PPP programme
Human measurement models

Call for PPP applications

Towards better human measurement models

In collaboration with:

and

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1 Introduction

1.1 Background of the PPP programme Human measurement models

Millions of people have to deal every day with the consequences of serious and sometimes life-threatening diseases. Health foundations are committed to achieving better and healthier lives for these people. Scientific research, to develop better treatments for example, plays a crucial role in this. However, the possibilities for carrying out experimental research in human subjects are limited. To gather the necessary knowledge at the various biological levels and to make predictions and understand causes, scientists often use model systems. A substantial proportion of current health research makes use of animal models. There are various reasons for this: for example, the use of animal models may be required by laws and regulations, the researcher may regard it as the best option for the research, or there may be few or no alternatives available yet.

Research models based on human material such as cells and tissues, or computer models based on data collected in humans, are expected to approximate more closely to humans than animal models do. The more closely a research model approximates to humans, the sooner the corresponding research results can be applied in practice. In addition, the (further) development of human models provides scientists with a wider range of opportunities to carry out relevant, high-quality research, without extensive use of laboratory animals.

New scientific insights and innovative techniques facilitate the (further) development of new human measurement models. Targeted funding is being made available for this under the Public-Private Partnerships (PPP) Programme “Human measurement models”. This PPP programme has been set up by the Association of Dutch Health Foundations (SGF) and the Top Sector Life Sciences & Health (LSH; Health~Holland) in collaboration with the Netherlands Organisation for Health Research and Development (ZonMw) and the NWO Domain Applied and Engineering Sciences (AES). This collaboration will lead to a long-term programme in the area of Human measurement models which will consist of two calls for applications. The current call (Call I) is being issued by SGF with funding by means of a PPP Allowance via the Top Sector Life Sciences & Health. The parties involved also intend to launch a joint second call under this programme in 2020.

The programme objectives are in line with the ambitions of the national “Transition Programme for Innovation without the use of animals” (TPI) coordinated by the Dutch Ministry of Agriculture, Nature and Food Quality (LNV). Partners in this transition include SGF, the Top Sector Life Sciences & Health, the Dutch Society for the Replacement of Animal Testing (*Stichting Proefdiervrij*) and ZonMw, together with various parties from government and society, industry and science. The TPI’s ambition is to make the Netherlands a forerunner in the international transition to animal-free innovation. The TPI is led by the Ministry of Agriculture, Nature and Food Quality in partnership with the Ministry of Education, Culture and Science, the Ministry of Health, Welfare and Sport, the Ministry of Economic Affairs and Climate Policy, and the Ministry of Infrastructure and Water Management. Further information on the “Transition Programme for Innovation without the use of animals” is available on its website.

1.2 Objectives of the PPP programme Human measurement models

The broad objective of the PPP programme Human measurement models is to facilitate the development of new, more efficient human measurement models for health research to ensure that research results can be applied better and faster in humans. This will make science less dependent on the use of animal models. The (further) development of human models will contribute to answering research questions that otherwise could not be answered or could be answered only by using animal models. These models may aim either at diagnosing and treating diseases or at disease prevention. The definition of “measurement model” includes both human *in vitro* and *in/ex vivo* models as well as *in silico* models.

Programme objectives:

- Development of human measurement models with good predictability for humans;
- Development of human measurement models for disease diagnosis, treatment and prevention;
- Development of combined models that, together, provide answers to larger issues (e.g. working towards replacement of an entire organ or organism);
- Application of valorised models and/or methods by stakeholders;
- Availability of (standardised) models and methods on a large scale;
- Impact in terms of reducing animal experimental research or preferably eliminating the use of animals in research.

2 Call I "Towards better human measurement models"

2.1 Objectives of Call I

The primary objective of the first call under this programme, entitled "Towards better human measurement models", is to develop innovative human-based measurement models (human material/tissue/cell lines/data) for disease-specific or multiple-disease research. Health research with health benefits for different patient groups is an advantage in this regard.

To facilitate the (further) development of human measurement models in the various research phases, this call has a broad scope, ranging from fundamental to industrial and experimental research (for an explanation, see the definitions of types of research in Appendix A, page 13). This programme aims to fund research of at least very good quality and relevance in different research phases and of different Technology Readiness Levels (TRL[1]) (see Appendix B, page 14).

The application should bring further an existing collaboration or create a new collaboration that brings innovative human measurement models closer to a clinical application. Applications are encouraged from multidisciplinary collaborations in combination with engineers.

2.2 Scope of Call I

The scope of the current call is:

- Projects aimed at the (further) development of models for research into health and disease;
- Proposed projects that (in the long term) demonstrably reduce the use of animals or eliminate the need for research involving animal experiments;
- Projects consist of a collaboration between at least one research institute and one private party with a for-profit status (see Section 3.1 for an explanation);
- The proposed project is a multidisciplinary collaboration;
- Projects that combine different models are preferred;
- Projects that achieve an impact for multiple patient groups are preferred.

Applications focusing on the topics listed below fall outside the scope of Call I:

- Toxicity and/or the improvement of toxicity studies;
- Prevention of diseases;
- Mainly aimed at improving animal welfare in existing measurement models;
- Improvement of a technique or application that does not require animal testing now or in the future, e.g. studies that are already taking place in humans;
- Improvement of surgical techniques, e.g. CT and MRI imaging.

[1] Technology Readiness Levels (TRLs) are used to indicate phases of research and innovation. Technology Readiness Levels indicate the degree of development of a technology, with TRL 1 standing for technology at the start of development and TRL 9 for technology that is technically and commercially ready.

Funding under this PPP programme aims to contribute to the development of better methods and models that have high predictability for humans and do not require animal studies. In addition, it is essential that these models and methods are applied by stakeholders. For many stakeholders (industry, researchers, authorities), the animal model is currently the gold standard and is in some cases legally required. Despite the shift towards models which do not involve animals, the large-scale application of such models is lagging behind. This is partly due to a lack of further development of human-based measurement. The aim of the research programmes to be launched here is to encourage the (further) development of such models and methods.

Together with its members and partners in the TPI, SGF will strive to ensure that Human measurement models are eventually developed sufficiently to be applied on a large scale and therefore replace the use of laboratory animals. SGF views this first call as a prelude and a transitional phase in which specific projects will be permitted to demonstrate the validity of an innovative model using the current (animal) standard. A condition for this is that the mechanisms and effects studied in the animal model are shown to be comparable to those in humans.
Where animal experiments form part of the proposed research then the ARRIVE guidelines must be adhered to.
Where an application concerns in vitro models, the use of Foetal Calf Serum (FCS)-free media is preferred.

2.3 Available budget for Call I

The SGF and the Top Sector Life Sciences & Health are making € 3.2 million in PPP Allowances available for new PPP projects under this call. This call is subject to the Health~Holland PPP conditions, including co-funding requirements.
The Dutch Society for the Replacement of Animal Testing is providing a contribution of € 75,000 as co-funding at project level, subject to additional conditions (see Appendix C, page 15).

3 Guidelines for applicants

3.1 Who can apply?

The project should be a collaboration between at least one Dutch research organisation[2] and at least one relevant private party with a for-profit status. The main applicant must be affiliated to a Dutch research institute and will be the point of contact for SGF and Health~Holland throughout the procedure. The other parties in the collaboration are co-applicants and, together, the partners form the consortium.

A person may be involved in a maximum of two PPP applications, in one of them as a main applicant. Exceptions to this rule are project members with a supporting role, such as statisticians, ethicists, laboratory staff, heads of GMP facilities and similar roles.

There must be effective collaboration[3] between the consortium partners. All consortium partners make a substantive contribution to the project and incur costs towards its implementation. Besides a possible cash contribution, all consortium partners should make an in-kind contribution.

[2] Examples of research organisations are universities, university medical centres, universities of applied sciences, TNO, and KNAW institutes. Definition of “research organisation” according to the Framework for state aid for research and development and innovation: “research organisation” means an entity (such as universities or research institutes, technology transfer agencies, innovation intermediaries, research-oriented physical or virtual collaborative entities), irrespective of its legal status (organised under public or private law) or way of financing, whose primary goal is to independently conduct fundamental research, industrial research or experimental development or to widely disseminate the results of such activities by way of teaching, publication or knowledge transfer. Where such entity also pursues economic activities, the financing, the costs and the revenues of those economic activities must be accounted for separately. Undertakings that can exert a decisive influence upon such an entity, for example in the quality of shareholders or members, may not enjoy a preferential access to the research capacity of such entity or to the results generated by it.

[3] Definition of “effective collaboration” according to the Framework for state aid for research and development and innovation: “effective collaboration” means collaboration between at least two independent parties to exchange knowledge or technology, or to achieve a common objective based on the division of labour where the parties jointly define the scope of the collaborative project, contribute to its implementation and share its risks, as well as its results. One or several parties may bear the full costs

In addition, public organisations (e.g. health foundations, the Dutch Society for the Replacement of Animal Testing, equity funds and hospitals) and regulatory authorities may be involved in the research proposal as private parties and make a financial contribution to the project. An explanation of the co-funding options available to these parties is given in Section 3.2. If these parties only make a financial contribution and do not themselves incur any costs in the project, they are not considered as consortium partners and are not required to co-sign the consortium agreement. Upon submission of the application, a letter of commitment will be requested from all parties making an in-kind and/or cash contribution.

All consortium partners should sign a consortium agreement before the start of the project. The model consortium agreement provided by Health~Holland is available for download from the Health~Holland website. Discussing this agreement with all partners during the writing of the application may help to ensure that the agreement can be signed promptly by all at a later stage.

3.2 PPP Allowance that can be requested

The minimum PPP Allowance that can be requested for a research proposal is € 500,000, and the maximum is € 1 million.
Of the total eligible project costs, a maximum of 75% of the PPP Allowance may be used for fundamental research, a maximum of 50% for industrial research and a maximum of 25% for experimental development. These maximum proportions are stated again in Table 1.

Additionally, this table shows the minimum percentage that a research organisation must contribute and the minimum percentage that a for-profit enterprise must contribute (in cash and/or in kind). In the case of industrial research and experimental development, the columns do not add up to 100% but to 90% and 80%, respectively. In these cases, the parties are free to decide how to obtain the remainder of the project funding required.

Summary of conditions and points to note for PPP Allowances:

- The conditions for a PPP project are described in the Health~Holland "TKI LSH Match Regulation for public-private partnerships in 2019". We recommend that you start by reading these conditions.
- The project proposal must be in line with the challenges as set out in the "Knowledge and Innovation Agenda 2018–2021" (KIA); see Health~Holland;
- Private parties such as health foundations and the Dutch Society for the Replacement of Animal Testing are not "for-profit enterprises". Co-funding by these parties does not count towards the compulsory company contribution based on which the PPP Allowance can be granted;
- For an explanation of the funding model by type of research, see Table 1;
- For definitions of the types of research, see Appendix A, page 13;
- Appendix D on page 16 provides some calculated examples for different budgets;
- The definitions of small and medium-sized enterprises (SME definitions) are explained in brief in Appendix E on page 17;
- If you have any questions about the PPP Allowance, definitions or conditions, please contact PPP Programme Manager Laila El Aziz directly and *at an early stage* via Aziz@health-holland.com or +31 70 205 1403.

Table 1: Funding by type of research

Type of research	**Fundamental research**	**Industrial research**	**Experimental development**
Maximum PPP Allowance to be deployed	75%	50%	25%
Research organisation(s)	min. 10%	min. 10%	min. 10%
For-profit enterprise(s)	min. 15%	min. 30%	min. 45%
- Large enterprise	- min. 2/3 in cash*	- min. 2/3 in cash*	- min. 2/3 in cash*
- SME*	- fully in kind	- fully in kind	- fully in kind

* At least 2/3 of the required minimum contribution from a large enterprise must consist of a cash contribution. This minimum contribution depends on the type of research and is based on their total project contribution.
** May be fully in kind. However, a cash contribution is encouraged.

3.3 Submission procedure

A registration procedure will be used for Call I. A research idea must be submitted by e-mail to humanemeetmodellen@gezondheidsfondsen.nl no later than September 5 2019.
The following information must be included in this e-mail:

- Name and email address of main applicant
- A description of the project idea in 200 words (in English)
- Names of potential cooperation partners

A full application, using the application form, should be submitted by 5 November 2019 (14:00 CE(S)T). The intervening period serves as an opportunity to develop the research proposal in more detail and, if necessary, to set up a research consortium. For the purpose of setting up research consortia, a networking meeting will be organised on September 16. This meeting will also be attended by health foundations, the Dutch Society for the Replacement of Animal Testing and other public organisations. Contact details of potential co-funders, including the members of SGF and the Dutch Society for the Replacement of Animal Testing, are attached to this call as Appendix F, p. 18.

3.4 Networking meeting

The networking meeting on September 16 will provide an opportunity for networking, finding new collaborative partners and obtaining information about the programme. Registration for the networking meeting is compulsory if you are a main applicant wishing to submit a full project application in November. If you are unable to attend the meeting, please send someone in your place.

4 Conditions

PPP applications are subject to the following requirements:

1. The project contributes to the objectives of the PPP programme Human measurement models;
2. (End) users are involved in the project;
3. Optimal use is made of existing knowledge and data;
4. Open access and open data principles are followed;
5. A data management plan is drawn up;
6. Diversity (age, ethnicity, sex and gender) is taken into account.

Explanation of the conditions

1. Contribution to the objective of the PPP programme Human measurement models: Describe clearly and explicitly how your research project contributes to the objectives of this call. The application includes an action plan consisting of a detailed step-by-step plan with a clear division of tasks, milestones and deliverables. There is also a clear and effective plan for the dissemination and implementation of project results during and after the project. The expected impact on animal use is demonstrated by a detailed justification describing the state of current practice, the intended application and the expected improvement of research as a result of the innovation to be developed. The quantification of the results in this area will be taken into account in the assessment of the elaborated funding application.

2. Involvement of users: The developed model must be in line with the expectations, wishes and situation of the (end) user (researchers, companies, healthcare providers, patients). User involvement is therefore essential, both while writing the application (co-design) and during implementation of the project (co-creation). At project level, users can help in fine-tuning the research question, gaining a clear picture of the societal and economic relevance, implementing the project, and valorising the results. In all research projects, a user committee must be set up in which, in addition to the consortium partners, other future users may also participate. Sometimes it may also be advisable to intentionally include non-users in the committee. The valorisation and capitalisation of the results should also be taken into account.

3. Optimal use of existing knowledge and data: It is important to show in your application that you are making good use of knowledge that is already available (nationally and internationally). The health foundations encourage optimal use of data. In your funding application, describe the options for using existing measurement models, including data files, and substantiate the need for any new data collection.

If setting up a new data collection, please indicate the rules for its accessibility after the end of the project.

4. Open access and open data: health foundations work hard to bring research results to the patient as quickly as possible. Open science contributes to this. This is a broad movement to make research results, articles and scientific developments freely accessible.
All articles resulting from the research should be accessible to all, free of charge. Research data must be easy to reuse. To promote this, we ask researchers to do the following:

- Research registration: researchers should enter their project in a register before starting the research;
- Sharing data: researchers are obliged – where possible – to make their research data suitable for reuse. In this respect we use the international FAIR principles to ensure that research data are findable, accessible, interoperable and reusable.

5. Data management: Within six months after the start of the project, researchers should draw up a plan for the storage, accessibility and potential for sharing and reusing the research data. This guarantees the quality and security of the data. The decision to reuse existing data or set up a new data collection should be substantiated.

6. Diversity: Good-quality research takes into account possible differences between people, such as in age, ethnicity, sex and gender. Attention to gender differences will be included in the assessment of your research proposal. If gender differences cannot be taken into account in your study, we will ask you to provide a motivation. For further information, see “Methods of Sex and Gender Analysis” from the Gendered Innovations project.

5 Assessment criteria

The assessment committee will assess the relevance and quality of all proposals against the criteria set out below.

Relevance criteria

1. To what extent does the project contribute to the objectives of the PPP programme Human measurement Models?
2. To what extent does the project contribute to the reduction and/or elimination of animal models?
3. Is the model to be developed applicable to multiple conditions and relevant to a broad group of patients?
4. Is sufficient support provided that the developed human measurement model is better and/or more efficient than current best practices and other innovations under development?
5. To what extent does the innovation differ substantially from what is already used in current practices?
6. Will relevant knowledge users (the intended user committee) be sufficiently involved in preparing the funding application and during implementation of the research project?
7. Are all relevant stakeholders included in the user committee?
8. In which phase of the innovation chain (TRL level) will impact be achieved?
9. Will it be possible to apply the results on a larger scale within five to ten years?
10. If applicable, is consultation with relevant regulatory authorities ensured? Where applicable, the coordination with relevant regulatory authorities, both before and during the research project, is included in the project proposal. The aim of this coordination is to increase the feasibility of the innovation’s practical application at national or international level.

Quality criteria

Project proposals will be assessed on:

1. Applicability of the innovation, clarity and scientific quality;
    - The applicability of the proposed research;
    - The clarity of the formulation of the problem and the proposed research;
    - The scientific quality of the proposed research;
2. Suitability of the action plan:
    - The feasibility of the project and completion of the proposed research within the duration of the project.
    - Detailed step-by-step plan with division of tasks.

- Effectiveness of the chosen approach.
- Soundness of the budget.
- Presence of a back-up plan.

3. Suitability and composition of the consortium:
   - Academic excellence, supported by relevant publications, grants and prizes awarded, training, mobility and supervision of staff.
   - The role and contribution of all public and private parties involved.
   - The intended consortium is vigorous, balanced and coherent.
   - The consortium is also focused agenda-setting, fund-raising and stakeholder engagement for the longer term.
4. Plan for dissemination and implementation of research results:
   - Clear plan for implementation/application of the method after the end of the project.
   - Clear plan for dissemination of the research results (for possible use by other research groups).

Brief explanation of the assessment of relevance and quality
The emphasis of the assessment is on relevance. Based on the assessment of relevance and quality, the assessment committee determines the ranking according to the following matrix. Proposals must be assessed as at least “Relevant” and “Very good” to be eligible for funding (green). Proposals not classed in the green cells are not eligible for funding.
It may not be possible to fund all proposals that are judged to be at least relevant and very good. If proposals are of equal suitability, the assessment committee will consider the spread of impact across different diseases and TRL levels.

Table 2: Relevance and quality criteria with the emphasis on relevance

		RELEVANCE			
		High relevance	**Relevant**	**Low relevance**	**Insufficient relevance**
QUALITY	**Excellent**	1	3	-	
	Very good	2	4	-	
	Good	-	-	-	
	Adequate	-	-	-	
	Inadequate	-	-	-	

Admissibility assessment
After the call has closed, SGF and Health~Holland will check whether the applications are complete and meet the PPP and other conditions. On this basis, the applications will be declared “admissible”, “provisionally inadmissible” or “inadmissible”. If an application is declared “provisionally inadmissible”, the main applicant will be given the opportunity to correct or supplement the application within three working days.

Assessment procedure
Health~Holland will assess whether the application meets the PPP conditions. As part of the substantive evaluation process, external national or international referees will evaluate the applications submitted. In addition, the programme council will set up an external assessment committee (including users) which will assess and rank the applications, based partly on the evaluation by national and international referees and any rebuttals.

In this phase, the programme council consists of staff from the parties involved, including SGF, Health~Holland, NWO Domain AES and ZonMw.
The external assessment committee advises the SGF board on the applications submitted. Based on this advice, the SGF board decides which applications to fund and then submits them to the Health~Holland board for funding approval. Applicants will be informed by the end of March 2020 whether their application has been awarded funding. If the applications submitted are not sufficiently relevant or of sufficient quality, the funders reserve the right not to deploy the entire PPP budget. The schedule for the assessment procedure is given in Section 8 of this call.

6 Application procedure

Registration before submission of an application
Applications will be submitted in an open competition. Before submitting a PPP application for Call I under the PPP programme Human measurement models, applicants are required to register via the SGF website. Registrations must be received by September 5 2019. The project idea should be described in 200 words. The setting up of a collaboration or the active involvement of for profit organisations, healthcare providers, patients' organisations or other parties is not yet necessary at this stage. Parties who have registered an application are expected to attend the networking meeting on September 16 to present a pitch on their project idea and explore opportunities for new collaborations. As a result, SGF may ask applicants with matching project ideas to submit a single joint proposal. If this is applicable, you will be informed by September 30.

Attendance at networking meeting
For Call I under the PPP programme Human measurement models, a networking meeting will be organised for researchers and companies. This meeting will take place on:
September 16, 13.30-16.30, location: NWO, Winthontlaan 2, 3526 KV Utrecht.

The meeting will also be attended by interested health foundations, the Dutch Society for the Replacement of Animal Testing and other public organisations. Information will be provided at the meeting, and there will be ample opportunity for networking, finding new collaboration partners and identifying opportunities for cooperation. Parties who have registered a project idea are expected to attend this meeting and will be invited to present a pitch on their project idea during the meeting. If you are unable to attend the meeting, please send someone in your place. As an outcome of the networking meeting on September 16, you may find new or additional collaborative partners with whom to submit a PPP application. Further information about registration and the networking meeting is available on the SGF website.

Submitting an application
The registration and full application should be written in English. Besides completing the application form, the main applicant should enclose at least the following annexes:

- Specified budget based on the Health~Holland budget form
- Letters of commitment in which the parties confirm the pledge of co-funding and the size of the cash/in-kind contribution per participant. Only the main applicant does not need to submit a letter of commitment. Letters of intent will not be accepted. A letter of commitment template is attached as Appendix G, page 19.

Submission of the application
The full application should be submitted to SGF (via humanemeetmodellen@gezondheidsfondsen.nl) by 14:00 CE(S)T on 5 November 2019. The SGF office will coordinate the applications before they undergo the assessment procedure via the programme council and towards Heatlh~Holland. In this phase, the programme council consists of staff from the parties involved, including SGF, Health~Holland, NWO Domain AES and ZonMw.

7 Funded projects

Consortium agreement and PPP Allowance Agreement
After the project award decision, the consortium agreement should be signed by all partners within eight weeks. Once the consortium agreement has been approved, Health~Holland will draw up a PPP Allowance Agreement. This agreement is a contract between Health~Holland and all consortium partners that states the rights/obligations and contributions of the various partners. The PPP Allowance Agreement will be drawn up by Health~Holland and should then be signed by all partners within four weeks. A data management plan should be supplied together with the signed version of the PPP Allowance Agreement. Health~Holland will assess the plan as quickly as possible.
Health~Holland will publish information about all projects awarded funding on the projects page of its website (http://www.healthholland.com/project). A broadly understandable summary of the project for publication on this page should be submitted together with the signed version of the PPP Allowance Agreement.

First payment
Once Health~Holland has received and approved the signed PPP Allowance Agreement, the data management plan and the summary for the Health~Holland projects page, the first advance of the PPP Allowance can be disbursed. The remaining payments will take place on an annual basis after a progress report has been received and approved. The disbursements will be made to the institution where the main applicant is employed; the main applicant is responsible for any further distribution of the funding to other consortium partners as well as the collective accountability for how the funding is used.

User committee
A specific user committee should be set up for funded projects to facilitate implementation of the project results. This user committee should meet at least once a year. The Dutch Society for the Replacement of Animal Testing, contributing health foundations and other co-funding parties may participate in this user committee in order to stay informed of the progress of the project and to contribute to the implementation possibilities.

Monitoring
SGF and Health~Holland wish to be kept informed of the progress of funded projects. Funded projects will therefore be monitored by means of (financial and other) progress reports and a mid-term and final evaluation.

Communication
At the request of SGF and Health~Holland the consortium will cooperate in activities aimed at raising funding for research and/or providing information about research results.

8 Schedule

Activity	Date
Opening of Call I Human measurement models	July 3 2019
Registration by e-mail via SGF: humanemeetmodellen@gezondheidsfondsen.nl	September 5 2019
Networking meeting	September 16 2019 (13:30-16:30) NWO, Utrecht
Funders' notification of any proposed collaboration for submission of application	By September 30 2019
Submission of applications via SGF: humanemeetmodellen@gezondheidsfondsen.nl	November 5 2019 (by 14:00)
Admissibility assessment by SGF and Health~Holland	November 5-8 2019
Evaluation of applications by referees	mid November 2019-January 2020
Feedback to applicants and rebuttal requests	early January 2020
Deadline for rebuttals	late January 2020
Assessment (external) committee meeting	February 2020
Notification of decision	Late March 2020
Return of signed consortium agreement to Health~Holland	within 8 weeks after decision
Return of signed PPP allowance agreement and data management plan to Health~Holland	within 4 weeks
Last possible starting date of projects	September 2020
Termination date of projects (no overrun possible)	August 2024

Questions about the call itself
For any questions about the call itself, please contact the SGF via humanemeetmodellen@gezondheidsfondsen.nl. Please include your telephone number so that we can contact you by telephone if necessary.

For any questions specifically concerning the PPP scheme and the associated conditions, please contact PPP Programme Manager Laila El Aziz via Aziz@health-holland.com or +31 70 205 1403.

Downloads and links:

- Link to Health~Holland PPP conditions
- Link to budget form (Excel) (in Dutch)
- The consortium agreement can be downloaded from the Health~Holland website
- Link to TPI website
- Link to SGF website

Appendix A Definitions of the three types of research

Fundamental research means experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts, without any direct commercial application or use in view.

Industrial research means the planned research or critical investigation aimed at the acquisition of new knowledge and skills for developing new products, processes or services or for bringing about a significant improvement in existing products, processes or services. It comprises the creation of components parts of complex systems and may include the construction of prototypes in a laboratory environment or in an environment with simulated interfaces to existing systems as well as of pilot lines, when necessary for the industrial research and notably for generic technology validation.

Experimental development means acquiring, combining, shaping and using existing scientific, technological, business and other relevant knowledge and skills with the aim of developing new or improved products, processes or services. This may also include, for example, activities aimed at the conceptual definition, planning and documentation of new products, processes or services. Experimental development may comprise prototyping, demonstrating, piloting, testing and validation of new or improved products, processes or services in environments representative of real-life operating conditions where the primary objective is to make further technical improvements on products, processes or services that are not substantially set. This may include the development of a commercially usable prototype or pilot which is necessarily the final commercial product and which is too expensive to produce for it to be used only for demonstration and validation purposes. Experimental development does not include routine or periodic changes made to existing products, production lines, manufacturing processes, services and other operations in progress, even if those changes may represent improvements.

Appendix B Technology Readiness Levels

The need to estimate the costs, timing and risk associated with research and development is becoming increasingly important and often guides the development of effective assessment systems to gauge the developmental level of science, industrial processes and medical treatments. Rather than developing a new system, it is more efficient to use an established system from another sector. The Technology Readiness Levels (TRL) system is widely used in other sectors of technology and can help companies, academics and drug developers to make decisions during the development of a potential medicinal product or innovation cycle. A TRL indicates the current or expected phase of a development project. Nine phases have been defined in total, spanning the entire development process. An overview of the nine phases with their translation to medical research is given below.

TRL level	Definition	Type of research
TRL 1	Basic principles observed	Fundamental research
TRL 2	Technology concept formulated	Fundamental research
TRL 3	Experimental proof of concept	Fundamental research
TRL 4	Technology validated in lab	Fundamental research
TRL 5	Technology validated in relevant environment (industrially relevant environment in the case of key enabling technologies)	Industrial research
TRL 6	Technology demonstrated in relevant environment (industrially relevant environment in the case of key enabling technologies)	Industrial research
TRL 7	System prototype demonstration in operational environment	Experimental development
TRL 8	System complete and qualified	Beyond the scope of the PPP Allowance Regulation
TRL 9	Actual system proven in operational environment (competitive manufacturing in the case of key enabling technologies; or in space)	Beyond the scope of the PPP Allowance Regulation

Appendix C Funding conditions Dutch Society for the Replacement of Animal Testing

The Dutch Society for the Replacement of Animal Testing endorses the objectives of the programme "Towards better human measurement models". In its view, this programme offers enormous added value for the transition to animal-free innovation. We create impact through collaboration. The Society is keen to work with parties aiming to bring about this paradigm shift and actively supports it. The Dutch Society for the Replacement of Animal Testing is a non-profit organisation that aims to replace all animal testing. In financial terms, it is wholly dependent on donations from its supporters.

To qualify for our co-funding under this programme, applicants must meet the additional conditions required by the Society's policy, which are set out below:

1. The research is both 100% free of laboratory animals and does not involve animals in any other way. This means that we do not co-fund projects that use slaughterhouse material or animal species falling outside the definition of the Animal Experiments Act (*Wet op de Dierproeven*);
2. The consortium partners are prepared to participate in communication about the research via the Society's channels. Examples include interviews, blog writing, photos, videos, etc. These forms of communication are always agreed in advance with the parties involved;
3. Where the application concerns *in vitro* models, the use of Foetal Calf Serum (FCS)-free media is preferred.

If interested in co-funding from the Dutch Society for the Replacement of Animal Testing, please contact Debby Weijers via weijers@proefdiervrij.nl.

Appendix D Calculated examples of project budgets using a PPP Allowance

In the case of a project consisting entirely of industrial research, a maximum of 50% of the PPP Allowance may be used. In addition, 50% matching is required. At least 10% of the total project budget should be contributed by the research organisation. In addition, at least 30% must be provided by companies and possibly the remainder (10%) by other partners.

Total project costs:	€ 1,000,000
Contribution from research organisation (10%)	€ 100,000
Contribution from companies (30%)	€ 300,000
Contribution from other partners	€ 100,000
Total matching (50%)	€ 500,000
Total use of PPP Allowance (50%)	€ 500,000

In the case of a project consisting entirely of industrial research, a maximum of 50% of the PPP Allowance may be used. In addition, 50% matching is required. At least 10% of the total project budget should be contributed by the research organisation. In addition, at least 30% must be provided by companies and possibly the remainder (10%) by other partners.

Total project costs:	€ 1,000,000
Contribution from research organisation (10%)	€ 100,000
Contribution from companies (30%)	€ 300,000
Contribution from Stichting Proefdiervrij	€ 75,000
Contribution from other partners	€ 25,000
Total matching (50%)	€ 500,000
Total use of PPP Allowance (50%)	€ 500,000

Appendix E European Commission Recommendation regarding SME definition

Micro-enterprises are defined as enterprises that employ fewer than 10 persons and whose annual turnover or annual balance sheet total does not exceed € 2 million.

Small enterprises are defined as enterprises that employ fewer than 50 persons and whose annual turnover or annual balance sheet total does not exceed € 10 million.

Medium-sized enterprises are defined as enterprises that employ fewer than 250 persons and either have an annual turnover that does not exceed € 50 million, or an annual balance sheet not exceeding € 43 million.

For more details, “The revised User Guide to the SME definition” can be downloaded here.

Appendix F Contact details of possible co-funders

Aidsfonds Contact: Marein De Jong	aidsfonds.nl/wat-doen-wij/aidsfonds-en-aanpak/subsidies/#weten research@aidsfonds.nl
Alzheimer Nederland Contact: Dinant Bekkenkamp	www.alzheimer-nederland.nl d.bekkenkamp@alzheimer-nederland.nl
Diabetes Fonds Contact: Rogier Van Gent	www.diabetesfonds.nl r.vangent@diabetesfonds.nl
Epilepsiefonds Contact: Martin Boer	www.epilepsie.nl boer@epilepsiefonds.nl
Hartstichting Contact: Karin Eizema	www.hartstichting.nl research@hartstichting.nl
Hersenstichting Contact: Esther Hosli	www.hersenstichting.nl ehosli@hersenstichting.nl
Johanna Kinderfonds Contact: Ellen Hanselaar	www.jkf-kinderfonds.nl hanselaar@jkfkinderfonds.nl
Longfonds Contact: Bas Holverda	www.longfonds.nl basholverda@longfonds.nl
MaagLeverDarm Stichting Contact: Marijke Boersma	www.mlds.nl marijkeboersma@mlds.nl
MS Research Contact: Kirstin Heutinck	www.msresearch.nl onderzoek@msresearch.nl
Nederlandse Brandwonden Stichting Contact: Carine van Schie	www.brandwondenzorg.nl cvanschie@brandwondenstichting.nl
Nederlandse Cystic Fibrosis Stichting Contact: Vincent Gulmans	www.ncfs.nl v.gulmans@ncfs.nl
Nierstichting Contact: Wouter Eijgelaar	www.nierstichting.nl/professionals/wetenschappelijk-onderzoek/calls-proposals/pionier-programma-voor-cofinanciering/ WouterEijgelaar@nierstichting.nl
Prinses Beatrix Spierfonds Contact: Simone Van den Berge	www.prinsesbeatrixspierfonds.nl onderzoek@spierfonds.nl
ReumaNederland Contact: Heidi Van Vught	www.reumanederland.nl research@reumanederland.nl
Stichting ALS Contact: Tom Bos	www.als.nl t.bos@als.nl
Stichting Proefdiervrij (Dutch Society for the Replacement of Animal Testing) Contact: Debby Weijers	www.proefdiervrij.nl/english weijers@proefdiervrij.nl

Appendix G Letter of commitment template

[Use headed paper of party]

[Name and address of the main applicants' duly authorised representative (“bestuurlijk verantwoordelijke”)]

[Date]

LETTER OF COMMITMENT

for the

[name of] PROJECT

Dear [main applicants’ duly authorised representative],

I, [first name and family name], in my capacity of [position in the organisation (has to be a duly authorised person)] at [name legal entity] hereby confirm that [legal entity] is committed to contribute to the [project name] project, on the condition that Stichting LSH-TKI grants the PPP Allowance as applied for by the main applicant, [first name and family name], [position] at [name organisation].

[Name legal entity] will contribute € [•] in cash towards the project costs in accordance with the budget in the project proposal and budget form.

[Name legal entity] will provide an in-kind contribution of [description of the contribution], representing a monetary value of € [•] and further detailed in the project proposal and budget form.

Yours sincerely,

_____

Name:

Position:

Date: