PPP programme
Human measurement models 3
Call for PPP proposals

Next steps in model development

In collaboration with

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1 Introduction to human measurement models programme

The Association of Collaborating Health Foundations (SGF) together with Top Sector Life Sciences & Health (Topsector LSH; Health~Holland), the Netherlands Organization for Scientific Research domain of Applied and Engineering Sciences (NWO domain AES) and the Netherlands Organisation for Health Research and Development (ZonMw) have set up the Human Measurement Models programme. The purpose of this programme is to stimulate more effective human health research, which is less dependent on animal testing. So far, two calls for proposals have led to funding of thirteen projects in the field of human measurement models. Now, a third call entitled: '*Next steps in model development'* is added to stimulate further development of promising human measurement models for health research on diseases and prevention.

This brochure provides the conditions governing proposals for funding of innovative research within this third call of the Human measurement models programme. It explains the objectives, scope, criteria, application and assessment procedure. This third call has been set up by the SGF and Health~Holland, in collaboration with ZonMw.[1] These organizations are referred to as Partners in this brochure. In Appendix A, more information is provided about the Partners including their mission statements. This call is financed with 4,430,574 Euro PPP Subsidy made available by Health~Holland, in strong collaboration with SGF, and 1M Euro by ZonMw.

SGF is the first point of contact for applicants in this third call. It receives the submitted proposals and coordinates the assessment procedure. This will be done in close collaboration with the other two Partners where Health~Holland is responsible for checking compliance with the terms and conditions regarding the PPP Subsidy.

1.1 Background of the programme

Millions of people deal with the consequences of serious and sometimes life-threatening diseases every day. The Partners are committed to achieving better and healthier lives for everyone. Scientific research plays a crucial role to develop better treatments. 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 on 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 may facilitate the (further) development of new human measurement models.

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, Health~Holland, the Dutch Society for the Replacement of Animal Testing (Stichting Proefdiervrij) and ZonMw, together with various ministries, parties from government and society, industry and science. The TPI's ambition is to make the Netherlands a catalyst 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 Health, Welfare and Sport, the Ministry of Defence, the Ministry of Infrastructure and Water Management, the Ministry of Education, Culture and Science, the Ministry of Economic Affairs and Climate Policy. Further information on the "Transition Programme for Innovation without the use of animals" is available on its website.

[1] Within the overarching Partnership programme, there is also a strong collaboration with NWO, which has led to the second call.

1.2 Programme objectives

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 measurement models will contribute to answering research questions that otherwise could not be answered or could be answered only by using animal models. These human measurement models may aim either at diagnosing and treating diseases or at disease prevention. The definition of “human measurement model” includes *in vitro* and *in/ex vivo* models (e.g. models based on human material/tissue/cell lines) as well as *in silico* models (e.g. models based on (big) data, systems biology and computational models).

The following programme objectives have been formulated:

- 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.

So far, two subsidy rounds have led to funding of thirteen projects in which over 9M Euro has been made available for public-private collaborations. These projects cover a wide range of techniques and applications which might in the end be of benefit for many patient groups. With this call for proposals, the Partners intend to stimulate ‘next steps in model development’. This concerns an open call in which everyone meeting the criteria as set in Section 3.1 can apply. The application should meet the submission requirements (see Section 3.2) and the criteria related to the PPP Subsidy (see Section 3.3). Projects that will be funded within this third call should meet the criteria for project execution (see Section 3.4).

2 Current call “Next steps in model development”

2.1 Objectives of this call

So far, limited human measurement models have been validated and accepted in health care research. There is a need for sufficient room to develop, improve and validate useful models and procedures. Therefore, the objective of this third call “Next steps in model development”, is to stimulate further development of promising innovative human measurement models for health research on disease and/or prevention of disease. The call focuses on human measurement model research that is already in development with a Technology Readiness Level (TRL) between 3 and 7 (as described below) and is considered as fundamental research, industrial research, experimental research or a combination thereof. In case of doubt between the definition of the TRL levels and the type of research, the definition of the type of research will always prevail. Please read the Glossary (Appendix B) for a brief explanation of a number of defined terms used in this call, including a definition of the three research types.

Within the current call, only projects that focus on further development of existing human measurement models can apply for funding. These models have been developed in previous research projects and knowledge has been gained about the feasibility and potential impact of the model. Besides further development of the model (for broader applications), research elements related to standardization and reproducibility are necessary for validation. Projects may concern the following TRL range:

- **Experimental proof-of-concept** (TRL-3): the first laboratory scale prototype or numerical model is realized or testing of an innovative technical element at laboratory level. Key parameters characterizing the model have been identified. Verification of the proof-of-concept through simulation tools or cross-validation with literature data;

- **Validation of technology in the lab** (TRL-4) by, for example, numerical analysis, measurement of Key Performance Indicators (KPIs) or demonstration of repeatable/stable performance. Also, integration of prototype in other systems at laboratory level is considered as TRL-4;

- **Validation of technology in relevant environment** (TRL-5): robustness of the model is proven in relevant environment, prototype shows repeatable/stable performance and/or the process is reliable. TRL-5 also includes research related to integration of supporting components to the prototype of the model. In this phase of model development attention should also be given to other relevant parameters, such as regulatory or socio-economic issues. These should be defined and qualitatively assessed;

- **Technology demonstrated in relevant environment** (TRL-6): demonstration of the model in relevant environment under a variety of conditions, or demonstration of reliable process which matches expectations. Interoperability with other connected technologies or processes is demonstrated. Environmental, regulatory and socio-economic issues are addressed.

- **System prototype demonstration in operational environment** (TRL-7): Pre-commercial system is demonstrated in operational environment and/or manufacturing approach is defined. The system is compliant with relevant environmental conditions, authorization issues (at least for the demo site). The integration of upstream and downstream technologies has been verified and validated.

Within the proposed project, substantial steps should be made in further development of the model. The project application should be sufficiently innovative, which may concern technology development as well as improving biological aspects (for example, adding immune system or vasculature to the model). With regard to the validation process, applicants are advised to make use of the knowledge and expertise of the EU Reference Laboratory for alternatives to animal testing (EURL ECVAM), which includes valuable validation resources, such as the EURL ECVAM library of reference chemicals.

This programme aims to fund research of very good quality, having scientific, societal and economic value. It should build further on an existing collaboration or create a new collaboration that brings innovative human measurement models closer to a clinical application. The concerned human

measurement model should be predictive for the human situation and preferably facilitate research that is applicable to multiple diseases (impact for multiple patient groups). If the demonstration of the validity of the model requires a disease-specific approach, this is allowed.

2.2 Scope

2.2.1 The scope of the current call

- The project aims at further development of existing/proof-of-concept models for research into health and disease;
- Project should pay attention to the reproducibility, standardization and/or validation of the developed model;
- Although the proposed project will build on previous research and knowledge gained about the feasibility and impact of the model, the project contains unique and innovative aspects;
- The project concerns innovative research, which can be categorized within TRL 3-7 (see Section 2.1)
- Projects that (in the long term) demonstrably reduce the use of animals or eliminate the need for research involving animal experiments;
- Within the project, multidisciplinary research will be performed: in the consortium, biological/medical expertise as well as (bio)technological expertise is represented and integrated. In case research is TRL-5 or more, expertise considered relevant for the applicant's project and future impact goals, such as regulatory expertise or business consultants should also be involved, at least in the user committee;
- Projects that might have an impact for multiple patient groups are preferred;
- Projects in which the validity of an innovative model using the current (animal) standard is demonstrated, are conditionally permitted. This is allowed only under the following conditions:
    - This research step is unavoidable for validation purposes of the innovative model
    - the mechanisms or effects studied in the animal model are proven to be comparable/relevant for humans.
- Projects in humans are allowed, as long as ethical approval is obtained.

2.2.2 Outside the scope of the call

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

- Technology development with research purposes/use only (no clear utilisation potential);
- Solely product development and/or testing (no clear technical scientific challenge);
- Research which can be categorised as Technology Readiness Level (TRL)-1 (fundamental research and desk research), TRL-2 (applied research), TRL-8 (product is complete and operational) or TRL-9 (deployment phase);
- Clinical trials, as defined by cohort studies or phase I/II studies and beyond;
- Projects mainly aimed at improving animal welfare in existing animal measurement models;
- Improvement of a technique or application that does not require animal testing or contribute to the reduction of animal testing now or in the future, e.g. studies that are already taking place in humans;
- Project applications not related to health and disease.

2.2.3 *Human measurement models and animal use*

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 golden 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. This is partly due to a lack of further development of human-based measurement models. The aim of this call is to encourage the further development of such models and methods towards validation and application.

SGF, ZonMw and Health~Holland, together with its members and partners in the TPI, 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. The previous calls and this call are considered as a prelude and a transitional phase in which projects will be permitted that 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- for validation purposes only- form part of the proposed research, the project consortium should, upon start, preregister the research protocols (for example CCD protocol(s)) in https://preclinicaltrials.eu/. In addition, they should adhere to the ARRIVE guidelines (https://arriveguidelines.org/) upon publishing the animal studies. Where an application *concerns in vitro* models, it is encouraged to take into account latest developments in the field such as the use of alternatives to Fetal Calf Serum (database is available here) and Matrigel.

2.3 Duration and available budget

The SGF and Health~Holland make 4,430,574 Euro PPP Subsidy available for new PPP projects under this call. ZonMw is making an additional 1M Euro available as part of the More Knowledge with Fewer Animals (Dutch acronym: MKMD) programme. ZonMw does not allow animal testing for validation purposes for its budget (see also Section 4.8.1).

Per project application, a minimum of 400K Euro PPP Subsidy must be requested and a maximum of 1M Euro can be requested.

The project has a minimum duration of two years and a maximum duration of four years, starting from the initial expenditure of the project's budget. The final start date of the project is September 1, 2025. The end date of the projects within this call of Human Measurement Models: *Next steps in model development* cannot exceed October 31, 2029, taking into account the PPP Subsidy 2024 conditions. Information on the final start and end date of the project will be included in the award letter.

2.4 Project application

In the application form, describe clearly and explicitly how your research project contributes to the objectives of the programme and specifically 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 description of the activities for the implementation and dissemination of project results during and after the project. The expected impact on reduction of animal use is demonstrated by a 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 application. For more detailed information see the application form.

3 Guidelines for applicants

3.1 Who can apply?

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

A person may be involved in a maximum of two applications, only in one of them as a main applicant. Exceptions to this rule are:

- Project members with a supporting role, such as statisticians, ethicists, regulatory expertise, laboratory staff, heads of GMP facilities and similar roles;
- Co-applicants or funding parties that do not receive funding from the project

Effective collaboration[3] takes place in the project. This means that the project is carried out at joint cost and risk and that all consortium partners make a substantive contribution to the project. A substantive contribution entails that each consortium partner should make an in kind contribution at least in the form of incurring payroll costs (which must be visible in the budget form). Please note that the SGF does not allow consortium partners that have collaborations and/or any other relevant connections with the tobacco industry.

In addition, public organisations (e.g. health foundations, the Dutch Society for the Replacement of Animal Testing, equity funds) and regulatory authorities may be involved in the research proposal as private parties and are allowed to contribute financially to the project. See Appendix C for more information about co-funding by the Dutch Society for the Replacement of Animal Testing. If these parties only make an in-cash contribution and do not themselves incur any costs in the project, they are not considered as consortium partners and are not required to 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.

3.2 Requirements for submission

Below, the requirements for submission are included and explained. Before reading the criteria below, please note that explanation of the used terminology is provided in the glossary of this call (see Appendix B).

Applications are subject to the following requirements:

- The obtained knowledge and results of the project should have high utilisation potential and contribute to the mission statements of Health~Holland, SGF and ZonMw (Appendix A).

[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.

- The research fits within the societal theme ‘Health & Care’, the central mission and at least one of the five focused missions that contribute to the central mission of this theme, as concretized in the Knowledge and Innovation Agenda 2024-2027.
- The research contributes to the objectives of the PPP programme Human measurement models and the objective/scope of the current call ‘Next steps in model development’ (see Sections 2.1 and 2.2);
- The proposal includes a consortium of at least two research institutes and one for-profit enterprise (see Section 3.1 and the Glossary (Appendix B) for an explanation). Foreign companies and foreign research/knowledge institutions are also encouraged to participate in the consortium, as long as the results of the research project benefit the Dutch knowledge infrastructure and economy
- (End) users are involved in the project. The developed model must be in line with the expectations, wishes and situation of the (end) user (researchers, companies, healthcare providers, regulators, patients). User involvement is therefore essential. In all research projects, a user committee must be set up in which, in addition to the consortium partners, other relevant users may also participate.
- The proposal consists of fundamental research, industrial research or experimental development, or a combination thereof (See the glossary for a description of the three types of research).
- Co-funding, by all consortium partners is required on project level. See table 1.A. ‘Funding by type of research’ (Section 3.3) for details.
- The project will be realised at joint cost and risk, and all consortium partners will make a substantive contribution to the project. This means that all consortium partners incur costs, at least in the form of personnel costs, and those costs are stated on the Budget Form (Excel).
- The use of animal models is only allowed for validation purposes, and only if can be shown that the effects and/or mechanisms studied in these animal studies are proven to be relevant for humans.
- The application should consist of all requested forms, among which a draft consortium agreement (according to the template as published with this call) and a letter of commitment of all involved parties, except the main applicant.
- The project or overlapping activities have not already been funded by other funding agencies.

3.3 Requirements related to PPP Subsidy

Since 2024, new PPP Subsidy rules apply, which are stated below. The maximum PPP Subsidy that can be requested for a research project is 1M Euro.

Organisations that meet the definition of research organisation (See Section 3.1) may fund up to 70% of their own costs[4] with PPP Subsidy in the case of fundamental and industrial research. Research organisations may fund up to 60% of their own costs with PPP Subsidy in the case of experimental development. Dutch SMEs (for-profit and not-for-profit enterprises[5]) may fund up to 60% of their own costs using PPP Subsidy to conduct fundamental and industrial research. Dutch SMEs may finance up to 40% of their own costs with PPP Subsidy to conduct experimental development.

Table 1.A shows these maximums in more detail. A project can consist of a combination of the three types of research. The Partners encourage consortia to jointly organise the activities and budget within the project, with both research organisations and enterprises contributing equally in terms of content to the project. In addition, Dutch SMEs are given an equal opportunity to apply for PPP funding for their R&D activities.

Large enterprises (Dutch and foreign), foreign SMEs and Dutch and foreign other parties are not

[4] All eligible costs incurred by that particular partner, except any in-cash contributions

[5] Each unit, irrespective of its legal form or manner of funding, that carries out an economic activity.

permitted to apply for PPP Subsidy; the expenses they incur should be equal to the in-kind contribution they provide.

Table 1.B illustrates the minimum percentage of total project costs that must be contributed by the research organisation(s) and enterprise(s) in the project. Appendix D provides two calculation examples applying the funding requirements to two different types of consortia.

Table 1.A: Funding by type of research

Partner level

Max % PPP Subsidy based on eligible costs partner	Fundamental and industrial research	Experimental development
Research organisation	70%	60%
Dutch SME	60%	40%
Large enterprises, non-Dutch SME, Dutch and non-Dutch other parties	0%	0%

The percentages listed in Table 1.A are taken over the total costs of the organisation in question.

Table 1.B: Minimal contributions

Project level

Minimal contribution based on total project cost	Fundamental and industrial research	Experimental development
Research organisation(s)	min. 10%	min. 10%
For-profit and non-profit enterprise(s)	min. 15%	min. 30%

The percentages listed in Table 1.B are taken over total project costs.

3.3.1 Calculating project costs

Eligible costs

Only those costs that are directly related to the R&D activities within the project (eligible costs) can be entered on the budget form. Examples include: scientific staff, technicians, support staff, consumables and the use of equipment specifically required for the project (depreciation system). Historical cost should be used when entering the cost of consumables. Entering commercial rates is not permitted. For an explanation of the (calculation of) eligible costs see the Commission Regulation (EU) No. 651/2014 of June 17, 2014, Article 25 and the Framework Decision National EZK and LNV Grants, Chapter 4, Article 10-14.

Parties that do not use PPP Subsidy are not required to use one of the payroll costing systems prescribed by the Framework Decision on National EZK and LNV Grants. These parties may also use their own hourly rate. A condition is that the calculation of the costs takes place on the basis of a customary and verifiable method and is based on business principles and standards that are considered acceptable in society and that the participants in a collaborative project apply systematically. On the budget form, these parties should choose "fixed hourly rate" and adjust the standard hourly rate of EUR 60 to an hourly rate that is customary and verifiable for them.

Examples of ineligible costs

The following are examples of ineligible costs. Therefore, these costs should not be entered on the budget form*:*

- Applying for and maintaining patents (costs for patents purchased on arm's length terms from or licensed from outside sources are eligible);
- Auditor's statement;
- Benchfee (note: costs for consumables are eligible);
- Travel within The Netherlands;
- Support staff, not directly related to the R&D activities, such as: project controller, business developer, administrative officer;
- Preparation of a business case;
- Costs related to implementation of the developed innovation;
- Carrying out effectiveness studies (Health Technology Assessment, HTA);
- Overhead;
- Non-scientific dissemination. However, scientific dissemination, including attending a scientific congress or publishing a scientific article, is eligible*;*
- Project management tasks, not directly related to the specific R&D activities, such as: escalation to a steering committee, preparing a risk management model, preparing reports to meet funding obligations, administrative accountability. Project management tasks that do relate directly to the R&D activities (e.g., discussions with staff, analysing technical risks, preparing research reports, preparing specifications) are eligible.

Costs attributable to third parties

If some of the activities are subcontracted, those costs due to third parties can be allocated to the project and entered on the budget form. Care should be taken to ensure that the costs due to third parties are in proportion to the rest of the budget. Should this cost category be particularly high, this could influence and become part of the evaluation committee's assessment.

Instructions Budget Form

A specific budget form will be used within this call. The budget form uses multiple built-in functions and redirects. Therefore, it is important to follow the instructions of the budget form (see the "Instructies" tab of the budget form).

3.3.2 Consortium agreement

The consortium must reach agreements on the intellectual property (IP) related to the products and services developed in the project. These agreements are recorded in the consortium agreement which all consortium partners should sign before the start of the project. A 'first option right' is among the possibilities. Agreements on IP follow the Framework Regulation on State Aid for Research, Development and Innovation (specifically article 2.2.2.) and the PPP Innovation Regulation (Staatscourant October 20, 2023, 28651). These state, amongst other matters, that enterprises and other private partners that participate in the project may acquire the IP from the research organization for a market-based fee (minus the amount already invested by them) and that results from which no intellectual property rights can be derived may be widely disseminated.

Note: Use of the model consortium agreement made available for this call is mandatory. Any modifications in the model must be immediately recognizable.

3.4 Criteria for project execution

3.4.1 Optimal use of existing knowledge and data

It is important to show in the application that the project consortium is making good use of knowledge that is already available (nationally and internationally). The health foundations encourage optimal use of data. In the detailed grant application, describe the possibilities of making use of existing data files and substantiate any stated need for new data collection.

3.4.2 Data management plan

The Partners want to raise awareness among researchers about the importance of responsible data management. Applicants should therefore answer a number of questions on data management under section E of the application form. After final approval of an application, applicants need to prepare a data management plan, using Health~Holland's template. Approval of the data management plan by Health~Holland is a condition for the provision of PPP Subsidy.

3.4.3 Open access and open data

The Partners 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. Via the website http://www.openaccess.nl/nl/node/644 you can check whether your organization has made agreements with traditional publishers regarding open access. Among other things, this website provides an overview of over 8,000 journals in which corresponding authors from Dutch universities and UMCs can publish in open access for free or at a discount. Costs associated with open access publishing fall under eligible project costs.

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 (e.g. Center for Open Science, Open Science Frame) 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. This means that the data generated in the projects can be found, understood and used by both humans and machines. The process of making data FAIR is explained by the GoFAIR foundation in the three-point FAIRification framework. When planning your project and its budget, take into account the opportunities and requirements set out at FAIR data & data management. If you do not intend to collect any data, please mention this in your grant application.
- All publications resulting from scientific research funded by this call must be made available in Open Access.

3.4.4 Animal experiments

If animal models are used, the research protocols (such as a CCD protocol) should be approved by the animal ethical committee and should be preregistered at Preclinicaltrials.eu at the start of the project. The ARRIVE publication or Gold Standard Publication Checklist (GSPC) guidelines should be followed in publications describing animal studies.

3.4.5 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.

3.5 Resubmission of proposals

Research proposals that were rejected in a previous SGF, ZonMw, NWO or Health~Holland evaluation procedure cannot be resubmitted to this Partnership programme automatically. When a research proposal is resubmitted, the proposal must comply with the requirements for the current call 'Next steps in model development' with respect to e.g. scope, applicants, criteria and co-funding. In addition, for proposals that were previously submitted to SGF, ZonMw, NWO or Health~Holland (including the two previous calls in the Human measurement models Partnership programme), the content has to be significantly revised. The earlier referees' comments and/or advice of the assessment committee may be used as a guideline in revising the proposal.

In case the research proposal is a resubmission of a previous SGF, ZonMw, NWO or Health~Holland proposal, the applicant is obligated to inform the SGF and attach a statement (in English) to the submission indicating the previous submission title and call submitted to and explaining the conducted revisions. If according to the Partners the research proposal has not been revised sufficiently, it will not be eligible for funding.

3.6 Submission procedure

3.6.1 Information meeting

For this third call of the Human measurement models Partnership programme entitled '*Next steps in model development'*, an online information meeting will be organised for researchers and other consortium partners and private parties. This meeting will take place on June 10th 2024.

The information meeting on June 10th 2024 will provide an opportunity to obtain information on the call in general and specifically on the new PPP Subsidy criteria. Moreover, it is an opportunity to ask questions for clarification. Further details about the information meeting is available on the SGF website.

3.6.2 Obliged contact with Health~Holland before submission application

For this call, PPP Subsidy rules apply, which involves requirements related to co-funding and own in-kind contributions. Since the PPP rules have been changed since 2024 and it is of benefit for the applicant as well as for the Partners to ensure that the rules are well understood and applied, it is obliged to contact Health~Holland at least two weeks before the application deadline for verification purposes and/or questions. Health~Holland can be contacted via tki@health-holland.com.

3.6.3 Submitting an application

The registration and full application should be written in English, according to the forms that can be downloaded from our website. Besides the **completed application form**, the main applicant should enclose at least the following documents:

- **Specified budget:** The template of the budget form can be found here.
- **Consortium agreement:** This should be an unsigned draft version, a blank format is not sufficient. The consortium is required to use the model consortium agreement made available by Health~Holland[6]. This is available for download on our website. Only non-essential changes and modifications that do not conflict with the Framework should be made to this model. When in doubt about changes, the consortium should consult an expert: e.g. the technology transfer office (TTO) of the research organization or a lawyer.
- **Letters of commitment** confirming per participant the commitment of co-financing and the amount of the in-kind and/or in-cash contribution by the parties, signed by an authorized person. The main applicant is not required to provide a letter of commitment. Letters of intent will not be accepted. The letter of commitment template can be downloaded from our website.

[6] Please contact Health~Holland when an existing consortium agreement is already in place

A full application, using the application form, should be submitted by 4 October 2024 (14:00 CE(S)T) via email to humanemeetmodellen@gezondheidsfondsen.nl. Please be aware that submissions received after 14:00 CE(S)T on the day of the deadline will not be considered.

3.6.4 Time frame

Activity	Date
Opening of Call Human measurement models 3	May 14, 2024
Online information meeting	June 10, 2024 (15:00 CE(S)T)
Applicants: Obligation to contact Health~Holland to discuss adherence to PPP rules	At last 2 weeks prior to submission deadline
Deadline submission of applications	October 4, 2024 (14:00 CE(S)T)
Admissibility assessment by SGF and Health~Holland	October 7-11, 2024
Applicants: Revision of proposal to fit formal requirements	October 14-18, 2024
Assessment by referees	November 2024-Mid January 2025
Feedback to applicants and rebuttal requests	January 13, 2025
Applicants: deadline for rebuttal	January 16, 2025
Interview selection	Mid-February, 2025
Applicants: interviews by assessment committee	March 13-14, 2025
Advice external assessment committee to SGF	End of March 2025
Decision by SGF and Health~Holland	April 2025
Return of signed consortium agreement to Health~Holland	Within 8 weeks after decision
Return of signed PPP Subsidy Agreement and data management plan to Health~Holland	Within 4 weeks after completion of signed consortium agreement
Last possible starting date of projects	September 1, 2025
Termination date of projects (no overrun possible)	October 31, 2029

4 Assessment procedure and criteria

4.1 Formal requirements

After the call has closed, SGF, ZonMw and Health~Holland will verify whether the formal requirements are met to determine whether the research proposal is eligible for consideration. If relevant conditions as mentioned in this call and/or application form are not fulfilled or the information requested is incomplete, the research proposal cannot be considered. In case adjustments are required, the SGF returns the research proposal to the main applicant within five to ten workings days with a request for adjustments or additional information to comply with the requirements. The main applicant is given **5 working days** – calculated from the date of SGFs notification – to submit a revised version via email. If the information required is not provided, or is incomplete by the deadline, the research proposal is considered as withdrawn.

In order to manage the programme together with the partners, SGF needs to collect personal data as present in the project (application) documents of the (co) applicants, personnel on the project, consortium members and/or users, (candidate) external referees and (candidate) committee members and share these data with the partners. This data will solely be processed for the purpose of the management of the programme and in accordance with the applicable data protection laws by the partners. See also the privacy notice on the SGF website.

4.2 Assessment by referees

The research proposal will be sent to (inter)national experts in the relevant specialist area (peer review). For the purposes of this Partnership programme, the aim is to have the research proposal assessed by three to five referees. These referees are drawn from the scientific world, large research institutes, and industry. Referees remain anonymous. They assess the proposal on the basis of specific questions about scientific quality and potential for utilization (see also Section 4.8).

In general, the number of referees consulted depends on the nature of the research proposal and the size of the budget requested in the research proposal. SGF gives applicants the opportunity to provide suggestions for referees. For this please add a list of the names and contact information for a maximum of five independent (according to the ZonMw Code of Conduct on Conflicts of Interests) international referees with relevant expertise.

4.3 Applicants rebuttal

All individual referees comments are anonymised and grouped together. SGF then requests the main applicant by e-mail to respond in English to the referees' comments provided. The main applicant should respond to each question or each comments raised by the referees individually.

Please consider the following guidelines when formulating your rebuttal:

1. Keep it short and to the point, do not include attachments;
2. The maximum length of the rebuttal is 2 A4 page. Use a minimum font size of 10, Arial, a minimum line spacing of 1.5 and a minimum margin of 1.27 cm;
3. Clearly identify which assessment report you are responding to;
4. Provide only substantive responses to the reviewers' comments. You may respond to questions or comments by providing additional information or clarification. The evaluators' comments may also be used as a basis for suggesting improvements in the implementation of your proposal. However, the evaluators' reports may not be used as a basis for rewriting your proposal or for major changes in the implementation of the project;
5. You are not allowed to introduce new figures in the rebuttal;
6. Only one rebuttal may be submitted.

The combined referees' comments including the responses from the applicant(s) will be used by the assessment committee for their final assessment of the proposal.

4.4 Interview selection by assessment committee

To guarantee objectivity of the assessment as much as possible, the Partners put together a multidisciplinary assessment committee consisting of approximately ten (10) to fifteen (15) independent national and/or international experts from the field drawn for example from universities, large research institutes or industry and other societal sectors to guarantee the assessment of quality of the proposal. The assessment committee is multidisciplinary, reflecting both scientific expertise relevant in the field of human measurement models as well as utilization expertise like clinicians, industry, patient representatives, ethics and/or regulators. Patient referees will base their rating on the extended layman's summary in the application form. Each assessment committee member will be assigned a maximum of six (6) applications to rate in this phase.

During the interview selection meeting of the assessment committee, all the project proposals submitted are discussed by the assessment committee members, taking into account the proposal, the review reports and the rebuttal, to evaluate each project proposal. After this discussion, the committee members assign two ratings (between 1 (excellent) and 9 (moderate / poor) to each assigned proposal, one for scientific quality and one for utilisation (prospects, including societal relevance). The two criteria are equal in weight and a ranking based on the sum of the calculated averages for both criteria is determined upon individual assessment by the assessment committee members.

A maximum of twice the number of proposals that can be funded will be selected for interview. The exact number depends on the budgets requested in the project proposals. The highest ranked proposals will be selected for interviews. The applicant will be informed about this decision before the end of February 2025.

4.5 Personal (conflict of) interests

Both the referees and the committee members have to confirm that they have no conflict of interest and are bound to confidentiality. For this call, the code of conduct for managing Conflict of Interest from ZonMw is applied, which can be found here: Laws and regulations concerning ZonMw.

4.6 Interview

During the interview, the consortium can briefly present the project plan, after which the assessment committee has the opportunity to ask questions. A maximum of 5 members of the consortium may be present during the interview including the project leader and a representative of the users. The interview is an important aspect of the assessment and might lead to adjustment of the scores of the assessment committee.

4.7 Final assessment by assessment committee

After the interviews, all project proposals are discussed again by the assessment committee members, taking into account the proposal, the review reports, the rebuttal and the interview to evaluate each project proposal. After this discussion, all committee members will have the opportunity to reconsider their two ratings (between 1 (excellent) and 9 (moderate / poor). The two ratings are equal in weight and a ranking is based on the sum of the calculated averages for both criteria. The ranking is determined upon individual assessment by the assessment committee members. A final prioritization for the research proposals is established, after which the advice of the assessment committee is formulated and presented to the SGF and Health~Holland board.

4.7.1 Minimal quality criteria, resolution of ex aequos and allocation of budget intended for animal-free research

Full proposals can only be considered for funding if both the utilisation quality criterion and the scientific quality criterion together score no more than 7.0 and the individual criterions score no more than 4.0. An explanation of the evaluation scores is provided in Appendix E.

The funding committed by ZonMw (1M Euro) is exclusively available for research projects that are free of animal testing and any other use of animals (as defined in Article 1.a of the Wet op de Dierproeven). The other part of the funding, 4,430,574 Euro, is available for funding of animal-free research as well as research in which animal studies are used for validation purposes (see criteria for submission). This budget is allocated in parallel and will be allocated to the highest ranked research projects which meet the quality criterion. This includes animal-free projects which could not be funded with the budget for

animal-free research.

The available programme budget may not be sufficient to award funding to all proposals that meet the eligibility criteria for funding and the allocation approach described here may result in funding of non-consecutive projects on the ranking list.

In order to ensure the disease overarching scope of this call, for all applications that have an end score between 3 and 7, the Committee retains the right to take into account that on a program level funding is appropriately distributed over a range of applicable diseases .

4.7.2 Ex aequo

Ex aequo is a situation in which two or more applications have similar end scores (based on 1 decimal), after prioritization by the assessment committee. In case of ex aequo around the limit of the funding ceiling or selection score, the proposal most relevant to the programme goals, as assessed by the assessment committee, will be prioritized. If this will not result in a distinction between the proposals on ex aequo position, the proposal with the best score for utilisation (prospects) will be prioritized.

4.7.3 Assessment criteria

The reviewers will base their score on the following criteria:

Utilization potential:

- **Fit for purpose:** Is the proposal in line with the goals, objectives and scope of the Human Measurement Models programme? Are next steps in model development being made within the project?
- **Reduction of animal use:** To what extent will the project contribute to the reduction and/or elimination of animal models?
- **Progress of project on model development:** In your opinion, to what extent will this project take the development of the concerned human measurement model a step further? How do you assess the elements related to the next steps in development, such as standardization, reproducibility and/or other validation aspects?
- **Output and outcome of project**[7]**:** How do you evaluate the expected output of the project and the role of involved stakeholders in achieving this output? How does the expected project outcome, including the outcome of eventual follow-up projects, aid in achieving the described impact goals?
- **Implementation and dissemination activities:** What is your opinion about the described activities for implementation/application of the research results and dissemination of the research results after the end of the project, in terms of clarity, feasibility and relevance?
- **Multiple diseases/patient groups:** To what extent is the proposed model (in potency) applicable to multiple diseases and relevant to a broad group of patients?
- **Users involvement:** How do you assess the involvement of (end) users in the project (both during the preparation phase as well as in the expected executive phase)?
- **Knowledge transfer:** What is your opinion about the potential plans for collaboration with the industry and knowledge transfer in the proposal, if the project is successful? To what extent is accounted for hampering factors (like commercial propositions, patents, societal acceptance) in the proposal?

Scientific quality:

- **Project design:** How would you evaluate the overall project design (including the goals,

[7] **Output**: Insights and conclusions derived directly from the project, e.g. publications, data and new methods. **Outcome**: Changes in behaviour, relationships, actions or activities of stakeholders as a result of the project's output, e.g. skill development, policy changes, people engagement.

hypotheses, research methods, risk mitigation and scientific feasibility)? How would you rate the innovative elements in relation to the current state-of-the-art?

- **Justification of animal experiments:** In case animal experiments are used for validation purposes, is the relevance thereof sufficiently substantiated? (if no animal experiments are used, you can ignore this question)
- **Feasibility:** To what extent do you expect the research project to lead to the anticipated deliverables, taking into account the described time schedule and project phasing?
- **Competence of consortium:** How do you judge the competence of the consortium to carry out the research?
- **Collaboration:** To what extent is collaboration between the participating partners substantiated and what is your opinion with respect to the level of collaboration? Is the expertise of the project members multidisciplinary and complementary to each other? Is sufficiently accounted for diversity aspects in the consortium composition? Is the proposed description of collaboration adequate for the execution of the proposed research?
- **Budget:** To what extent is the requested budget adequate and justified e.g. the number and category of requested personnel, budget for materials, investments and foreign travel? Are costs made by third parties in proportion to the rest of the budget (if applicable)?

4.8 Decision by SGF and Health~Holland

The advice of the assessment committee will be presented to the board of SGF, and for information to ZonMw, prior to the decision by the Health~Holland board. The Health~Holland Board does not assess the scientific content of the research proposals itself. The Health~Holland board bases its decision on the ranking of the research proposals and, if applicable, additional comments from SGF. The ranking established by the assessment committee is the primary starting point, however, the available budget for the Partnership programme may result in deviation from the advice of the assessment committee.

The motivation for the final decision will be sent to the applicants by Health~Holland. The Health~Holland Board may attach additional funding conditions to awarded projects. These conditions may relate to matters imposed by this call for proposals or conditions of the PPP Subsidy to SGF by Health~Holland, such as intellectual property, co-funding by (potential) users, major investments and/or special infrastructure facilities, accountability and financial reporting.

Applicants will be informed by Health~Holland by the end of April 2025 whether their application has been awarded funding or not. If the applications submitted do not score sufficiently, as defined in Section 4.8, the funders reserve the right not to deploy the entire PPP budget. The time schedule for the assessment procedure is given in Section 3.6.4 of this call.

5 Funded projects

5.1 Consortium agreement and PPP Subsidy Agreement

After the project award decision, the consortium agreement should be signed by all partners within eight weeks. Health~Holland receives and approves the final unsigned version of the consortium agreement before signing. Once the consortium agreement has been approved, Health~Holland and SGF will draw up a PPP Subsidy 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 Subsidy Agreement 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 Subsidy Agreement. Health~Holland will assess the plan as quickly as possible. The Partners will publish information about all projects awarded funding on the project page of its website. A layman's summary of the project for publication on this page should be submitted, together with the signed version of the PPP Subsidy Agreement.

5.2 First payment and monitoring

Once Health~Holland has received and approved the signed PPP Subsidy Agreement, the data management plan and the summary for the Health~Holland projects page, the first instalment of the PPP Subsidy can be disbursed. The remaining payments (up to 80% of the total awarded PPP Subsidy) will take place on an annual basis after a progress report has been received and approved. SGF will ask the main applicant for a progress report, upon which SGF coordinates the annual evaluation of the progress report in close collaboration with the partners. Health~Holland will pay the annual tranche upon approval of this evaluation process. The final tranche (20%) will be paid, if applicable, after approval of the final report.

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.

5.3 User committee

A User Committee should be established for the project by the main applicant, in which all consortium partners are represented including end users, such as patients, regulatory authorities and business consultants. In the application form, describe how you will involve (consult or collaborate with) stakeholders (industry, researchers, regulators, end users) in the project. This is to facilitate the implementation of the project results. The SGF and ZonMw should be invited to attend these meetings well in advance of the meeting. The User Committee meets at least once per year, preferably twice.

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.

5.4 Impact and dissemination plan

After the start of the project, a plan for impact and dissemination of the results needs to be formulated. The goal of this plan is to increase the social impact of the research and is expected to be formed in consultation with the user committee. More information will follow in the award letter.

5.5 Monitoring

SGF, ZonMw 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.

5.6 Programme days

SGF, Health~Holland and ZonMw will annually organize a human measurement models programme day for all the project consortia funded within the programme. The purpose of these days is to facilitate knowledge exchange, connection and stimulate validation and implementation of knowledge. Besides project presentations, the day might include workshops, interactive sessions or invited speakers in order to assist project consortia on the road to application of results. The attendance of each consortium on this day is expected.

5.7 Communication

At the request of SGF, ZonMw and Health~Holland, the consortia will cooperate in activities aimed at raising funding for research and/or providing information about research results. Before communicating about their project, the consortia will consult with ZonMw, SGF and Health~Holland to see if it is possible to communicate in common.

More detailed information will be provided in the PPP Subsidy Agreement.

6 Contact information

6.1 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 Subsidy and the associated conditions, please contact Health~Holland via tki@health-holland.com.

6.2 Downloads and links

All documents that are required for a full application can be found on the SGF website, including the following forms:

- **Application form**
- **Budget form**
- **Draft consortium agreement**
- **Letter of commitment**

Other important information can be found on these websites:

- **Knowledge and Innovation Agenda 2024-2027:** https://online.fliphtml5.com/gedjp/iwgv/#p=1
- **TPI website:** https://www.animalfreeinnovationtpi.nl/
- **Health~Holland:** https://www.health-holland.com/public-private-partnerships for more information about PPP

7 Appendices

Appendix A: About the Partners

SGF

The SGF consists of twenty-two independent public health organisations in the Netherlands that collectively address many of the most prevalent diseases in Dutch society. The SGF network was established in 2002 to streamline coordination and cooperation efforts across the foundations regarding commonly shared challenges. The **mission** of the SGF is to increase healthy life years for everyone living in the Netherlands. The SGF strives to make a difference on disease overarching themes such as prevention, quality of life and innovative treatments. To that end, the twenty-two foundations collaborate on research programs that aim to heal and treat different types of diseases, and to increase the societal impact of all efforts being made to improve overall health in the Netherlands.

The SGF is committed to stimulate animal-free research by investing in the development of human measurement models. These models use the human situation as starting point and are expected to act as better predictors than animal models in health care research, making the translation to an effective treatment easier and faster. Researchers are stimulated to look for human measurement models or find other animal-free innovations to test their hypothesis. Only if there is no non-animal alternative possible, research on animals is allowed, under the condition that the experiments comply with registry and publication guidelines that focus on maximizing quality and reliability of the research. More information can be found in the **vision** on animal research.

For more information about SGF and the aforementioned initiatives, please visit the website www.gezondheidsfondsen.nl.

Topsector Life Sciences & Health (Health~Holland)

Contributing to global societal challenges

The Dutch Life Sciences & Health (LSH) sector is one of ten “top sectors” in the Netherlands and part of the Dutch government’s Mission-driven Top Sectors and Innovation Policy. The top sectors are designated by the Ministry of Economic Affairs and Climate Policy and are selected on their ability to contribute substantially to global societal challenges.

Gaining economic and societal impact

Under the guidance of Top Sector Life Sciences & Health (Health~Holland) public and private partners combine nationally their investments and activities to gain economic and societal impact for Health & Care, one of the four challenges of the Dutch government's Mission-driven Innovation Policy. The common focus of the partners is formed by six Health & Care missions as formulated by the Ministry of Health, Welfare and Sport.

The central mission is as follows: By 2040, people in the Netherlands will live at least five years longer in good health, while the health inequalities between the lowest and highest socioeconomic groups will have decreased by 30%. There are five underlying missions that contribute to this central mission through changes to lifestyle and living environment, offering more care in the right place and better perspectives for people with chronic diseases, lifelong disabilities and dementia, and better protection against socially disruptive health threats. Furthermore, we support the economic opportunities within this societal theme.

Building on the strengths of the Dutch LSH sector

In order to realise its central mission, Top Sector LSH stimulates, facilitates and finances a variety of public-private partnerships (PPP's), thematic and programmatic collaborations between quadruple helix organisations. By attracting financial means, supporting businesses, sharing best practices and the

univocal (inter)national Health~Holland sector communication, the Top Sector builds on the strengths of the Dutch LSH sector.

ZonMw

ZonMw (The Netherlands Organisation for Health Research and Development) funds health research in the Netherlands and promotes the actual use of the knowledge this research produces. ZonMw promotes health research and care innovation throughout the entire knowledge chain from fundamental research to implementation. Through various subsidy programmes, we promote and fund development and practical application in the area of prevention improvement, care and health. The work field of the knowledge chain as a whole is broad, making ZonMw a unique organisation.

With regard to the call 'Human Measurement Models', ZonMw collaborates with the partners mentioned: NWO Domain AES, SGF and Top Sector LSH. ZonMw does so within the context of the funding programme 'More Knowledge with Fewer Animals'. This programme aims to develop new innovations free of animal testing and to encourage the use of existing innovations that do not use animal testing. The results of the projects funded under MKMD will also help with the development of new methods or models of safety and risk assessment. The ultimate aim is better and more relevant health and healthcare research for humans. For more info, see the webpage of the programme.

Within this context, funds committed by ZonMw for the current call 'Human Measurement Models' as described in this document, are exclusively intended and to be used for research projects that are free of animal testing and any other use of animals, preferably also without the use of Foetal Calf Serum (FCS).

Appendix B: Glossary

Animal testing: *(also referred to as animal research or animal experimentation).* This is the use of non-human animals in scientific experiments, aimed to control various factors that could affect the behavior or biological system being studied. Common purposes of animal testing are the research into basic biology and diseases, assessing the effectiveness of new medical treatments or testing the safety of consumer products. For more detailed information, please read Article 1 of the Wet op de Dierproeven. In this call, the use of invertebrates or slaughterhouse material is not permitted.

Consortium: Means a group of entities that work together on the research project as consortium partners, based on a clear and optimal division of tasks and risks, while retaining their own identity and responsibility. With respect to this programme, the consortium consists of at least two research organizations and one for-profit enterprise. Not-for-profit enterprises, foreign for profit enterprises and foreign research organizations are encouraged to participate in the consortium. Together, the consortium will prepare a project agreement.

Consortium partners: All project partners that contribute to the project by at least making an in kind contribution to the project (in the form of incurring payroll costs.

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.

Fundamental research: Experimental or theoretical research activities that are predominantly performed to gain new knowledge on the fundamental aspects of phenomena and observable facts, without the intent of achieving a direct commercial application or direct commercial use.

Human measurement model: human health research model which is based on human material or data. This includes human *in vitro* and *in/ex vivo* models (e.g. models based on human material/tissue/cell lines) as well as *in silico* models (e.g. models based on (big) data, systems biology and computational models).

In cash contributions: A contribution in cash from a consortium or another partner owed to one of the consortium partners to finance their R&D-related project costs.

Industrial research: Methodical research which is explicitly aimed at gaining new knowledge and skills with the intention of developing new products, processes or services, or to substantially improve existing products, processes or services. It encompasses the creation of parts for complex systems as well as the building of prototypes in a laboratory environment and/or an environment of simulated interfaces for existing systems, as well as pilot systems, when needed for the industrial research and in particular for validating generic technology.

In-kind contributions: In-kind contributions means capitalized personnel and/or material contributions from consortium partners. In kind contributions cannot be covered by PPP Subsidy.

Publication: The disclosure of results by any means, such as a text (including publications, abstracts, announcements on a website), illustration or an image or sound carrier, with the exception of disclosure resulting from a patent or patent application.

Reproducibility: A study is reproducible if someone re-analyses existing data using the same method

and thereby obtains the same results. This shows that the analysis was conducted fairly and correctly.

Small and Medium-sized Enterprises (SME): Enterprises which employ fewer than 250 persons and which have an annual turnover not exceeding EUR 50 million, and/or an annual balance sheet total not exceeding EUR 43 million as defined by the European Commission. For more information and if you want to determine whether your organisation qualifies as a SME, please visit this website.

Standardization: The process of achieving collaboration (interoperability) through (binding) agreements to achieve a shared goal. The agreements cover, for example, design, implementation, analysis, and reporting, which can be laid down in, for example, measurement standards, exchange standards and quality standards.

Technology Readiness Level (TRL): A system to determine the phase of technological development, from discovery phase (TRL 1) to deployment (TRL 9) of the product or service.

Total project costs: All costs that are directly related to the R&D activities within the project (eligible project costs).

Users: Means natural persons or legal entities that are able to use the results of the Project. Examples are: companies, NGO's, patient organisations, clinicians, authorities etc. Among the users, the consortium partners are included. However, the project may include more users who do not contribute in kind and/or in cash to the project.

Validation: Method validation is the process used to confirm that the analytical procedure employed for a specific test is suitable for its intended use. Results from method validation can be used to judge the quality, reliability and consistency of analytical results; it is an integral part of any good analytical practice.

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 Anne Burgers via burgers@proefdiervrij.nl.

Appendix D: Calculation examples of project budgets using PPP Subsidy

Calculation example 1 - Research organization and Dutch SME.

The calculation example assumes a project consisting entirely of industrial research.

Consortium partners	Costs
Research organization X	€ 600.000
Dutch SME Y	€ 400.000
Total	**€ 1.000.000**

Consortium partners	Max. % PPP Subsidy	Max. € PPP Subsidy
Research organization X	70%	€ 420.000
Dutch SME Y	60%	€ 240.000
Total	**66%**	**€ 660.000**

**Percentage of PPP Subsidy is calculated over the total cost of the partner in question.*

Minimal required contributions	% of total cost*	Minimal contribution (€)
Research organization(s)	10%	€ 100.000
Enterprises (for-profit and non-profit).	15%	€ 150.000
Open amount to be freely funded based on cost and minimum required contribution	***=€1.000.000 (cost) - €660.000 (max. PPP Subsidy) - €250.000 (min. contributions)***	**€ 90.000**

** Percentages for minimal required contributions are calculated over the total cost of the project.*

Funding per partner

Consortium partners	Total cost	In kind	In cash	PPP Subsidy
Research organization X	€ 600.000	€ 180.000	€ 0	€ 420.000
Dutch SME Y	€ 400.000	€ 160.000	€ 0	€ 240.000
Total	**€ 1.000.000**	**€ 340.000**	**€ 0**	**€ 660.000**

In this example, the open fundable amount of €90,000 is divided between the research organization and the SME, with both parties using their maximum allowable amount of PPP Subsidy.

Calculation example 2 - Consortium consisting of four parties

The calculation example assumes a project consisting entirely of industrial research.

Consortium partners	Cost
Research organization X	€ 500.000
Dutch SME Y	€ 150.000
Large enterprise Z	€ 250.000
Hospital A	€ 100.000
Total	**€ 1.000.000**

Consortium partners	Max. % PPP Subsidy	Max. € PPP Subsidy
Research organization X	70%	€ 350.000
Dutch SME Y	60%	€ 90.000
Large enterprise Z	0%	€ 0
Hospital A	0%	€ 0
Total	**44%**	**€ 440.000**

**Percentage of PPP Subsidy is calculated over the total cost of the partner in question.*

Minimal required contributions	% of total cost*	Minimal contribution (€)
Research organization(s)	10%	€ 100.000
Enterprises (for-profit and non-profit).	15%	€ 150.000
Open amount to be freely funded based on cost and minimum required contribution	***=€1.000.000 (cost) - €440.000 (max. PPP-subsidy) - €250.000 (min. contribution)***	**€ 310.000**

**Percentage of PPP Subsidy is calculated over the total costs of the project.*

Funding per partner

Partijen	Total cost	In kind	In cash	PPP Subsidy
Research organization X	€ 500.000	€ 125.000	(€ 25.000)*	€ 350.000
Dutch SME Y	€ 150.000	€ 60.000	€ 0	€ 90.000
Large enterprise Z	€ 250.000	€ 250.000	€ 50.000	€ 0
Hospital A	€ 100.000	€ 75.000	(€ 25.000)*	€ 0
Total	€ 1.000.000	€ 510.000	€ 50.000	€ 440.000

**The numbers in parentheses mean that these partners receive and use the private cash to cover part of their costs. In this case, the in cash contribution from the Large Enterprise is divided between Research Organization X and Hospital A.*

Appendix E: Evaluation scales

Utilisation

1 Excellent
• This will certainly lead to important new techniques or to very important applications in industry, society and other sciences.
• This research is urgently needed to make an estimate of the consequences of the use of this technology or technique.
• The utilisation is very well thought out and the approach ensures the greatest likelihood of an effective use of the results.

2 Excellent to very good

3 Very good
• This research will likely lead to important new techniques or to important applications in industry, society, or in other sciences.
• This research is highly desirable to make an estimate of the consequences of the use of this technology or technique.
• The utilisation is well thought out and the approach makes it plausible that the results of this work will be used well.

4 Very good to good

5 Good
• This work will possibly lead to new technologies or applications that might be useful for industry, society, or other sciences.
• This research will be needed to make an estimate of the impact of this technology or technique.
• The utilisation is sufficiently thought through, it can probably be improved during the execution of the work. The results of this work will probably be used.

6 Good to moderate

7 Moderate
• Technically this work could possibly be useful at some time or it is conceivable that in due course another science, industry or society or of the results could make use of it.
• The results of this research are not exactly awaited, but they may be useful in the future if an evaluation is made of the consequences of using this technology or technique.
• The utilisation is very unsatisfactory. This should certainly be improved, otherwise it is likely that the results of this work will not be used.

8 Moderate to poor

9 Poor
• Technically the work is bad and redundant, i.e. different, better or similar techniques, which are cheaper are already available.
• This study does not evaluate the consequences of using this technology or technique, moreover, it increases the confusion.
• The utilisation is completely wrong.

Scientific quality

1 Excellent
• An excellent researcher or outstanding research team.
• A well-chosen problem.
• The method is especially/pre-eminently effective and original.
• Very urgent.

2 Excellent to very good

3 Very good
• A competent researcher or competent research team.
• A significant problem.
• The method is original and effective.
• An urgent approach is important.

4 Very good to good

5 Good
• An average researcher or average research team.
• A routine problem.
• With the method, which has some original details, the project can be addressed, although other possibilities are conceivable.

6 Good to moderate

7 Moderate
• It is far from certain that this work is within the capacity of the researcher and / or the research team: the proposal itself contains no obvious errors.
• The problem is moderately interesting.
• Whether the project can be successfully tackled with this standard method, is questionable.
• The project may well be postponed.

8 Moderate to poor

9 Poor
• The competence of the investigator or research team is inadequate.
• The proposal contains serious errors or mistakes.
• This old method is not good for this project.
• Not to be executed, even if there is money left.