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 component 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 aiming 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 improvement..

Appendix B-I: Technology Readiness Levels

The Technology Readiness Levels (TRLs) indicate the maturity of a technology, ranging from basic principles (TRL 1) to a proven system in practice (TRL 9)**.** The scale is used internationally (e.g. by the EU and national funding agencies) to position innovations and determine the next steps towards market introduction.

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

Appendix B2: Ondersteuning *Technology Readiness Levels* voor bepaling type onderzoek

Let op: onderstaande richtlijnen zijn ter ondersteuning! Iedere aanvraag wordt op individuele basis beoordeeld; hierbij zijn de definities voor de drie typen onderzoek zoals gesteld door RVO in Appendix B1 altijd leidend.

Fase	TRL	Betekenis	Type onderzoek	Farma	Biotech	MedTech	ICT (AI)	Organ-on-Chip
Discovery	**1**	Fundamenteel onderzoek/ concept en ontwerp	Fundamenteel onderzoek (beperkt subsidiabel binnen de PPS-I regeling)	Biologisch principe/ Identificeren doelwit	Biologisch principe (enzym, *pathway*, biomarker) ontdekt / conceptueel platform beschreven	Klinische behoefte en technisch concept in kaart gebracht	Probleemdefinitie en opzetten *data dictionary*	Specificeren micro-omgeving, celtypes, *microfluidic layout*. Eerste CAD-ontwerpen
	2			*In vitro* tests resulterend in een experimenteel *proof-of-concept* *Target Discovery* en *Hit Identification* worden geclassificeerd als fundamenteel onderzoek (TRL 2 en/of 3)			*Proof-of-principle* en de ontwikkeling van het systeem zonder directe toepasbaarheid (TRL 2 en 3) Het ontwikkelen en testen van het *framework computational model* (model heeft nog geen specifieke taak en/of toepassing)	
	3	Toetsing (*proof-of-concept*)			Eerste haalbaarheidstesten resulterend in een *proof-of-concept* / eerste werkende assay-prototype	Proof-of-concept van de technologie nog zonder toepassing; lab-prototype op basale veiligheid/functietests		Eenvoudige in vitro *proof-of-concept* opstelling ter verificatie van barrièrefuncties en transportprocessen
Development	**4**	Implementatie en test prototype	Industrieel onderzoek (subsidiabel binnen de PPS-I regeling)	Verdere *in vitro* en *in vivo* studies om veiligheid en werkzaamheid aan te tonen *Hit-to-Lead conversion, Lead Optimization* en verder preklinische onderzoek tot aan de start van Fase I klinisch onderzoek wordt geclassificeerd als industrieel onderzoek (TRL 4 t/m 6)	Verdere preklinische studies *in vivo*/diermodellen om reproduceerbaarheid, veiligheid en werkzaamheid aan te tonen vallen onder de definitie van industrieel onderzoek.	De studies benodigd om *PoC* om te zetten tot een *minimum viable product*, inclusief eerste technische tests en gebruikstest voor veiligheid. Hieronder vallen o.a.: - Prototypeontwikkeling - Technische validatie - Eerste *usability study*	Toepasbaarheid-gedreven ontwikkeling valt binnen TRL4. TRL 4 t/m 6 bevat de verdere ontwikkeling van de (*machine learning*) technologie naar een productvorm, inclusief de applicatieontwikkeling.	Prototype fabricatie: Fysiek prototype met geïntegreerde basale sensoren
	5	Validatie prototype						Lab validatie: Meerdere celdonoren; meten van fysiologische parameters onder *flow*
	6	Demonstratie prototype in testomgeving		Fase 0 studies vallen binnen TRL6, zolang de studie niet gericht is op het bestuderen van het klinische effect (bv. farmacokinetiek)	Demonstratie functioneel prototype in een relevante testomgeving	*Usability studies* vallen onder TRL6 wanneer dit plaatsvindt in een gecontroleerde omgeving ((living) lab of testomgeving)		Optimalisatie: Verfijning extracellulaire matrix-coatings en *flow-parameters*; verhoogde levensduur en reproduceerbaarheid
Demonstration	**7**	Demonstratie prototype in operationele omgeving	Experimentele ontwikkeling (subsidiabel binnen de PPS-I regeling)	Fase I en II klinische studies worden beoordeeld als experimentele ontwikkeling (TRL7)	Opschaling Fase I en II klinische studies worden beoordeeld als experimentele ontwikkeling (TRL7)	(Pilot)studies in de operationele/realistische setting, t.b.v. klinische effectiviteit/waarde, inclusief bewijslast t.b.v. compliantie aan regelgeving. Verdere klinische studies	Start van de demonstratiefase Integratie van het product in bestaande systemen, inclusief het testen in een realistische setting	Validatie met *test-set reference compounds* (en relevante humane cellen); Simuleren van pathologieën
	8	Compleet en operationeel product/ dienst	**Niet** subsidiabel binnen de PPS-I regeling	Fase III klinische studies en verdere ontwikkeling	Fase III klinische studies en verdere ontwikkeling	Opschaling en regulatoire goedkeuring Volledig ontwikkeld product	Opschaling en regulatoire goedkeuring	Reproduceerbaarheidstest in meerdere laboratoria. Ontwikkeling gestandaardiseerde testprotocollen
Deployment	**9**	Marktintroductie product/dienst		Marktintroductie	Marktintroductie	Marktintroductie	Marktintroductie	Marktintroductie

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Appendix C: HH-tool National Technology Strategy

National Technology Strategy: Definitions key technologies

Key technology	Definition (NTS)
Biomolecular & cell technologies	*Biomolecular and cell technologies fall within the broader field of biotechnology, but the focus here is on molecules and cells. This key technology includes mapping, measuring and using molecules such as DNA, RNA, and proteins/metabolites. Sub-technologies include omics, gene editing, stem cell technology and synthetic cell technology.*
Imaging Technology	*Imaging technologiesdeal with the generation, collection, duplication, analysis, modification and visualisation of images (optical and non-optical). They involve the integral chain of imaging, requiring both hardware and software. They are widely used in the medical sector, semiconductor industry, security domain, agriculture, industry, traffic and aerospace.*
Artificial Intelligence & Data	*Artificial Intelligence (AI) is a systems technology aimed at realising behaviour by machines that resembles natural intelligence. Data science, data analytics and data spaces concern all aspects of collecting, managing, accessing, sharing and analysing data to create value.*
Optical Systems & integrated photonics	*Optical systems are engineered systems to refract, reflect or manipulate light to perform particular optical functions. For example, communication is possible using photons as information carriers.* *Integrated photonics is the technology that integrates various photonic functions (generation, modulation, sensing, etc.) in a functional photonic chip.*
Mechatronics & optomechatronics	*Mechatronics involves the integrated design of mechanical systems and associated control and regulation systems and combines physics, mechanical and electrical engineering, and ICT.* *Optomechatronics involves the integration of optical technology into mechatronic systems. Optomechatronic systems play an important role in semiconductor manufacturing, scientific instruments, 3D printing, medical equipment, aerospace and robotics.*
Semiconductor technologies (Microelectronics)	*Semiconductor technologies concern semiconductor components and/or highly miniaturised electronic subsystems and their integration into larger products and systems. They include the fabrication, design, packaging and testing of semiconductor components into microscale systems that integrate multiple functions on a chip and the development of machines for this purpose.*
Quantum technologies	*Quantum technologies utilise the dual nature of the smallest particles we know, such as photons, atoms and electrons, as well as similar systems that exhibit quantum properties. They facilitate the quantum computer, quantum communication and quantum sensing, which can be used to find solutions to complex problems.*
Cybersecurity technologies	*Cyber security technologies focus on the reduction of relevant digital risks, also including dealing with risks of damage or failure of digital systems and the availability, integrity and confidentiality of data. They are aimed at preventing cyber incidents and - when cyber incidents have occurred - detecting them, mitigating damage and making recovery easier.*
Process technologies, including process intensification	*This key enabling technology focuses on the optimal, stable and safe design of (green) chemical production processes. This includes matters such as: scalability, heat integration, safety, optimal downstream processing, space utilisation and cost efficiency. We want to make more use of sustainable raw materials, reduce by-products and waste streams and reuse and recycle them as much as possible.*
Energy materials	*Energy materials comprise all materials that facilitate the storage of (sustainably generated) energy, transport it, efficiently capture and transform it into another form of stored energy. They make an essential contribution to the energy and climate transition, for example in wind turbines, batteries or electrolysers.*

Appendix D: Definition of enterprise

English

According to established case law from the European Court of Justice, an enterprise is any unit that carries out economic activity irrespective of its legal status and manner of funding.

In this regard, the following points are important:

- The legal status (e.g. a private company or a foundation) of the entity is not decisive;
- A for-profit status is not required, competition on the market is sufficient (economic activities). This means that the entity participates in economic dealings and that there is business funding. Business funding means that the funding cannot consist entirely of grants, gifts and endowments. A turnover needs to be made and there has to be income from economic activity. *Please note: Startups/businesses fully funded by capital investments are not required to generate turnover yet;*
- An entity that carries out both economic and non-economic activities will only be designated as an enterprise with respect to the economic activities;
- The European Court of Justice has further determined that entities that (legally or de facto) fall under the authority of the same main entity should be viewed as a single enterprise;
- ANBI: Having a Dutch ANBI or charitable status (serving the common interest, no profit-making status, 90% rule) means that such an entity with ANBI status cannot also be an enterprise. That is because an entity with ANBI status enjoys fiscal advantages that a business does not enjoy.
- Foundations**:** A foundation can never be a for-profit enterprise, as pursuing profit is legally incompatible with the legal form of a foundation. If the foundation engages in economic activities, it may be regarded as a not-for-profit enterprise.

With respect to economic activity, the following aspects are, amongst others, considered in line with the Dutch Tax and Customs Administration:

- Registration with the Dutch Chamber of Commerce (KvK);
- Having a Dutch VAT (BTW) number and/or corporate income tax (VPB) number;
- Goods and/or services are delivered;
- The remuneration received for these is more than symbolic;
- The entity participates in the economic arena and enjoys income from this.

Nederlands

Volgens vaste rechtspraak van het Europees Hof van Justitie is een onderneming elke eenheid die een economische activiteit uitvoert ongeacht haar rechtsvorm en wijze van financiering.

Hierbij zijn de volgende punten van belang:

- De juridische status (b.v. BV, NV of stichting) van de eenheid is niet doorslaggevend;
- Er is géén winstoogmerk vereist, concurrentie op de markt is voldoende (economische activiteiten). Dit houdt in dat er wordt deelgenomen aan economisch verkeer en er ondernemingsfinanciering plaatsvindt. Ondernemingsfinanciering betekent dat de financiering niet volledig kan bestaan uit subsidies, giften en schenkingen. Er zal omzet en inkomsten uit economische activiteit moeten plaatsvinden. *Uitzondering: Startups/bedrijven die volledig worden gefinancierd door kapitaalinvesteringen hoeven nog geen omzet te genereren;*
- Een eenheid die zowel economische als niet economische activiteiten verricht, wordt alleen met betrekking tot de economische activiteiten aangemerkt als onderneming;
- Het EU Hof van Justitie heeft verder bepaald dat entiteiten die (juridisch of feitelijk) onder de zeggenschap staan van dezelfde entiteit, als één onderneming dienen te worden beschouwd.
- ANBI-status: Het hebben van een ANBI-status (algemeen belang dienen, geen winstoogmerk, 90% regel) sluit uit dat een entiteit met ANBI-status ook een onderneming is. Een entiteit met ANBI-status geniet namelijk fiscale voordelen welke een onderneming niet heeft;
- Stichtingen: Een stichting kan nooit een onderneming *met* winstoogmerk zijn, omdat het voeren van een winstoogmerk juridisch onverenigbaar is met de stichtingsvorm. Indien de stichting economische activiteiten verricht, kan zij mogelijk aangemerkt worden als onderneming zonder winstoogmerk.

Bij economische activiteit wordt, in lijn met de Belastingdienst, onder andere gekeken naar:

- Inschrijving KVK;
- Het hebben van een BTW-nummer en/of VPB-nummer;
- Er worden goederen en/of diensten geleverd;
- Hier staat een meer dan symbolische vergoeding tegenover;
- Men neemt deel aan het economisch verkeer en daar komen inkomsten uit.

Appendix E: European Commission Recommendation 2003/361/EC regarding SME definition

Engels

The European Commission's Recommendation 2003/361/EC, adopted on 6 May 2003, provides a standardized definition of Small and Medium-sized Enterprises (SMEs) across the European Union. This harmonized framework ensures consistency in eligibility for support programs, regulatory exemptions, and statistical reporting. The criteria are based on three main factors: **staff headcount**, **annual turnover**, and **annual balance sheet total**.

The classification of SMEs is as follows:

> **Micro-enterprises** are defined as enterprises that employ fewer than 10 persons and whose annual turnover or annual balance sheet total does not exceed EUR 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 EUR 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 EUR 50 million, or an annual balance sheet not exceeding EUR 43 million.

For more details 'The revised User Guide to the SME definition' can be downloaded here.
Or use the European SME Wizard.

Health~Holland may verify the outcome of the self-assessment questionnaire using the three main criteria: staff headcount, annual turnover, and annual balance sheet total.

Nederlands

De Aanbeveling 2003/361/EG van de Europese Commissie, vastgesteld op 6 mei 2003, bevat een gestandaardiseerde definitie van het midden- en kleinbedrijf (MKB) binnen de Europese Unie. Dit geharmoniseerde kader zorgt voor consistentie bij de vaststelling van de voorwaarden voor steunprogramma's, vrijstellingen in regelgeving en statistische rapportages. De criteria zijn gebaseerd op drie hoofdindicatoren: aantal werknemers, jaarlijkse omzet en jaarlijks balanstotaal.

De indeling van MKB-ondernemingen is als volgt:

> **Micro-ondernemingen**: ondernemingen met minder dan 10 werknemers en een jaaromzet of balanstotaal van maximaal €2 miljoen.
>
> **Kleine ondernemingen**: ondernemingen met minder dan 50 werknemers en een jaaromzet of balanstotaal van maximaal €10 miljoen.
>
> **Middelgrote ondernemingen**: ondernemingen met minder dan 250 werknemers en óf een jaaromzet van maximaal €50 miljoen, óf een balanstotaal van maximaal €43 miljoen.

Voor meer informatie kan de Revised User Guide to the SME definition worden geraadpleegd.
Daarnaast kan gebruik worden gemaakt van de European SME Wizard.

Health~Holland kan, indien nodig, de resultaten van de zelfevaluatie controleren aan de hand van de drie hoofdcriteria: aantal werknemers, jaaromzet en balanstotaal.

Appendix F: Conflict of Interest

This Appendix is also available in Dutch and can be requested by sending an email to tki@health-holland.com

1. Introduction and Legal Framework

According to Articles 29.d and 30.c of the Framework, applicable to the PPP Subsidy regulation, research organisations must receive remuneration equivalent to the market price for the intellectual property rights generated during the project. The absence, or inadequacy of agreements pertaining to a remuneration based on the market price leads to the indirect granting of state aid to the participating industrial parties.

'Remuneration equivalent to the market price' entails a best-effort obligation for the parties involved. It means that the research organisation and the participating industrial parties are expected to actively negotiate this remuneration on so-called 'arm's length' terms – conditions that reflect what would reasonably be agreed upon between unrelated parties in a competitive, commercial setting. Any transaction resulting from an open, transparent and non-discriminatory procedure will be deemed to comply with the arm's length procedure.

2. Definition of Conflict of Interest (COI)

Every project has the potential for a conflict of interest between the research organisation and one or more industrial partners. A conflict of interest can exist on a personal (individual) level or on an organisational (institutional) level. An objective conflict of interest exists when a situation has the potential to create undue advantage or disadvantage – regardless of whether harm or benefit actually occurs. The presence of a conflict of interest means that the arm's length conditions are potentially not met.

Conflict of Interest often arises when financial interests are present that may influence the objectivity of decision-making or project execution. Examples of financial interest may be: the PI or its direct family member have shares, options and/or other participation in any of the industrial participant(s); a participating company is a recent spin-off from the research organisation with, for example, overlapping personnel, shared IP rights, or ongoing financial interests

Individual Conflict of Interest: *An individual conflict of interest arises when a person's personal interests — such as financial gain, intellectual property rights, or family ties — have the potential to influence their professional responsibilities and objectivity within the project*.

Examples, but not limited to:

- A researcher, for example, the Principal Investigator (PI), working on the project holds shares in or has a formal role (founder, advisor, or board member) within a (spin-off) company participating in the consortium.
- A researcher receives royalty payments from a patent licensed to an industrial partner within the consortium.
- A project member has been paid over €10,000 in consulting fees by a partner company in the last year.
- A researcher is employed by both the research institution and a company in the consortium.
- A close relative of a researcher is a shareholder or executive at one of the participating industrial partners.

Institutional Conflict of Interest: An institutional conflict of interest occurs when an organisation involved in the project has financial, structural, or governance-related ties to another participating organisation, which could affect objective project decisions or create preferential outcomes.

Examples, but not limited to:

- A participating company is a recent spin-off from the research organisation, with, for example, overlapping personnel, shared IP rights, or ongoing financial interests.
- A research organization and a participating industrial partner share employees, board members or management.
- One consortium partner holds equity in another partner without being a formal affiliate.
- An industrial partner funds sponsored research in the same department that is executing the PPP project.
- Decision-making authority within the consortium is disproportionately influenced by a single institution.

It is up to the parties concerned – and in particular the directors of the participants – to recognize, interpret and report such an objective conflict of interest. This obligation to report may already exist at the time of the application being made.

3. Identifying Conflicts of Interest

To help identify potential conflicts of interest, the following questions can be used as a reference. These are not exhaustive but aim to prompt transparent disclosure.

3.1 Individual potential COI

- Is any individual involved employed by both (one of) the research organization(s) and (one of) the industrial partner(s)?
- Does the Principal Investigator (PI) in the project have any financial interest in (one of) the industrial participant(s)? If so, how many shares, options and/or other financial benefits do the PI (or the relatives) have rights to?
- Does any other investigator(s)/employee(s) of the research organisation have any financial interest in the industrial participant(s)? If so, how many shares, options and/or benefits do the investigator (or the relatives) have rights to?
- Have the PI or their immediate relatives received financial benefits (e.g. shares, patent rights, consultancy fees) from any industrial participant(s) involved in the project?
- Does the Principal Investigator (PI) have an inventorship role in a patent that has been licensed to, or is being developed by, a participant in the project?
- In the last 12 months, did any commercial entity or any of the entities that are participating in the project pay for or reimburse you (your employer, or your relatives) for consulting services, salaries or otherwise? If, so does such payments exceed €10.000 per year? If so, will the company in question benefit from the outcome of the Project?

3.2 Institutional potential COI

- Are any of the consortium partners in the project affiliated or associated with another consortium partner in the project? If so, how?
- Does any consortium partner have directly or indirectly any shares, options and/or any other participation in another consortium partner despite not being an affiliated entity? If so, how many shares, options and/or participations?
- If the financial interest as stated in the two points above does not apply, would a consortium partner exercise any control over any of the other consortium partners' decision-making? If so, how?
- In the last 12 months, did any Industrial partner in the Project pay for or reimburse any sponsored research or services to the Research Organisation(s) to the same research group(s) involved in the Project? If, so does such payments exceed €10.000 per year? If so, will the company in question benefit from the outcome of the Project?

4. Reporting Obligations

Upon identification of a (potential) conflict of interest, the Program group must be notified immediately. This includes situations already present at the time of application.

The following questions must be answered **in a separate document:**

- What is the nature of the potential conflict of interest? Please use the questions in 3.1 and/or 3.2 to describe the nature of the potential COI.
- Have the involved participants, including relevant directors, adequately weighed the interests?
- Has the potential conflict of interest been adequately addressed?
- Is there a transparent procedure in place to ensure that the participants, PI's, researchers or directors can abstain from involvement in certain decisions (which may involve a conflict of interest)?
- How are the arm's length conditions adequately met?
- Has the participant/director provided for the involvement of other researchers who can make these decisions without bias?
- Can the director involve his or her fellow director(s) in the decision-making process and is it possible in the management relationship for the director concerned to abstain from making management decisions (four eyes principle)?

The responsibility for answering these questions rests exclusively with the consortium partners. This means that the consortium parties involved have to assess whether and to what extent the potential conflict of interest has been adequately addressed and whether they are satisfied with the precautionary measures that the director(s) concerned have taken.

5. Role of Program group and Health~Holland

The Program group, and by extension Health~Holland, will not subjectively evaluate the conflict of interest. The Program group will assess whether the performance of the consortium will be hindered or compromised by the existence of such a potential conflict of interest. The Program group, and by extension Health~Holland, will therefore require full transparency if and when an objective conflict of interest arises or is likely to arise.

If, as a result of a conflict of interest, situations occur that violate the arm's length conditions, the consortium parties are liable for any resulting damage, including implications of indirect state aid.

6. Legal Support

For the sake of completeness, Health~Holland recommends involving legal support from the consortium partners, preferably from the research organisation, in order to adequately address a potential conflict of interest.