

Review of TPI

**Self-evaluation of the
acceleration programme
Transition Programme for
Innovation without the
use of animals (TPI)**

**2018
2020**



Contents



Management
summary



Introduction



The effort to
accelerate the
transition



Measuring the
acceleration



Directing the
acceleration of
TPI



Conclusions and
recommendations
for a follow-up

1 Introduction	10
The effort to accelerate the transition	12
2.1 The ambition, philosophy and method of TPI	13
2.2 Results of the TPI approach	14
2.3 The recommendations predating TPI were taken to heart	19
2.4 The partners look back on a special process	21
3 De versnelling gemeten	22
3.1 Accelerating is mainly done together	23
3.2 The transition is in a phase of pre-development	25
3.3 Process indicators show the movement	29
3.4 The ambition has been achieved: TPI is an international frontrunner	31
4 Directing the acceleration of TPI	32
4.1 Funding	33
4.2 The cooperating TPI partners	34
5 Conclusions and recommendations for a follow-up	39
The Netherlands is an international frontrunner in open dialogue	39
The transition has entered a phase of pre-development	39
Follow-up recommendations: going in-depth, embedding and broadening	40
Appendix: References	44

Management summary

TPI is a programme that seeks to accelerate the transition to innovation without the use of animals by encouraging alternatives and innovations. The partners Health-Holland, NFU, RIVM, SGF, the Dutch Society for the Replacement of Animal Testing, VSNU, ZonMw and the national government – with the Ministry of Agriculture, Nature and Food Quality (LNV) as director and the Royal Netherlands Academy of Arts and Sciences and NCad as observers – are cooperating on the ambition of 'the Netherlands as a frontrunner in the international transition of innovation without the use of animals'. The mission is to develop alternative models and tests that better predict the effectiveness and safety of medicines and substances, thus making animal procedures increasingly redundant.

In 2018, the TPI partners set up a guiding Core Group and a coordinating Transition Group for TPI. Directors and staff of the Ministries involved hold interdepartmental consultations, referred to as (D)IWAD, on alternatives for animal procedures. In the present self-evaluation, the cooperating TPI partners answer the question of whether they have fulfilled their promises made in 2018, whether the transition has been accelerated, what its current situation is, and whether the Netherlands is an international frontrunner. Based on this, conclusions and recommendations are given on what is needed to continue the TPI programme.

Result 1:

The TPI partners together have a lot of impact and organisational power

A spectrum of networks, projects and initiatives for innovation led to the exchange of knowledge among pioneers in the chain, and to the empowerment of various stakeholders working on animal-free innovation. At a national meeting in March 2019 stakeholders contributed their own agenda items, and an international conference in November 2019 saw an open dialogue with a large number of stakeholders about ownership, trust and confidence in alternative models and corporate opportunities. Tools were developed for promoting open discussion and, in its wake, innovation. What has been most striking are the so-called helpathons. These are intensive brainstorming sessions about specific cases, guided by the auxiliary question: Assuming you are not allowed to carry out animal procedures, how could this research still be done? Further, there is the television channel TPI.tv, a learning network on the Internet for the exchange of knowledge among professionals. Various partners actively sought to collaborate and even pooled resources in a number of calls for animal-free research, something that was not happening before TPI. The call for Humane Measurement Models was included in the knowledge and innovation covenant of the Health & Care societal theme for mission-driven innovation policy.

Result 2:

There is now a strong network in which there is an open dialogue

At the outset, the TPI partners deliberately chose to shift the focus from reducing animal procedures to building up alternatives. This allowed animal-free innovation in a broad sense to be discussed, as well as enabling cooperation between stakeholders with different interests and focus areas from very different research domains, target sectors, technologies and policy dossiers.

The TPI partners also deliberately opted for a philosophy and method for the open exploration of animal-free innovation avenues. This was needed in view of the complexity and large number of actors in the field of animal procedures. Accordingly, many different areas of expertise are involved in the conversation. This is initially confusing and demands an effort on the part of those involved in the conversation, but it consistently proves to be enriching. The open dialogue with a variety of stakeholders from the relevant sectors and research domains can provide an overview of and insight into options for animal-free innovation.

The open dialogue between stakeholders from the entire chain – not just the usual suspects – creates space for nuance. The combination of various points of view also increases the likelihood of innovation. Moreover, using data from various methods – in vitro (Petri dish) and in silico (computer) in interaction with in vivo (animal model) – creates a foundation for the development and acceptance of alternative models and safety tests.

Result 3:

A direction with promising transition routes was found

The open search has since led to a direction to follow. Under the leadership of the Dutch Research Institute For Transitions (DRIFT) and in cooperation with a number of innovators from the TPI network, two promising transition routes were identified: a) the personalisation of healthcare (personalised medicine), and b) safety assessment based on knowledge about human beings (from in-vitro and in-silico methods). These have broad support. The TPI partners are still busy fleshing out the steps to take in following these two transition routes, but they see the end goal increasingly clearly: a solid translation into better predictive models.

Conclusion 1:

As a director among stakeholders, the Netherlands is an international frontrunner

The Netherlands is ahead of other countries in putting the philosophy and method of the cooperating TPI partners into practice. The open dialogue this generates, with a variety of stakeholders from the entire chain and from different sectors and domains, is special. Other countries have not yet taken this approach. What is especially innovative is that the government, in this case LNV, acted as director of the transition's acceleration. The Dutch approach has since attracted the attention of various stakeholders from abroad.

Conclusion 2:

The transition has entered a phase of pre-development

TPI, we find, has effectively fomented the transition using tools for an open dialogue. All sorts of things are happening, there are energised networks and there is pressure to change. What is important now is to have a breakthrough in the system that leads to the actual implementation of the alternatives. According to DRIFT, transitions usually take one or two generations, and the transition to animal-free innovation is now in the phase of pre-development. The TPI partners agree.

Recommendation:

Going in-depth, embedding and broadening

Going forward, the TPI partners state they would like to:

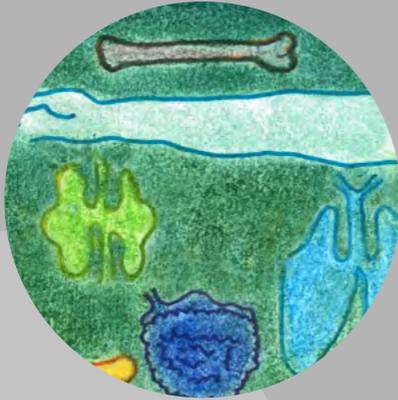
- see a subtitle referring to the importance of developing humane measurement models, so that the shift from animal procedures to humane knowledge is clear from the title;
- enter into a dialogue with more scientists, more large companies and more regulators from the EU: what are their choices and considerations?
- look for additional resources to develop humane measurement models rather than redirecting funding flows for animal procedures;
- request greater involvement from other Ministries, in particular those of Health, Welfare and Sport and of Education, Culture and Science.

It is important for the TPI partners to shift from an open search to a focused search:

- *going in-depth* with regard to current alternative and innovative practices;
- *embedding* existing animal-free possibilities in policies and guidelines;
- *broadening* the dialogue to include more scientists and researchers who deal with animal procedures, and to the general public.

While openness, organisational power and vision were in evidence and there was good and pleasant cooperation, the composition of the network could be improved. The development of medicines is the predominant angle in the current Core Group and Transition Group. In the coming months, the TPI partners will be collaborating on a concrete, subject-specific follow-up agenda for TPI. On the basis of this agenda it can be decided how the partners will organise themselves and what support on the part of the government is needed to further accelerate the transition.

1



Introduction

TPI is a Transition Programme for Innovation without the use of animals. TPI stands for substance, but also for cooperation among partners. This evaluation discusses both the substance of the acceleration programme and the cooperation. At the start of the acceleration programme, the collaborating partners explicitly decided on the philosophy and method of TPI and deliberately avoided setting specific goals and milestones. As a result, this evaluation of the TPI programme is a self-evaluation of the method of the TPI partners and the programme agency.

'The fact that not much was committed to in advance benefited creativity and cooperation.'

Wouter Dhert VNSU, University of Utrecht

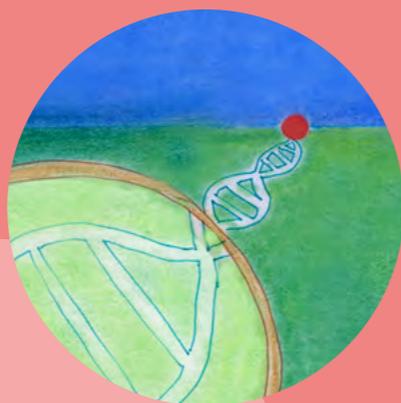
The TPI programme agency carried out the evaluation based on bilateral conversations with all TPI partners: the Core Group and Transition Group members, and the policy officers and directors of the Directorates involved in TPI at various Ministries (see Section 4.2 for the composition). This was done by asking them about the activities thus far, asking what they estimate has been accelerated, and asking about the collaboration between the TPI partners.

This makes this self-evaluation a collective review of the period from June 2018 to October 2020. The evaluation has two aims: to account for what has been accomplished and to learn lessons for the future. The results of this evaluation will be used when deciding on the follow-up of TPI after 2020.

Structure of the document

First, the TPI partners' document 'Philosophy & method' is revisited, with a description of how the partners look back on the activities that took place. As a baseline measurement, we will look at what was done with recommendations from documents that formed the foundation of TPI. Following this description of the efforts made, the partners estimate whether the activities have led to acceleration, followed by the opinion of DRIFT transition experts as to the current situation of the transition. Next, the acceleration is measured by transition process indicators: the formation of new approaches, new connections and a shared vision. The key question is whether the ambition has been fulfilled: in what respects is the Netherlands a frontrunner? Lastly, we describe how the partners look back on their collaboration.

2



The effort to accelerate the transition

On 1 June 2018, TPI began formally with the publication of an initial Letter to Parliament. In this letter, Minister Schouten set out how she and a group of partners would go about accelerating the transition to animal-free innovation. A guiding Core Group and an operational Transition Group were set up in which the partners are represented.

'I will accept the governing role in this transition process, but I must be realistic: I definitely cannot do this alone. Both in the Netherlands and on the international stage, we need to pool our strengths, knowledge and influence.'

Carola Schouten, ministry of Agriculture, Nature and Food Quality

2.1 The ambition, philosophy and method of TPI

The Core Group of TPI partners considered that the ambition formulated by then State Secretary Martijn van Dam in 2017 needed adjusting. For example, the objective of 'the Netherlands as an international leader in animal-free innovation in 2025' became the joint ambition of Minister Schouten and the TPI partners of 'the Netherlands as a frontrunner in the international transition of innovation without the use of animals'.

This adjusted ambition, without a target year and using the term frontrunner instead of leader, is more realistic. The emphasis in the acceleration programme was placed on building up alternatives rather than on reducing animal procedures. The rationale was that all stakeholders, from activists to researchers, would be able to support and cooperate with this. As a result, it was possible to cooperate with a broad range of stakeholders with a variety of interests, focus areas and bodies of knowledge.

'We saw a switch from an activist file to a formational file.'

Nico van Meeteren, Health Holland top sector LSH

TPI Philosophy and Method (June 2018)

For the purpose of the open search the partners drew up the document 'Philosophy & method', sent as an appendix to the Parliamentary Letter.

It states that TPI:

- looks for a viable route towards possible solutions, rather than following a predetermined route;
- accelerates the transition to options for animal-free research and testing;
- uses transition experts to support innovation networks in which leaders, interested parties and relevant stakeholders explore and shift their range of actions;
- searches for new insights across the entire chain, that is: involving knowledge institutions, the business community, NGOs and governments. It is about acquiring new technical insights, such as the development of humane measurement models, and process-related insights, such as new ways of funding and regulating;
- has an international context with international legislation and regulations, decision-making forums, science and research;
- is interdepartmental, with consultations involving the Interdepartmental Working Group on Alternatives to Animal Testing (IWAD) and directors of relevant policy directorates at six ministries in the Netherlands.

'For LNV it is exciting to facilitate this transition in a field with many interests. Pioneering a transition approach outside of the regular system is really a different way of working'

Lieke Hendrix, ministry of Agriculture, Nature and Food Quality

2.2 Results of the TPI approach

In a political context, evaluation mainly means accounting for what one has done. Accordingly, in this evaluation we want to examine the specific outcomes of the 'viable route' approach. This question is answered below by way of the effort indicator: which activities were developed under the flag of TPI? What effects did they have in a communicative, financial, regulatory and management sense?

The activities of TPI

The recent TPI progress report for 2020 sent to Parliament describes the actions taken under the flag of TPI. The actions are carried out by learning innovation networks and as part of innovation projects.

'In these innovation networks, leaders and interested parties in the chain explore how methods that are free of animal testing can be developed and accepted. They look at the content, process and/or system and develop experimental ideas.'

Philosophy & method, TPI partners 2018

According to the progress report, a central thread running through the activities carried out under the flag of TPI is the combination of data from different technologies for alternative methods, both in vitro (Petri dish) and in silico (computer). Multidisciplinary scientific research, including biomedical science, toxicology and data science, is also considered promising. Change management methods such as the open-space dialogue and the helpathons proved effective in enabling stakeholders and professionals from different domains to contribute their own agenda items, to have fruitful conversations and to cooperate.

Communication for empowerment and exchange

As to communication, animal-free innovation has become an issue that is open to discussion in the various networks and initiatives. This required those involved to step outside of their comfort zone; fortunately, many different stakeholders were able to do so. Many partners see exchange across the entire knowledge chain and using different angles, methods and research domains as key for achieving animal-free innovation.

The target situation for education being developed, as well as initiatives such as the recently started TPI Utrecht, increases the options for dialogue among scientists as well. In addition, sharing data is considered essential. With TPI.tv a start has been made to match the supply and demand of information, knowledge and data by way of an online platform.

'TPI is important to have other predictive models generate more new data and to allow more available data to be.'

Jurgen Mook, Ministry of Social Affairs and Employment

This communication is particularly supported by the 'helpathon' tool that was developed and that, in view of the COVID-19 pandemic, was given a hybrid format with a crew that meets in person as well as online participants. This tool offers an intensive session in which specific research cases are helped ahead using an auxiliary question: Assuming you are not allowed to carry out animal procedures, how could your research (e.g., into the deepening of burns) still be done adequately? The helpathon also offers general lessons: as a researcher, evaluate with others when the results you have obtained could be applied before you decide on follow-up research.

'It becomes possible to bring forward the step of applying your research results to people.'

Case owners from helpathon #2 at the Dutch Heart Foundation in 2019

International attention

With regard to the international situation, at the pioneer2policymaker conference guests from abroad said that they found TPI's chain approach to be a strong one, and that our government acting on this issue is an eye-opener.

'The international conference received enthusiastic feedback. The participants from other countries admired the conversation taking place between all of the various relevant stakeholders. They admired that this conversation is going well.'

Saskia Aan, Dutch Society for the Replacement of Animal

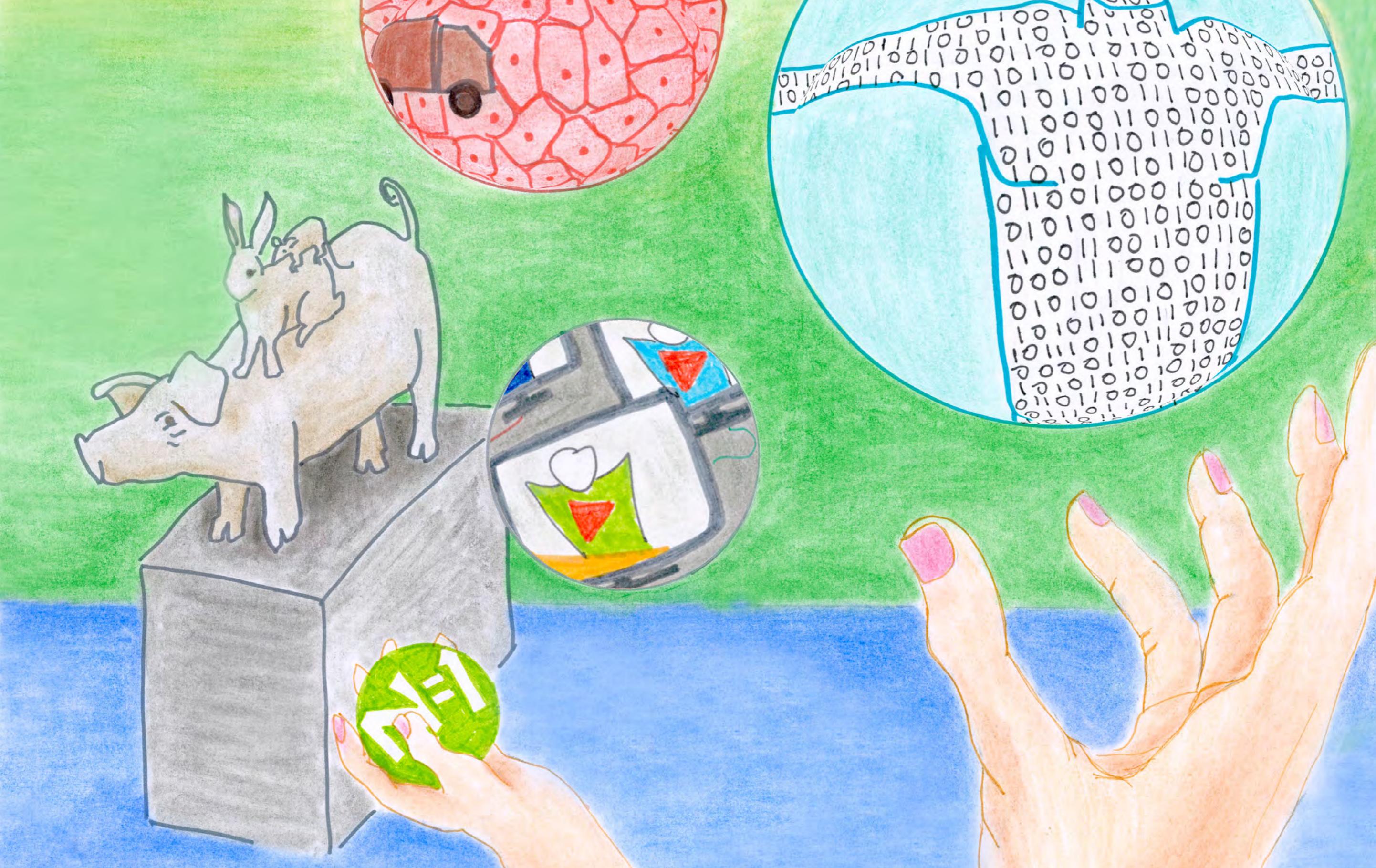
The TPI network was broadened during the international conference. New connections were made with interested parties in the chain. The attendance gave one indication of the international interest: there were over 190 participants, of whom one third came from 15 different countries. They represented research, research funding, large companies, start-ups, governments, risk assessors and NGOs. Invitees also took part in the 2020 helpathons. In addition, the programme agency explained the TPI approach in various international webinars.

Pioneer2policymaker conference: video impressions (November 2019)

In late November 2019, the TPI network organised the conference 'Accelerating the transition towards animal-free innovation' in Utrecht. Three videos were made at this pioneer2policymaker conference recording impressions of the dialogue. The first issue addressed in the dialogue was showing ownership. This was registered in the video Looking beyond borders. A second issue is that test developers, regulators and end users can learn from one another. This was discussed in the trust & confidence workshop as show in the second video, Invisible walls. A third session revolved around the exchange of experiences of start-ups with advancing their innovation; this was recorded in the video about Business development opportunities

The pioneer2policymaker conference revealed a pressing need for dialogue, as this is still prone to getting 'lost in translation'. This is logical with a multi-stakeholder approach involving various research and testing methods in different target sectors. The discussion about the transition to animal-free innovation involves participants whose areas of expertise are highly distinct from one another. This allows for a better insight into and overview of the complex subject matter.

The word 'validation' is a good example of lost-in-translation dialogue in the varied TPI network. Very different meanings are assigned to it, depending on the sector one works in, the type of research one is involved with, the phase the research is in and the legal requirements faced.



Booklet: 26 x better and faster without use of animals (November 2019)

To meet the need for more knowledge about the various innovations developed by start-ups, late 2019 saw the publication of a booklet with 'calling cards' of Dutch start-ups and scale-ups. This guide, 26 x better and faster without use of animals, was distributed at the international conference in November 2019 and on other occasions. In it, start-ups and scale-ups explain their animal-free innovations and what motivates them to carry these out. This paints a picture of what the Netherlands has to offer in the field. The guide also includes articles about the context in which start-ups in the Netherlands operate. Some start-ups in the guide have already been contacted by invitees from abroad. In 2021 a venture challenge will be issued specifically to start-ups engaged in animal-free innovation, and one start-up made use of the communication channels of TPI and its partners to organise a competition in which scientists can win the use of their chips.

Combined forces for animal-free research

From the financial point of view, several calls for animal-free research were launched in the past year. In this respect the TPI partners are demonstrating their organisational power. They pooled their vision and resources into:

- calls regarding Humane Measurement Models by SGF, NWO, ZonMw, with the Dutch Society for the Replacement of Animal Testing as a co-funder;
- the COVID-19 call of NWO, ZonMw and the Dutch Society for the Replacement of Animal Testing for animal-free virus research and diagnostics;
- the submission of a plan for a Virtual Human Platform (VHP) by a consortium led by UU, HU and RIVM in action line 1 of the Dutch Research Agenda (NWA);
- setting up an interdepartmental call in action line 2 of the NWA, 'Towards a new safety assessment based on pathological and physiological knowledge about human beings'.

'By getting health research to match human beings to the greatest extent possible, thus making it more applicable, it becomes possible in the long term to prevent or cure an increasing number of diseases. This is why SGF is investing in 'humane measurement models.'

Amy Davies, Association of Dutch Health Foundations

From a regulatory point of view, the members of various networks indicate that safety assessments require adjustment to improve the prediction of the effects of medicines and chemical substances in people. There is a need for human-related models and a new framework so that the reproducibility and relevance of these models can be determined without recourse to animal procedures. In addition to the two NWA calls mentioned, a large Partnership for Chemicals Risk Assessment (PARC) is being set up in the EU. Animal-free innovation, humane biomonitoring and the involvement of regulators are priorities in this partnership.

Policy-wise, the deliverable of 'animal-free innovations' forms part of the Knowledge and Innovation Covenant. This covenant seeks to contribute to the complex Social Theme of Health & Care, for which the Ministry of Health, Welfare and Sport formulated a mission in the context of mission-driven innovation policy. Its sub-missions about the chronically ill and Alzheimer's are relevant here. They state that the development of medicines against dementia is proving a remarkably difficult terrain so far, among other reasons because preclinical (animal) trials have turned out to be insufficiently predictive of clinical success. The mission also encompasses the goal of approaching care for individual persons (personalised medicine) as closely as possible. Humane measurement models and accumulating knowledge about human pathology and physiology are relevant to this goal.

'We have system responsibility for research and for the mission-driven innovation policy. TPI is important for this.'

Luuk Klomp, Ministry of Economic Affairs

Lastly, from a managerial point of view, a way was found with the help of DRIFT to combine efforts towards promising transition routes that also deal with humane knowledge. See Section 3.3.

2.3 The recommendations predating TPI were taken to heart

Before the formal start of TPI, three documents were drawn up that can be taken as a kind of baseline measurement:

- In October 2015, the Think Tank on Supplementary Financing for Alternatives for Animal Procedures (*Denktank Aanvullende financiering alternatieven voor dierproeven*) released *'In Transition! The Netherlands leads the way in innovations without laboratory animals'* ('In Transitie! Nederland internationaal toonaangevend in proefdiervrije innovaties').
- In December 2016, NCad issues a recommendation, 'Transition to non-animal research methods – on opportunities for the phasing out of animal procedures and the promotion of innovation without laboratory animals' (*'Transitie naar proefdiervrij onderzoek, over mogelijkheden van het uitfaseren van dierproeven en het stimuleren van proefdiervrije innovatie'*);
- In March 2018, RIVM published the 'Agenda for animal-free innovations in the regulatory field (*'Agenda proefdiervrije innovaties in het regulatoire veld'*)', or PIRV Agenda.

Each of these documents had a somewhat different scope. NCad referred to phasing out animal procedures and stimulating animal-free innovations, while the PIRV Agenda contains RIVM's explicit statement that the complete

replacement of animal procedures is not yet realistic. This Agenda wants to achieve innovation in which the level of safety stays at least the same in case of a reduction of animal use and the stimulation of economic growth. In addition to reducing animal procedures and stimulating business, the Think Tank also discussed increasing the relevance of research for people, animals and the environment.

These three documents contain a number of specific recommendations, such as a time horizon. Below, we indicate generally for each document which recommendations have been followed up on and which ones have not yet. We see that many recommendations got off to a good start, and some were elaborated thoroughly.

In Transition! The Netherlands leads the way in innovations without laboratory animals (2015)

The Think Tank introduced transition studies to the field. Specific recommendations involved matters we now know as the preclinical trial register, the Beyond Animal Testing index (BATi), the calls for humane measurement models and the innovation network for health research with its helpathons, although this was then referred to as gezond@. There was a call for challenge-driven research and data sharing. We see this reflected to some extent in the programme More Knowledge with Fewer Animals (Meer Kennis met Minder Dieren, MKMD) and 'safe harbour'. Remarkably, the think tank represented a virtual network and a fund back then as well; these are action lines also mentioned in the DRIFT arena process. Part 3 gives a wide range of options for funding by a large number of actors. In the end, when animal-free research requires funding the option chosen everywhere seems to be the reallocation of funds.

'Increased funding of humane measurement models and their validation in a central programme are needed to generate more mass. Ideally, this funding would not just come out of big research budgets but also from patrons, crowdfunding and the business community. Better healthcare, better safety and better science are an interesting proposition, making this a good business model for the business community.'

Tom Oostrom, SGF, Dutch Kidney Foundation

'There is free space in which rats predict nothing about people. That free space also exists with in-vitro models, but in a different location. It does not mean these models are better or worse. One can choose to make alternatives the standard, accepting that the risks will be different ones.'

Jurgen van Belle, Ministry of Health, Welfare and Sport – Nutrition, Health Protection and Prevention Department

Transition to non-animal research methods – On opportunities for the phasing out of animal procedures and the promotion of innovation without laboratory animals (2016)

NCad advocated the development of target scenarios for fundamental research, including one for education, as well as calls around humane measurement models. We clearly see these activities reflected in the progress report. An index modelled on the Access to Medicine Index is coming about with the BATi, also mentioned by the Think Tank.

Another recommendation concerned innovation policy: now that animal-free innovation forms part of the knowledge and innovation covenant for the Health & Care mission in the framework of mission-driven innovation policy, links can be identified with – as recommended by NCad – parties that take a chain-oriented and multidisciplinary approach to animal-free innovation and valorisation and the acceptance of animal-free methods.

Lastly, ZonMw at the request of LNV is looking into the establishment of an AI platform for finding data from humane research. Helpathons and TPI.tv are also contributing to the diffusion of knowledge and the exchange of views on this topic.

In 2020, the recommendation to aim for the review of regulatory risk assessments started nationally with the NWA – albeit not as a separate track, but as part of the aforementioned request for a Virtual Human Platform and the elaboration of an interdepartmental call for safety assessment based on alternatives. A condition for this call – to be met by consortia that will be signing up – is to involve the international regulatory field and businesses. The recommendation made then to adopt a radically different approach to risks is the only one that has not yet been actioned.

Agenda for animal-free innovations in the regulatory field (PIRV Agenda) (2018)

The PIRV Agenda published by RIVM deals with the development of an animal-free safety assessment of substances. In addition to a number of preconditions such as commitment and coordination, RIVM is augmenting this process with items that a significant start was made on in the innovation networks around the virtual human (under constructed in the VHP), TPI.tv, ATMPs and 'safe harbour'. The organisation of the 'trust and confidence' workshop at the international conference fits in with this as well: in this workshop it was discussed that regulators, test developers and end-using companies should exchange opportunities for the acceptance and application of alternative models at an early stage (see the video Invisible walls).

The actual enshrinement in law of animal-free innovation in the safety assessment regime is complex and requires a lengthy process. An example of what has been achieved, however, is the modification of an ICH guideline on side-effects of medication during pregnancy which the Medicines Evaluation Board and RIVM have worked on: the so-called 'double animal test' can be replaced with an in-vitro test in the first phase of this safety study.

'It should be the other way around. First prove that an animal test is better than a human.'

Susan Janssen, National Institute for Public Health and the Environment Ministry of Health, Welfare and Sport

2.4 The partners look back on a special process

The members of the Core Group look back on a positive, inspiring process. TPI had the characteristics of a voyage of discovery and had a well-structured, well-facilitated process.

'A lot of energy has now been released. We need to show and transmit that energy.'

Debby Weijers, Dutch Society for the Replacement of Animal Testing

Many partners refer to TPI as positive in view of the emphasis on looking for alternatives rather than phasing out animal procedures. In this way the TPI approach enabled an open dialogue and harnessing the power of combining divergent experiences and interests. Separate initiatives were ranged under the same heading, and stakeholders from across the development chain were involved in the dialogue. In view of the large differences in context and the diversity of interests, it is remarkable that this succeeded. As many have concluded, the dialogue has as a result become nuanced. 'TPI created a buzz'. 'Things have been shaken up'. These are some of the comments heard from the Core Group members. The acceleration programme is of great importance to the parties in the field; they are proud of it.

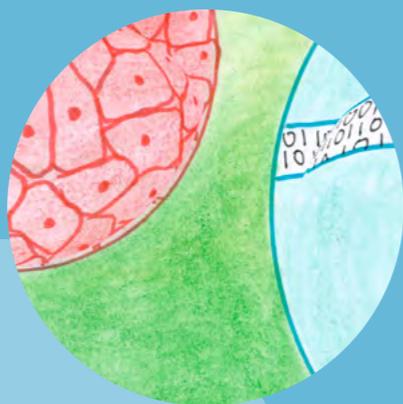
'Everyone has their own perspective, but in the end TPI everywhere is about health.'

Marijke Valstar, Ministry of Defence

All policies related to animal use – except those for animal welfare – are ultimately aimed at the health of people. To be sure, these people come from very different target groups: not just patients, but producers, consumers, employers and citizens as well. Consequently, TPI partners deal with highly divergent interests. The variety of sub-interests is mainly seen as an opportunity, as it sharpens up the dialogue and a greater number of angles means a greater chance of innovation.

3

Measuring the acceleration



Having reflected on the effort in the previous chapter, in this chapter we will discuss how the TPI partners look back on the movement that is TPI. Has the transition been accelerated? We will then look at what an expert authority says: How does DRIFT interpret the current situation of this transition, and do the TPI partners recognise this? Next, we will name the process indicators for acceleration: have new perspectives, new connections and a joint vision come about? We will then pose the key question: is the Netherlands a frontrunner and if so, in what area exactly?

3.1 Accelerating is mainly done together

Various TPI partners express their satisfaction about the results obtained by TPI in the past years. The reduction of animal use is not the yardstick here; after all, the development of more alternatives is not linear and is not directly related to the reduction of animal use.

'Maybe we first need more laboratory animals to develop innovations, and then a big reduction will suddenly become possible.'

Han van de Sandt, Netherlands Organisation for applied scientific research (TNO)

This is also emphasised in the latest progress report (over 2020), which further states that the transition is differently paced in different domains. Not all researchers say they have the option of using alternatives to animal procedures. Also, some tests are required by law. The position is that as long as the transition to animal-free methods is ongoing and laboratory animals remain needed in addition to alternatives, it is necessary to protect the welfare of laboratory animals. What is special in the TPI network is the emphasis on what is promising for animal-free innovation. The well-being of laboratory

animals is identified as a push factor for animal-free innovation, in addition to pull factors such as personalised medicine and open science.

'We have a good story, we are not against anything, we contribute something.'

Henk Smid, Netherlands National Committee for the protection of animals used for scientific purposes

The approach in which stakeholders from the entire spectrum can enter into a dialogue with each other about building up alternatives is considered to serve acceleration. We hear, for example, that TPI having become more open to discussion has made it possible to consider which model, with or without laboratory animals, best fits a specific study. Some are happy that this has brought the message across that TPI strives for 'better science' with better predictive value about efficacy and safety, while a greater number of animal procedures can become redundant.

'It is possible to see things from a different perspective. Helpathons and the international conference were important to get this started. It created openings. Now we have to carry on.'

Carine van Schie, SGF, Dutch Burns Foundation

Conversely, others consider 'better science' to go without saying, as scientists are always working on improvement and animal procedures are well-organised and carried out with care, with permit procedures in place.

'One size fits all does not work. This risks alienating many scientists.'

Rita Struhkamp, ZonMw

We also see divergent perspectives in connection with the COVID-19 pandemic. Some partners expect the research into COVID-19 to boost open science and the exchange of data from methods with and without animal procedures. According to others, the COVID-19 research seems to rely more strongly on animal procedures, and research phases more often take place in parallel in order to speed up vaccine trials.

'The issue is validation: this is tricky.'

Hans van Leeuwen, Netherlands Federation of University Medical Centres, Erasmus Medical Centre

We are dealing with a firmly enshrined system of international safety assessment. Not all stakeholders who are embedded in that system want to or are able to walk the road towards applying animal-free innovations, as this takes additional effort, time and money.

'The sowing has been done. We will reap when scientists are actually allowed to put innovations into practice.'

Anne Kienhuis National Institute for Public Health and the Environment Ministry of Health, Welfare and Sport

At a webinar titled 'use of and need for animal procedures' ('*nut en noodzaak van het gebruik van proefdieren*') organised by the Royal Netherlands Academy of Arts and Sciences on 8 June 2020, part of the participating scientists turned out to be relatively unfamiliar with the TPI approach and to have their concerns about it, including in connection with their own

research. Various participants believed the Dutch government's goal is 'no more animal use by 2025'. They did not know that since 2018 the emphasis in the ambition has shifted to spearheading alternatives and innovations. In this webinar, scientists emphasised that animals procedures are important to their research.

In the TPI network, those scientists who prioritise the importance of animal-free innovation see the value of exchanging and pooling knowledge and data both about animal procedures that translate well and about alternative models and methods.

Royal Netherlands Academy of Arts and Sciences inventory: 'The importance of animal procedures' ('Het belang van dierproeven', June 2019)

The Royal Netherlands Academy of Arts and Sciences submitted its inventory 'The importance of animal procedures and options for reducing these in fundamental neuroscience research' to Parliament following the request for a target scenario from the Ministers of Education, Culture and Science and of Agriculture, Nature and Food Quality. This inventory includes an underlying exploration by the Bijker Committee, 'Excellent brain research with fewer animal procedures, Opportunities and challenges for animal-free research in neuroscience' ('Excellent hersenonderzoek met minder dierproeven, Kansen en uitdagingen voor proefdiervrij onderzoek in de neurowetenschappen'). The Academy stresses the great importance of animal procedures and has expressed its wish to contribute, where possible, to a dialogue between politics, civil-society organisations and the scientific community on the continued development of animal-free alternatives. Chapter four of the inventory describes developments that in the next 10 years can contribute the most to fundamental neuroscience research with fewer animal procedures:

- (i) Organoids and complex cell and tissue cultures;
- (ii) Non-invasive studies in humans;
- (iii) Invasive studies in humans;
- (iv) Use of existing (big) data and collected human brain tissue;
- (v) Computer models and artificial intelligence.

'We also find that drawing up the inventory has led to a spirited debate at the Academy and in the field about animal-free innovation in fundamental research. It is of great importance that we continue to have this dialogue in a broad setting.'

ministers of Science and of Agriculture Engelshoven and Schouten in their response to the Academy's inventory, 4 July 2019

The Transition Group suggests that scientists find the discussion about ending animal use a valuable one, but they themselves want to be able to choose the best model to answer their research question. The fact of there being a discussion can, however, be interpreted as a sign that things are on the move.

'Rather than barging your way through, at an early stage facilitate the discussion between proponents in the movement and people who put up resistance. Discuss their fears, for instance about the interests at stake. It is logical to protect one's own interests, but also look for the common greater interest. Go one step at a time. This kind of evolutionary movement creates the space for change.'

Jan Rotmans, Dutch Research Institute for Transitions

Many TPI partners insist strongly that in the coming years many more scientific researchers should become and remain involved in the debate about the facts, opportunities, possibilities and impossibilities of animal-free innovation.

In parallel, in order for the movement to grow we should actively seek the discussion with parties that have concerns.'

From a letter by SGF to the director of Animal Agricultural Chains and Animal Welfare (Direction of the ministry of Agriculture, Nature and Food Quality), July 2020

As an issue for consideration, some point out that TPI is making an effort to ensure that broadening the dialogue also leads to concrete new actions and to progress.

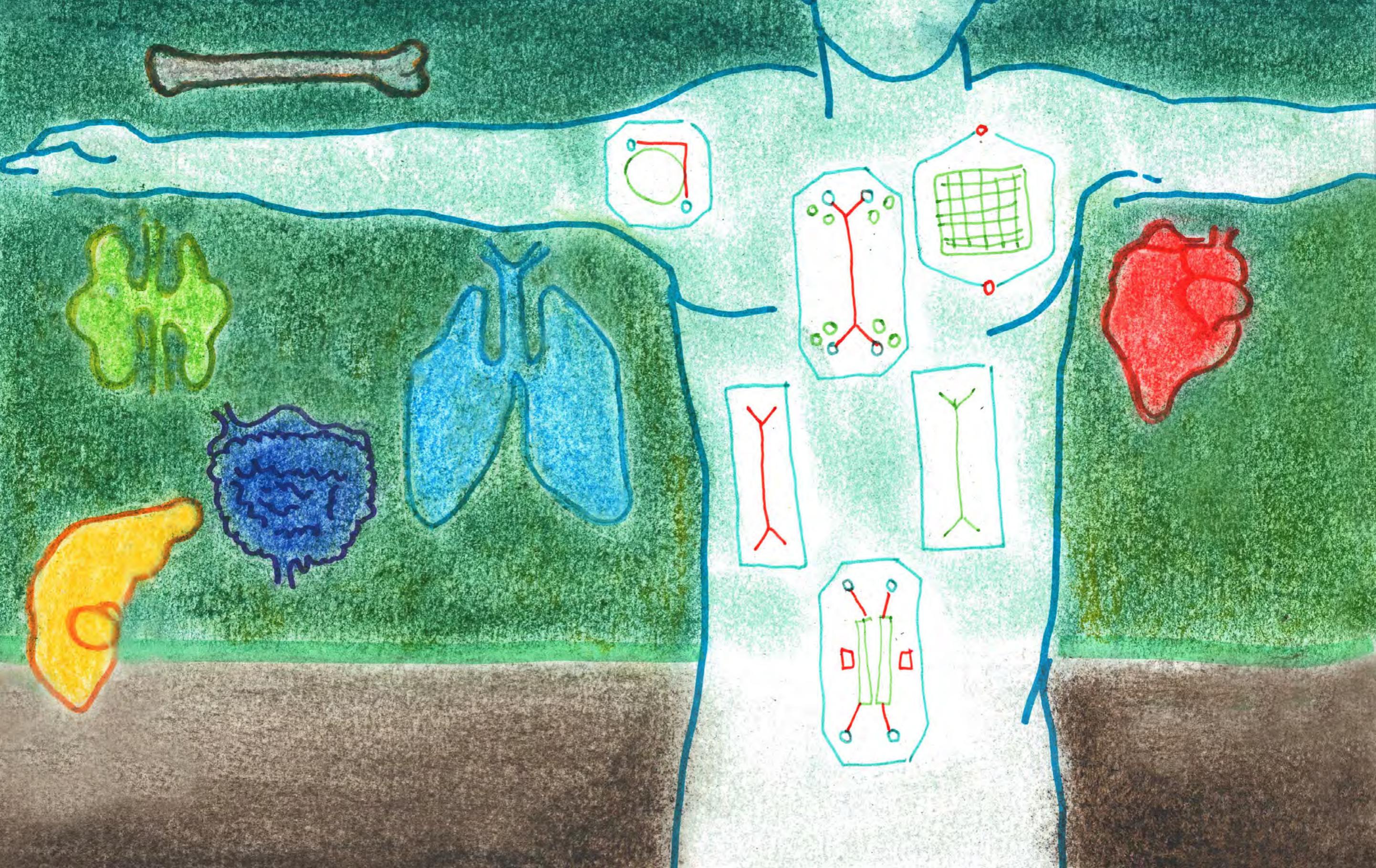
3.2 The transition is in a phase of pre-development

DRIFT was asked to conduct an analysis of the current situation of the transition to animal-free innovation. In the winter of 2019-2020, three so-called arena sessions took place with members of the Core Group and Transition Group and with innovators from various domains and organisations.

DRIFT arena about the current situation and the direction of TPI (spring 2020)

DRIFT approaches the analysis of transitions at the macro level in 'the landscape' of big, autonomous developments, at the micro level in 'niches' of individual innovations and at the meso level in institutions that constitute current governmental structures. At the micro level we see many technological innovations. At the macro level there are developments such as digitisation or the changing relationship between humans and animals. There is also a remarkable political involvement with this transition. At the intermediate meso level, however, no institutional developments towards this transition are seen yet; for instance in legislation and regulations, in education or in ethics. There is now a narrow, deep support base for the transition to animal-free innovation, but there has not yet been a breakthrough at the systemic level. The outlines of the transition's potential development, however, can be made out. Transition routes that are about the big 'from ... to' movement are the routes from animal use to personalised healthcare and safety assessment using in-vitro and in-silico methods. DRIFT explained its findings at a webinar in May 2020.

An important concept in the DRIFT analysis is that transitions usually take up a generation or two. The transition to animal-free innovation is currently in the phase of pre-development: all sorts of things are happening, there are energised networks and there is pressure to change. What is also important is to get the system moving, with a breakthrough towards the large-scale implementation of alternatives.



'Many people still think in terms of improving the current system rather than a real.'

Merel Ritskes-Hoitinga, Radboud, Syrcle

The Core Group members participated actively in the process involving DRIFT's transition management approach and arena approach. They concur with the analysis that we are at the start of the transition to animal-free innovation. They realise that this transition is a matter of perseverance. Animal procedures appear to be the 'golden mean', and particularly in fundamental research there do not seem to be many alternatives.

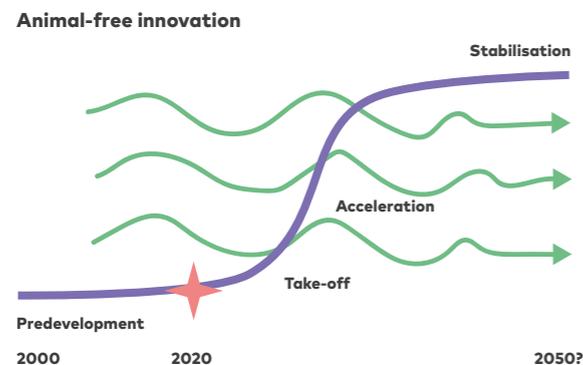


Figure 1, source: DRIFT analysis

'It has to be clear that TPI's ambitions require generations, and that true acceleration therefore lies twenty years in the future rather than five.'

Hans van Leeuwen, Netherlands Federation of University Medical Centres

Reference is made to the new generation of scientists. Everyone considers education to be important to learn to make decisions regarding animal procedures or possible alternatives. The younger generation of researchers are being educated in a period in which humane measurement models are seen as options among the available models. They do not

experience the animal procedures model as the 'gold standard'. Given that the development and acceptance of humane measurement models requires an extra effort and therefore extra time and money, their work is the work of pioneers.

At the webinar about the DRIFT analysis, several partners also named education as an important action, with the current generation considered to be an area of attention. Earlier, at the international conference in 2019, one of the partners had already suggested setting up a retraining task force to facilitate the switch from animal procedures to alternatives. The transition routes towards 'personalised medicine' and a 'safety chain based on in-vitro and in-silico methods' described by DRIFT are almost universally considered promising.

'Personalised medicine is an important route for drawing more attention to successful and useful medical innovations. The knowledge underpinning it is often derived from animal procedures as well. In some areas of expertise, the use of entire organisms for experiments will remain necessary for a long time to come.'

Dov Ballak, Netherlands Federation of University Medical Centres

DRIFT finds it remarkable that it is politics advocating the transition to animal-free innovation. As said, many scientists are unfamiliar with the issue. Many companies are not talking about this transition, probably to avoid being associated with animal use. Also, there seems to be less activism in this field than there was decades ago.

'There is no broad public awareness yet of the issue of animal-free innovation, but it appears there is awareness among politicians and policymakers. Usually, politics is the last sector to become involved in an issue. The issue of animal-free innovation gives this conventional situation the lie.'

Jan Rotmans, Dutch Research institute for Transitions

Most transitions have their origin in societal focus and concern. TPI began with political involvement. Possibly, COVID-19 and the attendant information flow about vaccine development are leading to change in scientific and/or societal involvement. Whether this is the case, and the direction in which this change is going, is still hard to predict.

3.3 Process indicators show the movement

Autonomous developments in ethics, science and healthcare have a significant impact on the transition. The impact of TPI on the transition's acceleration was measured by asking for the partners' opinion on qualitative process indicators identified for determining the speed and direction of movement in transition projects.¹

The following aspects are characteristic of a transition:

- uncertain, complex and dynamic processes;
- innovation of the system, not just incremental change;
- various actors, with the government being one of the partners involved;
- experimentation in order to develop new practices and structures by searching and learning.²

We see that these characteristics also apply to TPI.

This evaluation succeeded in: addresses the following process indicators for transitions and then answers the question of whether it has

1. starting experiments, or causing experiments to be started, that lead to changes in the behaviour, perceptions and attitudes of those involved;
2. creating (new) connections in the TPI network
3. letting visions converge into a common vision.

The partners' evaluation of these process indicators is described below.

1) A new way of seeing things came about

We learned from the conversations that various partners would like to experiment by exchanging ideas in a safe environment. The network for innovative healthcare, which together with the agency Meneer de Leeuw developed the helpathon tool, is particularly suitable for this. At exchange sessions the following practice question was answered: If we were not allowed to carry out animal procedures, what could we do in a given research case? This helped the cases discussed in helpathons ahead. At a meeting of this network at the end of last year another question was discussed: 'Does one need a living complex system to research a living complex system?'

'As soon as you find yourself wanting to repeat opinions or abstract statements you have already repeating for a long time, please consider refraining from doing so. As soon as you find yourself moved to share a thought that is new to you, that you not completely understand the meaning or consequences of yet, please consider sharing it!'

Mister Lion, programme booklet pioneer2policymaker conference november 2019

1 Based in part on <https://transitiepraktijk.nl/nl/programma/evalueren-en-monitoren/wat-monitor-of-evalueer-ik>
 2 NSOB (2018) – Project-oriented evaluation: policy evaluation for systems change (Opgavegericht evalueren: beleidsevaluatie voor systeemverandering)

Vooruitgangsrapportage innovatief Progress report on innovative health research (January 2019)

Animal-free innovation is easier if those engaging in it are able to join forces: from patients and citizens through to healthcare professionals, researchers, financiers and policymakers. This is set out in the progress report of which Director-General Marjolijn Sonnema of LNV received the first copy in January 2019, when it was presented to a varied audience of network participants and interested parties. The report, not distributed digitally in the interest of the confidential exchange of ideas, shows two perspectives when literally flipping the book: that of a preference for animal-free innovation on the one side and that of one hundred per cent animal-free innovation on the other.

The report advises research backers to work towards the structural promotion of animal-free innovation in health research. They can do so, for example, by communicating openly about research involving animal procedures, setting out their own innovation strategies, earmarking 'slow money', compiling 'challenge lists' of research models that should and should not be used, and organising coincidence.

2) New connections were made in the network

The Core Group members further note that the network has been expanded to include more and different stakeholders, such as transition experts, data scientists and a few patients. The network has also drawn international attention. The pioneer2policymaker conference saw a big attendance. A number of guests from abroad discuss their practice on TPI.tv and participate in the helpathons. Conversely, TPI introduced itself at some meetings in Europe.

'It's a good thing that the conversation got going with the involvement of others than just the usual suspects.'

Debby Weijers, Dutch Society for the Replacement of Animal Testing

3) A shared vision has been developed

In spite of all differences, the vision from the arena process with DRIFT is shared broadly: the transition is in a phase of pre-development, and the two formulated transition routes are recognisable and viable in the eyes of many. Which specific steps are possible and required on these routes is still in the discussion stage. It is becoming clear that the end goal is good translation into better predictive models.

'TPI is about pooling knowledge in order to improve to human.'

Wouter Dhert, The Association of Universities in the Netherlands, University of Utrecht

Fortunately, there is respect for each other's different views and interests. This leads to a more nuanced dialogue and a greater chance of innovation through the combination of insights and the use of data from different methods (in vitro and in silico, preferably interacting with in vivo). This promotes the acceptance and application of animal-free innovations.

3.4 The ambition has been achieved: TPI is an international frontrunner.

In addition to the question of whether, and to what extent, the TPI programme has accelerated the transition to animal-free innovation, there is the question of the extent to which the Netherlands – in accordance with the 2018 ambition – is an international frontrunner in this transition. In the neighbouring countries, too, many people and organisations are hard at work to limit animal procedures, to develop innovative, animal-free methods and to make use of the opportunities offered by those innovations. In the 2020 progress report Minister Schouten writes: 'Our ambition is for the Netherlands to be the frontrunner in the international transition, but as far as I am concerned this is not a race. In fact, it is important to join forces with frontrunners in other countries – hence the international conference.'

The most striking difference with other countries is the role the Dutch government has taken on in this transition. As far as we are aware, in no other country has the government explicitly positioned itself as a transition director and actively brought together many different parties in this capacity. At the 2019 international conference, participants from other countries expressed their admiration of this. In this respect the Netherlands is clearly a frontrunner in opening up animal-free innovation to discussion.

'European sister organisations of NCad see the Netherlands as a frontrunner. We are being watched closely.'

Henk Smid, Netherlands National Committee for the protection of animals used for scientific purposes

The Dutch approach has since attracted the attention of various other stakeholders from abroad. For example, foreign invitees at the pioneer2policymaker conference took part in the online helpathons in 2020, and TPI was asked to feature as a showcase at an online conference organised by Cruelty Free Europe about human-relevant science on 11 September 2020, appearing alongside the institutes ICCVAM (US), ECVAM (EU) and an initiative from the Brussels region.

4



Directing the acceleration of TPI

4.1 Funding

Even before the start of the TPI programme, government funds were being spent structurally on stimulating animal-free innovation, and this will continue to be the case after the current TPI programme (in 2021 and beyond). For example, LNV annually spends over €5.5 million on animal studies and animal-free innovation, such as on the ZonMw research programme 'More Knowledge, Fewer Animals' ('Meer Kennis, Minder Dieren'), knowledge-oriented questions for RIVM and Intravacc, and the WOT food safety programme. Besides LNV, the Ministries of Education, Culture and Science, of Health, Welfare and Sport and of Defence annually spend an amount on alternatives to animal procedures, as well as contributing to research using animal procedures. Parliament has always been informed about this when discussing the LNV budget.

At the start of TPI, it was agreed the programme would receive an annual budget of €1 million from LNV as 'process money' for accelerating the transition to animal-free innovation. In 2018 Parliament was informed separately about the allocation of these funds ³. The actual amount spent was lower, among other reasons because the programme used its own expertise and human resources.

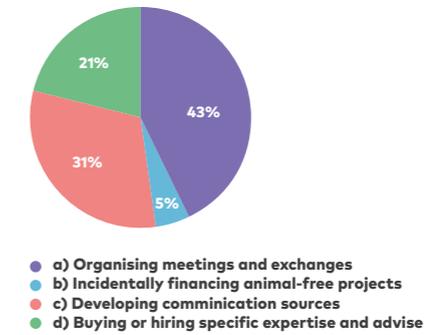
2018	2019	2020 (until October)
€840,000	Approx. €698,000	Approx. €352,000

³ See the Letter to Parliament dated 29 October 2018, 'Transition Programme for Innovation without the use of animals: 2018 costs' ('Kosten 2018 Transitie Proefdiervrije Innovatie') 32 336 No. 85

⁴ For a more extensive description, see the appendix to the progress letter sent to Parliament in 2020.

4.1.1. LNV spending on TPI over 2018-2020

Percentages spending TPI-budget in 2018, 2019 and 2020



4.1.2. Distribution of TPI funds from 2018-2020 ⁴

These funds were distributed as follows:

43% for organising encounters and exchanges, such as in the various innovation networks, helpathons and an international conference;

5% for (co-)funding the interdepartmental NWA research call;

31% for developing communication tools such as the TPI newsletter, the website transitieproefdiervrijeinnovatie.nl, TPI.tv and the booklet '26 x better and faster without use of animals';

21% for buying and hiring specific expertise and advice, such as transition and change management advice, supporting innovation networks and helpathons, and communication advice.

The Ministry's spending on TPI is lower in 2020 because the COVID-19 pandemic made it practically impossible to organise meetings.

4.2 The cooperating TPI partners

Setting up the consultation structure

In 2018, TPI's consultation structure was set up as a guiding administrative Core Group and a more operational Transition Group. Both include representatives from Health-Holland, the agency for the top sector Life Sciences and Health (HH), the Royal Netherlands Academy of Arts and Sciences, the Netherlands National Committee for the protection of animals used for scientific purposes (NCad), the National Institute for Public Health and the Environment (RIVM), the innovation grants organisation ZonMw, the Association of Dutch Health Foundations (SGF) and the Dutch Society for the Replacement of Animal Testing. The Association of Universities in the Netherlands (VSNU) and the Netherlands Federation of University Medical Centres (NFU) joined this Core Group on 25 March 2019. With the VSNU and NFU joining, the Academy and NCad became advising observers. The Core Group discussed the mission and direction of the acceleration process. The members actively involve their own network and report on developments, initiatives and activities relating to animal-free innovation. The Core Group is where the members strike a balance between personal ambition and their position on behalf of their constituency.

'The recommendations made on the basis of transition management – to bring together pioneers in animal-free innovation – were taken to heart.'

Bea van Golen, ministry of Agriculture, Nature and Food Quality, TPI programme agency

The members of the Transition Group are active in the innovation networks and initiatives, and together have an overview of these. A transition expert was appointed for each innovation network; these experts met on occasion to deepen their insight into the transition.

The partners look back on a fruitful collaboration

'A network was successfully set up. There was no hint of that when we started out; the field was highly fragmented and people barely knew each other.'

Pepik Henneman, Mister Lion

It proved possible to create a robust, diverse network that includes not just the obvious organisations, but also such parties as transition experts and data scientists, who are often relative novices in the field of animal studies and the development of alternatives. This is seen as adding value, given the fresh angles they contribute.

Especially striking is the cooperation between SGF, NWO, ZonMw and the Dutch Society for the Replacement of Animal Testing in various research calls that involve animal-free innovation and in which this is preferred or even required. These organisations are admired for their willingness to cooperate. Their solidarity and vision have been strengthened, as is shown by their pooling of resources for the research call on humane measurement models.

'The cooperation exceeds expectations. Just look at the changes and breakthrough achieved by the health funds!'

Henk Smid, Netherlands National Committee for the protection of animals used for scientific purposes

The Core Group is happy to see politics taking an interest in this issue. It also seems positive that other spokespersons than those for animal procedures discuss the transition as well. After all, TPI is about more than animal welfare alone: it is also about sharing data and practising open science, and about recent biomedical innovations that dispense with animal procedures. Members of Parliament who are also spokespersons for science, healthcare or innovation are especially relevant.

The Core Group members would also like to see a greater involvement from other Ministries than ministry of Agriculture, Nature and Food Quality. In particular they are thinking about the Ministry of Education, Culture and Science (in view of the science policy) and the Ministry of Health, Welfare and Sport (in view of the Health & Care mission). They especially hope that these Ministries will highlight the scientific and economic opportunities of animal-free innovation in Brussels in the circuits that are setting up the big EU framework programme for research.

'Animal-free innovation is not just important to LNV. Other important incentives include new economic activity for Economic Affairs, medicine development for Health, Welfare and Sport and safety around chemicals for Infrastructure and Water Management. The government has a crucial role in uniting the sub-interests.'

Han van de Sandt, Netherlands Organisation for applied scientific research (TNO)

According to the Ministries, the Core Group seems to be focusing on medicine development. They think it would be a good idea if it broadened its scope to include policies and safety assessment around chemical substances to which, for example, consumers and employees are exposed.

Collaboration between ministries

The participating policy directorates at the Ministries of Economic Affairs; Health, Welfare and Sport; Education, Culture and Science; Infrastructure and Water Management; and Defence work together in the Interdepartmental Working Group on Alternatives to Animal Testing, (D)IWAD. They are elaborating a common theme for the previously mentioned interdepartmental NWA call and have discussed the outcome of the DRIFT arena process.

In the policy directorates' view, it is certainly important to use innovation to develop better medicines or to improve the safety assessment of substances. If this can be done without animal procedures, so much the better.

'The desirable perspective is: using the best possible test. This might be an animal procedure, but clearly it often is not.'

Jasper Claessen, Ministry of Health, Welfare and Sport, Pharmaceutical Affairs and Medical Technology Directorate

Accordingly, they support the analysis. While the viable route approach chosen for TPI was certainly not self-evident to policymakers, they increasingly see the relevance of this approach.

'Improved predictions: this is language we can work with.'

Peter Munters, Ministry of Health, Welfare and Sport, Nutrition, Health Protection and Prevention Directorate

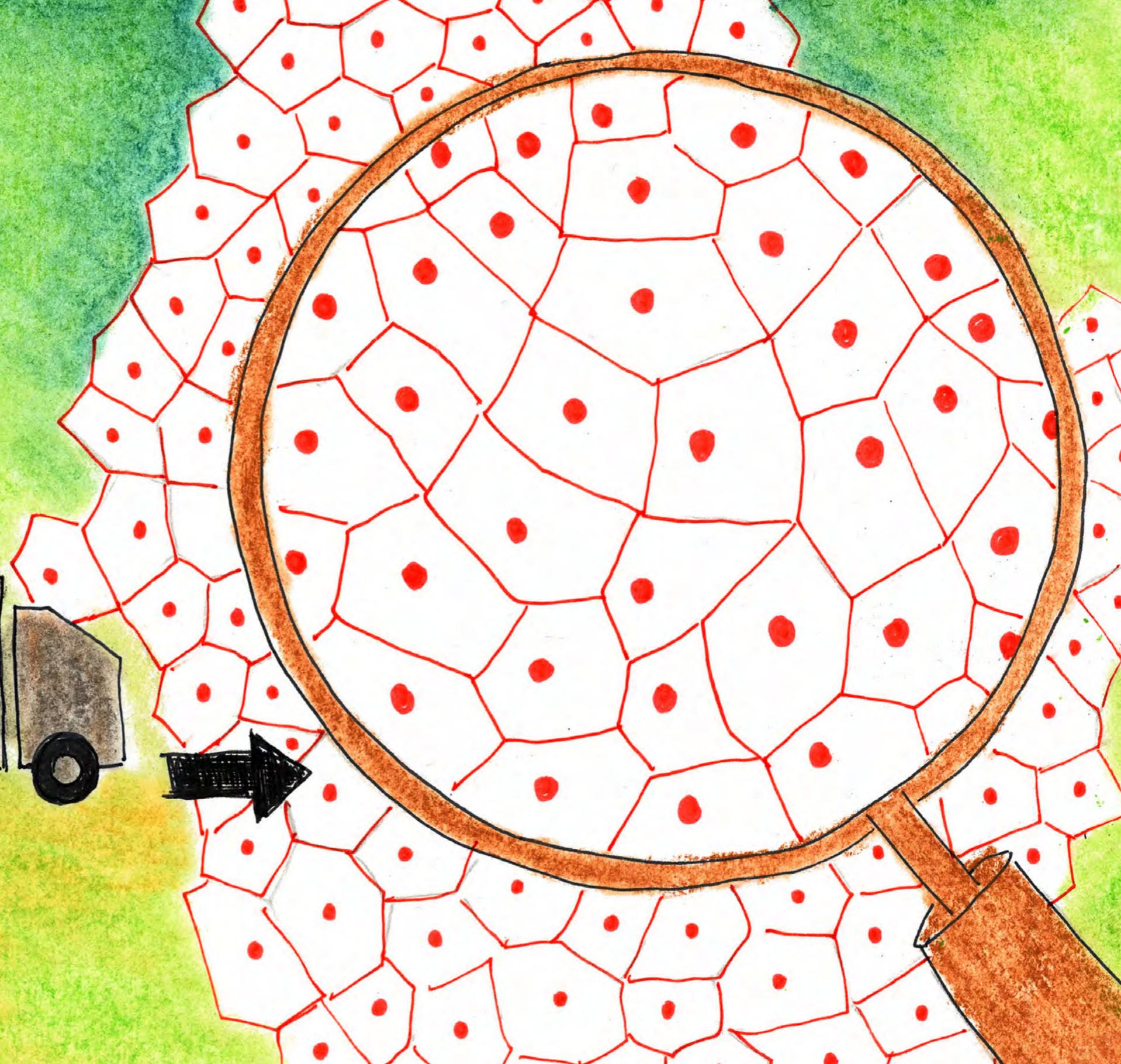
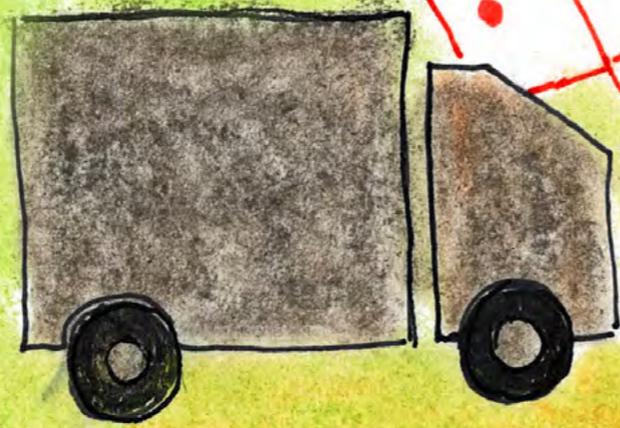
'What we currently have in place, using animal procedures, is not necessarily optimal.'

Judith Elsinghorst, Ministry of Infrastructure and Water Management

'The current methods are insufficient. If we want to press on with animal-free innovation, TPI has to continue and has to involve international stakeholders more.'

The Netherlands cannot do it on its own.'

Heddy Lindeijer, Ministry of Infrastructure and Water Management



In addition to elaborating the joint interdepartmental NWA call, there is an opportunity for collaboration in the above-mentioned EU partnership, PARC, for innovating the assessment of chemical substances. This is currently being set up with the involvement of ministry of Agriculture, Nature and Food Quality and the Ministries of Infrastructure and Water Management; Health, Welfare and Sport; and Social Affairs and Employment. RIVM and ZonMw also look for practical cooperation with partners in the field of Health, Welfare and Sport on the social theme of Health and Care for mission-driven innovation policy.

Structure of the programme agency

LNV has a governing role in TPI on behalf of the national government. Accordingly, a 'programme agency' with a limited number of employees was set up in 2018 to support TPI. This agency keeps an overview of and insight into actions and developments, it stimulates, it connects parties inside and outside of the existing frameworks and it communicates about progress and results. The agency acts as secretary for the Core Group, the Transition Group and (D)IWAD. It is led by the director of Animal Agricultural Chains and Animal Welfare (Dierlijke Agroketens en Dierenwelzijn, DAD), who acts as a commissioning authority. The director of DAD is also the chair of the Core Group and of DIWAD.

The programme agency staff all work to foment and accelerate the transition, working in different areas of expertise and roles. These range from knowledge about transition management to communication, from agile and programmatic work to stakeholder management. With the exception of a few permanent members of staff, most employees were assigned briefly and efficiently from an internal labour pool.

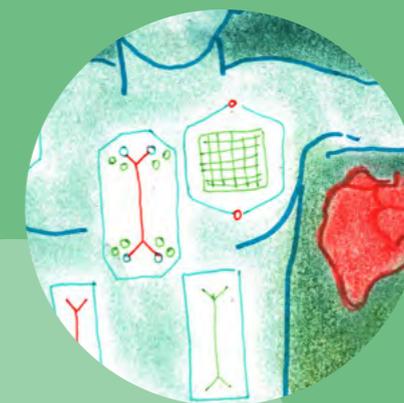
General knowledge was built up within the programme agency about the different domains and policy dossiers related to animal use or the in-vitro, in-silico and clinical alternatives, about technological developments such as organoids and artificial intelligence, and about concepts such as open science and personalised medicine. In addition, the linkage with LNV provides access to a large body of knowledge about animal welfare.

Throughout the entire course of the programme attention has been paid to communication and to reaching more people and organisations of various backgrounds. Ways of doing so have included the development of a website and a newsletter. The variety of target groups – from scientists in a broad range of disciplines to large and small businesses and regulators in different contexts – makes it challenging to convey a single fitting message.

Due to the COVID-19 pandemic it was tricky in 2020 to get people together for cross-fertilisation. The postponement of the World Congress on Alternatives and Animal Use in the Life Sciences also made it harder to export the TPI philosophy to partners in other countries. Medicine and vaccine development for COVID-19 may offer new opportunities for the (online) exchange of insights into the use of laboratory animals and alternatives in the development of a vaccine. The Minister of LNV requests advice from NCad on this topic.

'Animal-free innovation also comes about without TPI. But don't let go! Central support, nationally and internationally, speeds up this development and its implementation.'

Han van de Sandt, Netherlands Organisation for applied scientific research (TNO)



5

Conclusions and recommendations for a follow-up

The Netherlands is an international frontrunner in open dialogue
Compared to other countries, the Netherlands is ahead with the practical application of the philosophy and method formulated by the partners. It is remarkable that this has led to an open dialogue with various stakeholders from across the chain and from different sectors and countries. What is especially innovative is that the government, in this case the Minister of ministry of Agriculture, Nature and Food Quality, acted as the director of the transition. Other countries have not yet taken this approach. The Dutch approach has since attracted the attention of various stakeholders from abroad.

The transition has entered a phase of pre-development

Significant steps have been taken, and the changes to be observed are the following

- Many stakeholders are at work under the flag of TPI. Their collective activities form an open search in which a thousand flowers bloom. Participants stepped outside of their comfort zone in sessions using tools such as the helpathon and the open-space dialogue. The stakeholders themselves chose what to discuss and were open to different perceptions and contexts.
- Many new connections were made in the TPI network. It proved possible to create a diverse network with new connections between professionals from very different disciplines and organisations such as transition experts, data scientists and a few patients. There is awareness within the network that exchanging and pooling knowledge and data from different models and test methods helps innovation ahead. Different partners pooled resources in joint calls for animal-free innovation.

- They have found a direction in which to move. The two transition routes from the DRIFT analysis are broadly recognised as promising:
 - a) the personalisation of healthcare (personalised medicine) and
 - b) safety assessment based on knowledge about humans (from in-vitro and in-silico methods).

The transition has entered a phase of pre-development, with many innovative activities and tapping into opportunities for change on the basis of autonomous developments such as digitisation. The institutional systems change, in which animal-free innovations will become more accepted and more frequently applied, will occur at a subsequent stage. The end goal is better translation into a practice in which resources are developed and substances are safety-tested using humane knowledge and data.

Follow-up recommendations: going in-depth, embedding and broadening

The many different partners must 'continue to hold each other' on their way towards the end goal. Various partners argue for a subtitle for TPI that refers more clearly to the end goal. They have made suggestions such as 'Innovation in translation' or 'Transition to humane models'. In the coming period the TPI partners will look into a suitable name for a follow-up to TPI.

'The strength is in the combination of 'innovation' and 'animal-free'. This points to the opportunities for a practice with human data coupled with limiting the practice of animal studies.'

Pepik Henneman, Mister Lion

The TPI partners would also like to start up a dialogue with parties not yet involved: what are their choices and considerations? How can we inspire and involve them?

'A focal issue is for TPI to continue to connect with the regulatory field, which is international by definition.'

Marcel van Raaij, Ministry of Health, Welfare and Sport

'We need to connect with the scientists to be able to help the transition ahead.'

Peter Steenhuis, Ministry of Education, Culture and Science

'It is often easier to connect with companies at the level of an issue than at the administrative level. True commitment in parts is preferable to a global obligation.'

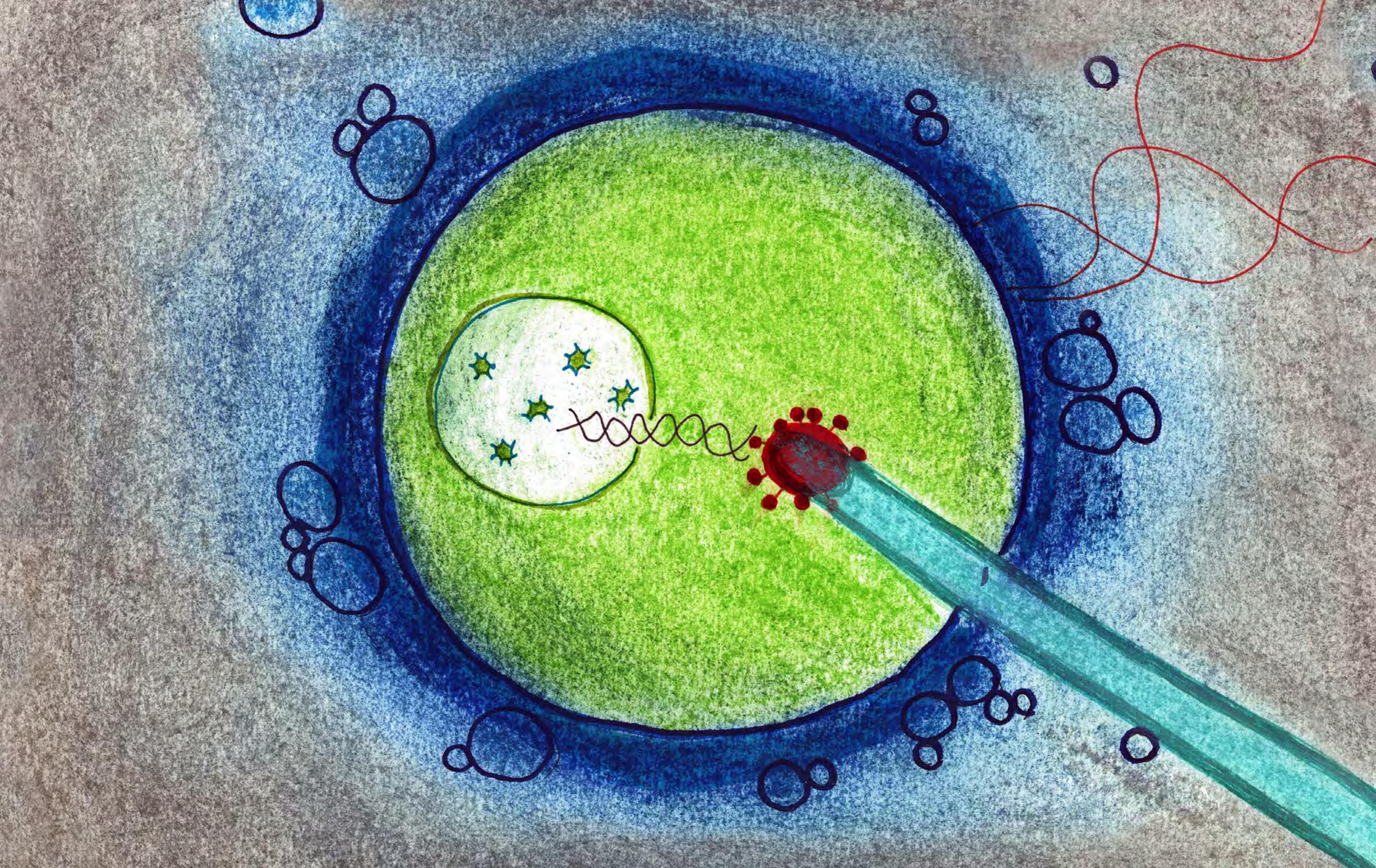
Erica van Oort, Netherlands Organisation for Health Research and Development

The partners prefer to look for additional resources to develop humane measurement models rather than redirecting funding flows for animal procedures.

Additionally, they want to request greater involvement especially of the Ministries of Health, Welfare and Sport and Education, Culture and Science.

In a subsequent phase it will be important for the TPI partners to shift from an open search to *going in-depth* on alternative and innovative practices in a targeted way, *embedding* existing animal-free options in policies and guidelines, and *broadening* the dialogue to include the general public as well as more scientists and researchers who deal with animal use.

While openness, organisational power and vision were in evidence and there was good and pleasant cooperation, the composition of the network could be improved. In the current Core Group and Transition Group, the angle of development of medicines predominates. It is also important to involve more scientists, more large companies and more regulators from the EU.



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Invisible Walls

Interview with Jan Rotmans, I never saw government spearhead a transition before (Nooit eerder zag ik de overheid een transitie aanjagen) (2020)

Report of the DRIFT webinar, Jointly choosing promising transition routes towards animal-free innovation (Samen kansrijke transitiepaden in slaan naar proefdier vrije innovatie) (2020)

Royal Netherlands Academy of Arts and Sciences webinar programme, Use of and need for animal procedures (Nut en noodzaak van dierproeven) (June 2020)

Royal Netherlands Academy of Arts and Sciences webinar programme, Use of and need for animal procedures (Nut en noodzaak van dierproeven) (June 2020)

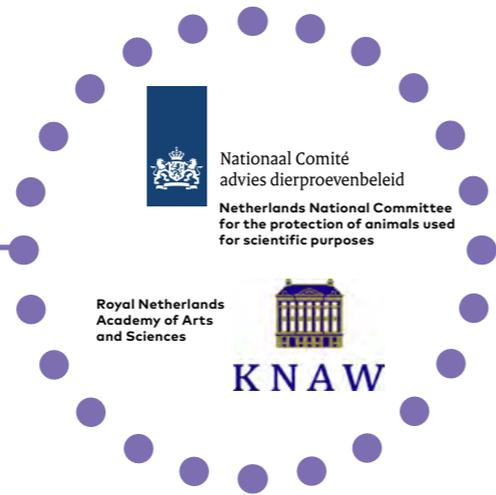
Request from Minister Schouten for NCad advice on COVID-19 and animal procedures (2020)

Partners

The TPI partners:

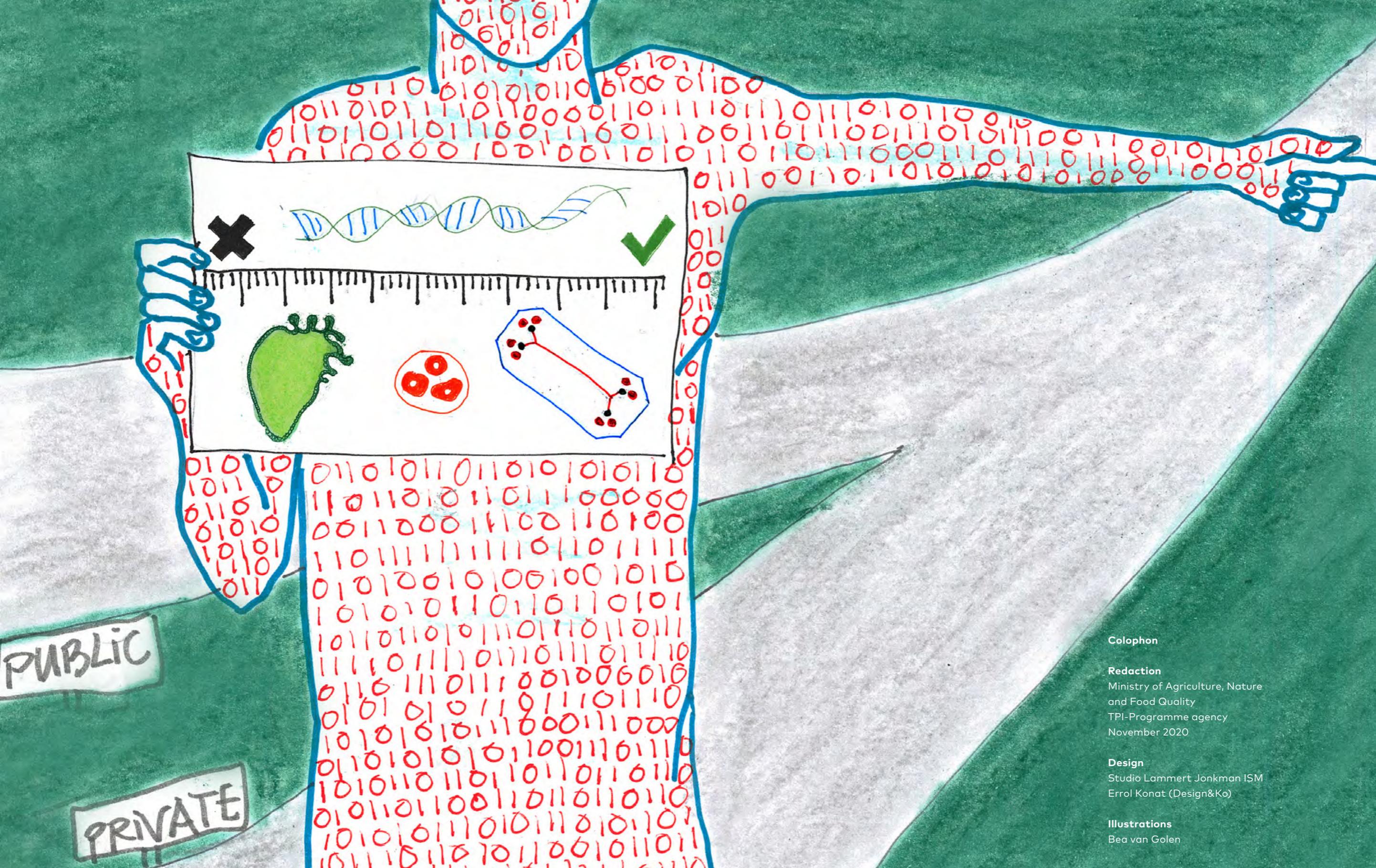


Core Group observers:



Transition experts:





Colophon

Redaction

Ministry of Agriculture, Nature
and Food Quality
TPI-Programme agency
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