences between boys and girls, men and women in the prevention, diagnosis and treatment of cardiovascular diseases.

Research proposals on new technologies should identify how these technologies can potentially be applied for cardiovascular diseases both in men and women. See the website of [Stanford university](#) for tools that can be used to integrate sex and gender aspects in research applications.

### *Open access/ open science*

The DHF and Hartekind Foundation have the ambition that all publications that are the result of research that is funded by the DHF and Hartekind Foundation is published in an open access journal. Find out more on our Open Access in publications policy (see also the [website](#) of the Heart Foundation (in Dutch)).

The proposal should contain a detailed description on how the acquired data will be handled (data stewardship). Therefore, the consortium is strongly advised to involve a data-expert in their consortium and is obliged to allocate resources for data-management (KinCor and CONCOR) into the budget. After having been awarded the grant, the consortium will be asked to hand in a Data Management Plan (DMP; format will be provided by the Durrer Center). This DMP is considered to be a dynamic document and will also be used to monitor progress on data management.

### *Development of talent*

Stimulation/ development of talent within the consortium is an aspect that has to be addressed. To stimulate the appointment of postdocs within the consortia, the ratio of requested postdocs vs requested PhD students is at least 1:2. The success of the first phase talent program should be demonstrated by providing an overview of PhD students and postdocs that obtained prestigious (postdoc) positions internationally or were offered prominent research positions in academia or industry.

The consortium has to take into account that next to a consortium specific part, the consortium is also required to participate in a collaborative program with the other CVON consortia (e.g. network meetings as organized by Young@Heart and NL-HI congress). The aims of the talent program and which criteria are used to assess talents should be made clear both in children and adult congenital cardiology.

### **3.8 Budget/ duration**

The maximal available funding will be 3 million euro of which 10% should be dedicated to the talent program. The consortium contributes and participates to the activities organized in collaboration with the other CVON/DCVA consortia and allocates at least 25 % of the talent program budget for their contribution.

A minimum of € 500.000 (made available by Hartekind Foundation) should be dedicated to research or activities that contribute to the fight against congenital heart diseases during



childhood. Please include separate budget lines for the research parts in children and in adults where possible.

Make sure budget is allocated to all activities described in the proposal. When no budget is allocated, please motivate in the proposal how the consortium will acquire additional funding. The duration of this granting period is a minimum of 4 to a maximum of 5 years.

#### **4 Submission of proposal**

The deadline of submission is **25 June 2019 14:00 h**

We explicitly advise you to carefully read the agreements and discuss them with the consortium partners before submitting your proposal. Upon submitting the proposal all consortium partners/institutes agree with the agreements.

On submission we expect you to deliver the following documents:

1. Application form
2. Budget sheet
3. Flowchart technology transfer trajectory
4. Intra-consortium agreement

The start of the project will be within 6 months after approval.

#### **5 Time schedule**





**September 2019**

Compilation of the reviews and CSQ sent to consortium



**October 2019**

Meeting, including interview with ISAC and CSQ members



**November 2019**

Decision by board of DHF

## **6 Review process**

### **6.1 First check by DHF and Hartekind Foundation**

DHF and Hartekind Foundation will first check:

- if the application is in line with the purpose of the call;
- if the consortium has correctly addressed all the important elements in the application;
- if all conditions of the DHF and Hartekind are included in the application;
- if the application is eligible in terms of the format used.

If the application is not eligible but can be amended on short notice the DHF and Hartekind Foundation will invite the applicants to amend the application before the review process will be started.

### **6.2 Combined role of International Scientific Advisory Committee (ISAC) and Committee Societal Quality (CSQ)**

After the first check is done and if the application is eligible, members of the committee, consisting of members of the International Scientific Advisory Committee (ISAC), a member appointed by Hartekind Foundation and members of the Committee Societal Quality (CSQ), will evaluate the application on the main criteria (paragraph 3). The criteria are specified in annex one. When necessary other external reviewers will evaluate the proposal on certain specific topics.

The ISAC members will review the application from a more scientific point of view.

The CSQ members will review the application from a more societal quality point of view.

The applicants will receive a compilation of the reviews of the external reviewers, including possible remarks of CSQ in order to prepare for an interview with the ISAC /CSQ. During this



meeting the applicants are requested to present their application, information about this meeting will be send when the application is eligible.

### **6.3 Code of Conduct on Confidentiality and Conflicts of Interest**

The DHF and Hartekind Foundation invite active researchers from knowledge institutes and specialists from other knowledge intensive organizations to participate in assessment procedures. These people are themselves involved in ongoing or new research and often belong to large organizational associations and research networks. Therefore, any conflict of interests, or anything that remotely resembles this, must be avoided in the assessment of research proposals. Additionally, the confidential treatment of all information must be guaranteed.

To ensure a fair assessment and transparency for researchers, the DHF and Hartekind Foundation use a Code of Conduct on Confidentiality and Conflicts of Interest. This code stresses the necessity of confidentiality, identifies possible forms of conflicts of interest and indicates the steps to be taken to avoid conflicts of interest. Parties subject to the code of conduct are: referees, jury members, committee members, members of decision-making bodies, DHF officers and Hartekind Foundation officers. The full text of the code of conduct on conflicts of interest is available at:

<https://www.hartstichting.nl/wetenschappers/subsidiewijzer> (in Dutch).

## **7 Committee Advice**

Only if the consortium scores very good/ excellent for the proposal on all the criteria mentioned above, the consortium will be considered for a grant and the ISAC/CSQ is requested to formulate an advice of: must be funded.

If the scores are lower and/or there are serious doubts about (parts of) the proposal the ISAC/CSQ is requested to formulate the advice of: not to be funded.

If an application can be re-written for 'minor' issues within two months the advice 'not to be funded, unless' can be given. It has to be very clear what should be improved within the program and/or consortium.

## **8 After decision/ after granting**

### **Complaints procedure**

A research leader can submit a complaint about the procedure by completing a form that is sent to the Complaints Committee of DHF. It is not possible to appeal against the outcome of the procedure. The form can be found on the DHF website. Complaints should be submitted within four weeks after receiving the notice from the CEO of DHF.

### **After granting**

After granting, the consortium partners have to sign two legal documents:



1. A consortium agreement between the DHF, Hartekind Foundation and the consortium partners in which the legal and financial conditions are stated. This agreement is non-negotiable.
2. An intra consortium agreement (ICA) (see appendix) containing a.o. paragraphs on IP, organizational and publication arrangements. The ICA becomes part of the consortium agreement. The ICA has to be submitted with the research proposal.

The agreement and ICA have to be signed and returned to the DHF office within 6 months after receipt of the grant approval letter. The project must start when the agreements are signed and within 6 months after approval.



## **Annex 1 Checklist for the evaluation**

Below the specific questions that will act as a checklist for external reviewers and the ISAC/CSQ to evaluate the application are mentioned. As stated above the following criteria will be used for the grant for the congenital heart disease consortium:

- Clear definition of the theme the consortium contributes to, including well-defined ambitions for the short and longer term, including male-female differences.
- Scientific Excellence including boys-girls, male-female differences.
- Realistic strategy for technology transfer or valorization and (future) implementation. Also, collaboration with users, private partners and patient involvement will be reviewed.
- Proof of effective collaboration with added value within the consortium and other relevant consortia and partners. Including open access/open science and development of talent.
- Specific criteria for this consortium as described in this brochure.

All criteria are regarded equally important and will have equal impact on the final verdict.

### **Clear definition of and ambitions for the theme of the consortium**

#### *Description of theme*

Are the long-term ambitions and milestones, visionary and realistic?

#### *Match of science-healthcare problem*

Do the (main) results of the former scientific program contribute to the described healthcare problem? Are the results differentiated by sex?

To what extent is the described healthcare problem relevant for men and women? Is the proposed scientific program contributing to solving the healthcare problem as described in the proposal? How and to what extent does the research contribute to solving the specified healthcare problem in the short- and/or long-term for boys and men as well as for girls and women?

#### *Sustainability of theme*

Is the long-term impact and sustainability of the cardiovascular research theme sufficiently described as well as the future contribution of the research leaders and PIs in the development of the theme? Consortium prospects and contribution to the specific research field have to extend beyond the duration of the scientific program with (at least) 5 years.

### **Scientific quality**

#### *The achieved main results*

Are the achieved main results a) internationally competitive (and do they have a scientific significant impact) and b) (potentially) relevant for healthcare/ patients?

Are the main results linked to the milestones/ deliverables? Is there a convincing rationale for choosing these results as the main results?



### *Synergy preclinical- clinical*

Are both basic and clinical research parts strong and synergistic?

### *Internationally competitive*

Is the proposed scientific program and the constitution of the consortium internationally competitive?

### *Feasibility of aims*

Are the set aims, as laid out in the proposal, feasible in the manner suggested? Are (potential) differences between men and women addressed and linked to (the described literature on) the healthcare problem?

### *Plan of work*

Opinion about plan/ involved and required disciplines/ realistic budget/ timeframe. Are (potential) differences between men and women addressed and linked to the described literature and aims? Will the generated results and data be managed according to the FAIR principles?

### *Infrastructure*

Will the investments in this research proposal strengthen the infrastructure to such an extent that it will support more than just the research proposal?

### *Quality of research leaders and workpackage leaders in international perspective*

The research leaders have to show strong and inspiring leadership (as mentioned before). The ISAC judges the leadership of the research leaders during the presentation of the program and the following discussion.

- Is there sufficient confidence that the research leaders and the workpackage leaders will complete the research proposal satisfactorily?
- Is there a good balance and integration in the collaboration between the research leaders and the workpackage leaders?

### *Development of talent*

Is the talent program inspiring and effective?

## **Realistic trajectory for strategy of knowledge application**

### *Plan of translation: next step realistic*

Has attention been paid to translation of the findings, and are the described plans to do so in the future clear and sufficient? Is the next step clearly described? Is the envisaged end product, process etc. realistic? How and to what extent are the differences between men and women considered?

The entire translation axis must be clearly described, but the present proposal should not cover the entire axis, but should enable translation to at least one step higher technology readiness.





*Impact of the envisaged end product*

Does the consortium make clear that the envisaged end product, process will have an impact on healthcare? Is the impact the consortium hopes to generate realistic? Is the strategy for valorization/knowledge transfer time- and cost-effective? Is HTA expertise during the term of the proposed project guaranteed?

*Knowledge transfer*

Does the consortium make clear how they plan to make translatable findings available for clinical research and ultimately application?

Does the proposal clearly describe how and to what extent the researchers will actively engage in disseminate knowledge, and not only to immediate colleagues, but also to scientists/(end) users who could take the next step in the research or its implementation, or to professionals (in the broad sense) who could start working with the research results (Next Step)? Are all the appropriate stakeholders involved?

To what extent is the specific knowledge, experience and expertise of professionals and patients incorporated?