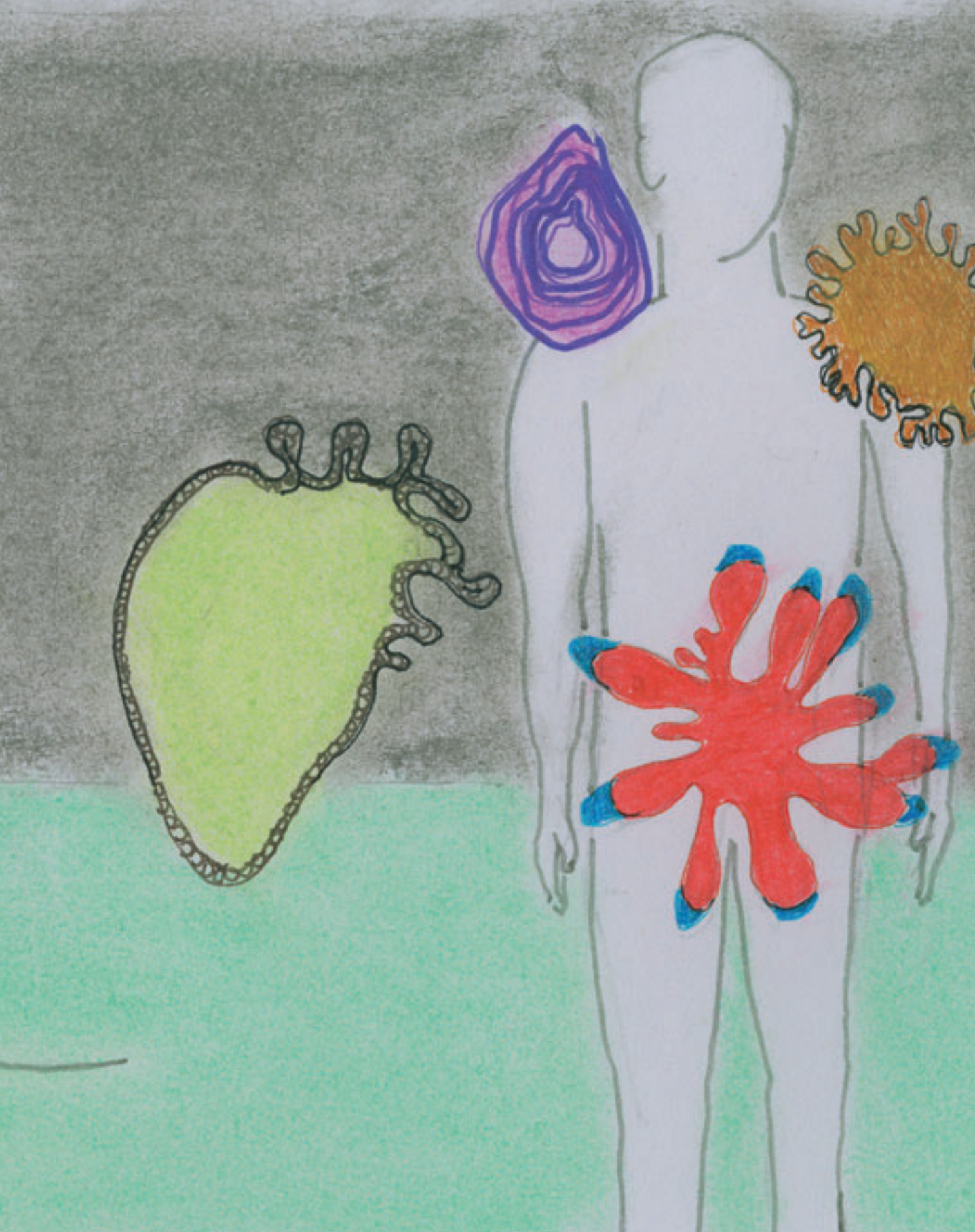
26 X BETTER AND FASTER WITHOUT USE OF ANIMALS

Dutch start-ups and scale-ups 2019

tpi.

The question must be: can better, smarter, cheaper alternatives be devised?



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Dutch start-ups and scale-ups 2019

Foreword

How can we improve research in the development of medicines, food safety and chemical risks without the need for laboratory animals? Representatives from the realms of science, health care, government and industry have joined forces to answer this challenging question. Various actors are involved, and many changes are needed. We are at the start of a new transition period. Transition Programme animal-free Innovations (TPI) is aimed at accelerating the change process.

Start-ups and scale-ups are of utmost importance in this transition. In an Innovation Network aimed at this target group, we are inviting start-ups and scale-ups to jointly tackle problems that stand in the way of animal-free innovations. At several meetings, we defined the biggest challenges and searched for specific solutions. You are looking at the result of one of these solutions: 26 'positive stories' and examples of producers of animal-free testing methods. These start-ups and scale-ups are going out on a limb. In addition to the usual obstacles faced by start-ups, they also overcome the obstacles of a sector that has long been structured around animal testing. Read their profiles, look at their technologies, and contact them if you are interested!

Collaboration between all stakeholders is key to further development, implementation and acceptance of these technologies, whether they involve Organs on a Chip, smart ex-vivo techniques or computer models.

We think the Netherlands has a positive role to play here, in Europe and around the world. A fine example of this is the Dutch OoC Consortium hDMT, which is hard at work to create an ecosystem with a growing European network of research groups in over 17 countries (European Organ-on-Chip Society).

To give you an impression of the lie of the land of start-ups and scale-ups working on animal-free innovations, this booklet includes reflections, visions and initiatives from the top sector LifeScience & Health (Health Holland), platform hDMT, trade association HollandBio, the Dutch Society for the Replacement of Animal Testing, and multinational contract research organisation Charles River.

We hope that you will find this booklet inspirational and that you will make useful contacts!

the Start-ups and Scale-ups TPI-innovation network

Transition Programme animal-free Innovations (TPI)

Why

The Transition Programme for animal-free Innovations (TPI) brings together people and organisations aiming to accelerate this transition. Together, we are working on:

- improved applicability and reliability of chemicals;
- improved predictability and reproducibility of scientific research;
- better treatment methods and efficacy of medicines;
- better and more accessible research information;
- applications for promising technologies;
- solutions to problems within the chain;
- a platform for debate.

How

When it comes to science and technology, every day we are learning and discovering more and more. Entrepreneurs, researchers and civil society organisations are becoming increasingly aware of the opportunities for research and testing without laboratory animals.
New medicines and chemicals can be tested for safety and efficacy in different ways. In this transition from animal testing to animal-free methods and technologies, the existing scientific and regulatory system based on animal testing will gradually be replaced – part by part – by the new way of working without animal testing, until the entire system has eventually been renewed. This process is facilitated by incremental changes and initiatives outside the existing frameworks.

What

A transition is a social development rather than a policy decision. However, policymakers can speed up, guide and supervise this process.
In this light, the Ministry of Agriculture, Nature and Food Quality has stepped up to the plate. On 1 June 2018, Minister Schouten wrote a letter to the Dutch House of Representatives explaining the philosophy and approach. Since then, several individuals and organisations have been working hard to accelerate the transition towards animal-free innovation by starting innovation networks and projects.
Innovation networks connect and support pioneers, enabling them to explore and expand their horizons within a safe environment, and so to stimulate disruptive changes. The start-up and scale-up network is one of these TPI-related innovation networks.

Quintessence & Appreciation

Why do you want to speed up the transition towards animal-free innovation?

Minister Schouten: I think it's very important that we work together on alternatives to animal testing. Many scientists believe that tests using alternative methods are much better at predicting whether something works and is safe for people. Alternatives often save time and costs. We also see a growing concern in society about the welfare of laboratory animals.

What is the importance of animal-free innovations?

Prince Constantijn: Animal testing is often comparatively more expensive and slower than alternative testing. Animals need to be cared for. Impacts take time to emerge. Animal-free tests can be performed much faster at the same time, a substantial cost saving can be realized.

Have you had a response yet to your call to work together on speeding up the TPI?

Minister Schouten: The drive to speed up the TPI has had a first response, which I'm very happy about. Association of Dutch Health Foundations and Health Holland are now spending over 3 million euros on a research programme for 'human measurement models and animal-free innovation'. Since more partners wish to join, this amount will grow in the coming years.

Why is it important that start-ups have a podium?

Prince Constantijn: Start-ups and scale-ups are the creative, driving force behind the technological revolution. Start-ups turn new technologies into scalable products and build future companies. That's why it's important that we focus on opportunities by showcasing promising start-ups and scale-ups. Real change starts with visibility and awareness.

What do you know about Start-ups in the Dutch topsector Life Sciences and Health?

Prince Constantijn: The Dutch increase at the Genome Global Start-up Ecosystem Ranking (from #19 in 2017 to #15 in 2019) is partly due to our strong performance in Life Sciences and Health. Dutch universities and businesses are continuously looking for ways to make the country's 'Life Sciences and Health print' leaner and better.

What is the urgency of finding alternatives to animal testing?

Minister Schouten: As said, animal tests often fail to predict the disease process in humans accurately. Also, internationally validated alternative tests are not always available yet. Together we must find ways to make it easier for start-ups with innovations in this field to access the market, to stimulate real change.

Prince Constantijn: The presented start-ups and scale-ups in this booklet not only provide alternatives for animal testing, but also demonstrate that the Netherlands is the home for tomorrow's leaders in tech. Of course, their potential will only materialize when they get sufficient (legal) room for experimentation and acceleration. Any support provided can help bridge the 'valley of death' between proven technology and scalable products that really have a global impact on animal free testing innovation.

Why do you want the Netherlands to be an international leader in these developments?

Minister Schouten: Laws and regulations around animal testing are Europe-wide, and scientists and the business community are operating in an international context, so proving that an alternative is safe to use is an international quest. That's why the Netherlands is keen to bring other countries on board. Let's bring our forerunners together. Alone you go faster, but together we can make real progress!

Prince Constantijn: The Netherlands has an excellent starting position to present itself internationally as a forerunner in the field of animal-free innovations. This position can be used to accelerate the transition to animal free research on an international level as well.

At its core, what should the TPI dialogue be about?

Minister Schouten: I've found that everyone involved in the chain wants there to be a conversation about just what can be done differently, and what it would take. How do we actually implement animal-free innovation? The emphasis in this conversation is on increasing alternative tests, rather than on reduction of animal tests.

Prince Constantijn: It's important that all involved parties start the dialogue on what is needed for animal-free testing innovations to be acceptable. Knowledge sharing between start-ups and scale ups with contract research organizations and pharmaceutical companies should be improved. Ultimately, the question must be: can better, smarter, cheaper alternatives be devised? If we find solutions, all parties benefit.

Minister of Agriculture, Nature and Food Quality: Carola Schouten

His Royal highness Prince Constantijn van Oranje, Special Envoy TechLeap.NL

Working together on animal-free innovation is essential.

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Taking the lead together on alternatives to animal testing

Working together on animal-free innovation is essential, say Wilbert Frieling and Erik Baltussen of American contract research organisation Charles River Laboratories (CRL). That's why they collaborate with innovative start-ups and advocate collaboration between various stakeholders.

'You must join forces to achieve your goal,' Baltussen believes. Frieling adds: 'The goal is to be a leader in alternatives to animal testing in roughly five years' time.'

At CRL, Frieling is in charge of early development and pharmacology in the international discovery division. A few years back, Baltussen took over from him as director of the branch in Den Bosch. Further down the development path, this branch carries out safety research for new medicines and other substances.

What does CRL do?
In Groningen and Leiden, CRL's Discovery division tests the efficacy of new medicines in vitro (culture dish), in silico (computer), in chemico (chemical analysis) and in vivo (entire animals). For example, when the academic world has developed a new enzyme: how do molecules react to it? How does it behave at the cellular level? And it is effective in taking on the targeted disease in a live animal?

In Den Bosch, CRL – also through a combination of in-silico, in-vitro and in-vivo methods – tests whether new substances are safe and can be marketed. This is done by following procedures regulated by law. Baltussen: 'We may be asked to investigate whether a new medicine does not have the side effect of causing liver cancer. It is not uncommon for substances we look at not to make it past our tests.'
Development takes place within the legal framework for the assessment of medicines (CBG, EMA, FDA), pesticides (CTGB) and chemical substances (ECHA).

Predictive value

'Nobody likes animal testing. Since 1977, the law has prohibited animal testing if there is a valid alternative. In-vitro methods can test more in a shorter period of time than in-vivo tests can. Moreover, animal tests don't always yield 'data that correlate with the human situation'.
If something turns out not to work in people, it's a waste of the effort put into laboratory animals. After all, they need looking after, veterinary care and feeding. Tests performed in a stand of test tubes therefore save money.
But Frieling is doubtful about the proposition that in-vitro testing generally has better predictive results than in-vivo testing.

'A lot of Alzheimer research is disappointing', he observes. 'On the other hand, the harmful substance Softenon appeared to have no detrimental effects on rats.'
Baltussen: 'There are no outcomes that can be predicted with 100% certainty.' He is hesitant to call animal testing a gold standard as long as not everything can be seen in a Petri dish.
In very many cases, the safety of alternatives has yet to be demonstrated, while we have 60 years worth of experience with animal testing. For this reason, the in-vitro models are first compared with animal tests. As more data are collected, the predictive value improves.

'There's a lot of work still to be done. All the more so because society is less and less willing to take risks', Frieling points out.

Trend towards greater complexity

Erik Baltussen explains that the number of in-vitro methods and chemical analyses is growing. At the same time, in-vivo tests are replacing live animals with slaughterhouse waste where possible. The BCOP (Bovine Cornea Opacity/Permeability) test, for example, uses the eyes of slaughtered cows. Similarly, the ICE (Isolated Chicken Eye) test uses the eyes of slaughtered chickens.

'The relative proportion of animal tests has decreased, and this trend is set to continue', Baltussen believes. 'Excellent alternatives are already available for relatively simple end points such as eye irritation. In 95% of cases, in-vivo tests are no longer needed for such things.'

'I predict that alternatives will be used in increasingly complex situations', Baltussen ventures.

Smart partners

CRL increasingly entering into new forms of collaboration with start-ups. Acquisition does not always work straight away, as contract research organisations and start-ups have very different starting principles. Frieling: 'Start-ups that come up with an innovation see a big future ahead of them, but have yet to prove themselves. Collaboration may be a better option to further develop the innovation.
Later on, the parties can decide whether acquisition is an interesting option for both of them. DistributedBio is a current partner of ours. Their innovation consists of a file in which they've collected 70 million unique human antibodies. Our partnership is such that, at the moment, we're also selling their product to our customers.' CRL also works on the continued development of the innovation. Further down the line, both parties may start on an acquisition process if they so wish.

CRL is looking for partnerships with several start-ups at the same time. As Baltussen explains: 'one single technique is never the solution for everything. Various innovations by different start-ups can complement each other.' Accordingly, CRL is also looking to team up with a start-up that creates 3D models.
'Where previously we'd introduce tumour cells into a mouse to grow a tumour for testing a new medicine on, we can now create 3D organoids from specific patient material.
In these 3D models, we can test thousands of

substances at once on different types of tumour cells, but also on such cells as liver cells and tissue cells. You pick the most promising substances and only these are then used in animal tests.'

'Testing on these new 3D models saves a lot of mice and a lot of time. And time is precious for patients', says Frieling.

Helping each other move forward

Aside from private cooperation in technical innovation, the actual use of alternatives requires a kind of systematic innovation across the chain. Scientists feed the innovations, companies can scale them up and governments can assess these innovative tests and permit them in an international context.
Without joining forces, you won't be able to meet your goal of being a leader in alternatives to animal testing in roughly five years' time.
The innovative cooperation in the chain mainly involves safety research, in which CRL does not want to keep exclusive control of Intellectual Property (IP). It's only in this way that progress can be made.

CRL, then, advocates systematic innovation with different stakeholders but finds public-private partnership to be difficult, as the business community can only invest profit in a still uncertain venture up to a point.
Other parties will have to share the risk.
The Netherlands, however, is good at forming PPP constructions. A lot of experience has been gained regarding how the scientific and business communities can draw up constructive contracts. This is done by first deciding what they want, and only then working out a proper legal arrangement – not the other way around.

Pioneering the past

As early as the 1980s, Frieling was active in the Platform for Alternatives to Animal Testing *(Platform Alternatieven voor Dierproeven)*.
'At the time, this united the industry, academics and animal rights activists. The difference with now is that back then, the government did not have a clear position on what we wanted to achieve, in contrast to its current goal of being a pioneer.

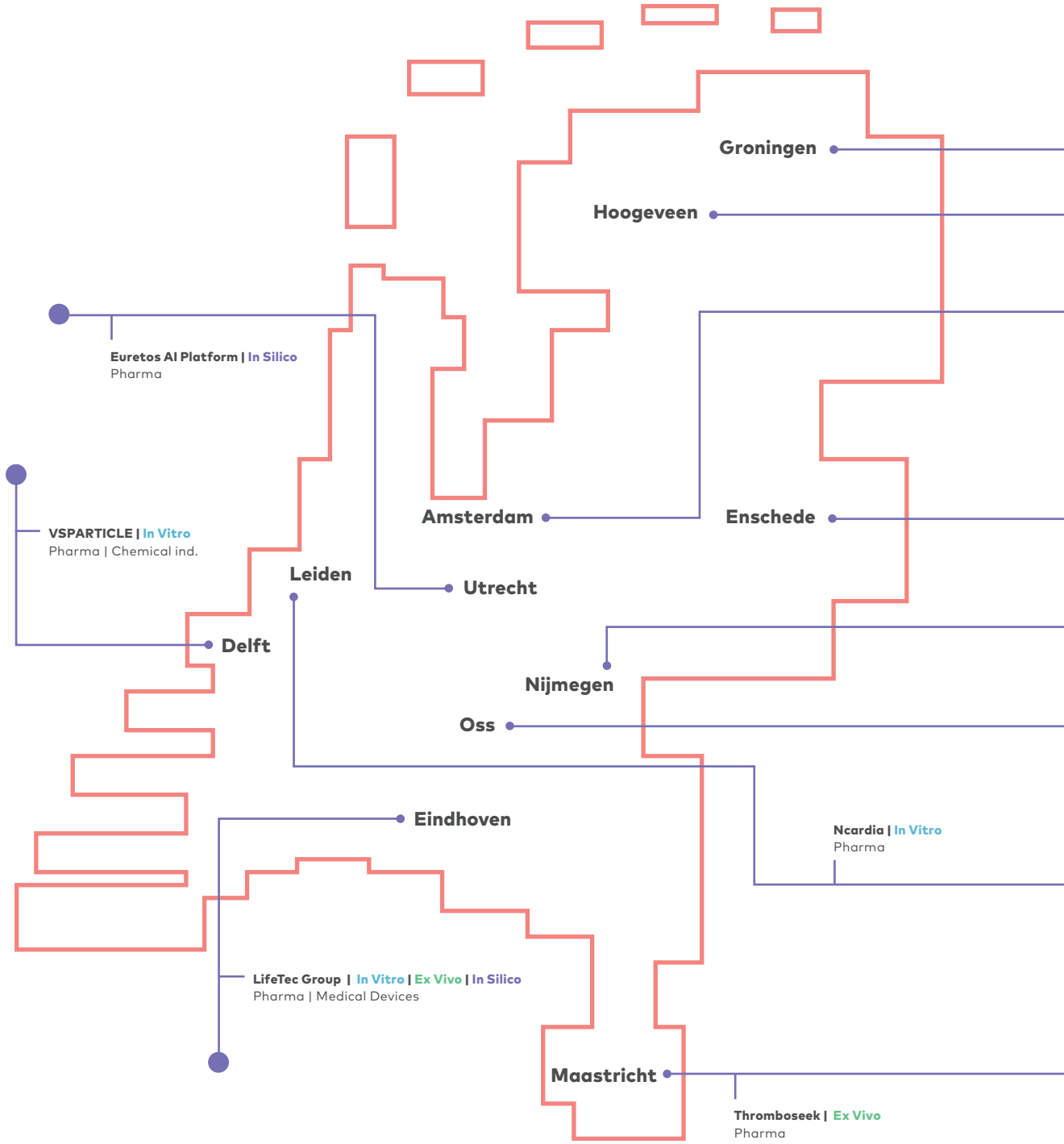
The international community was not clear on whether the Netherlands wanted to phase out animal tests by 2025. If such tests were to be banned altogether, everything would stop, as all activities are interrelated. The TPI approach in which the focus is on scaling up of alternatives with pioneers is a good one that everyone can rally behind.

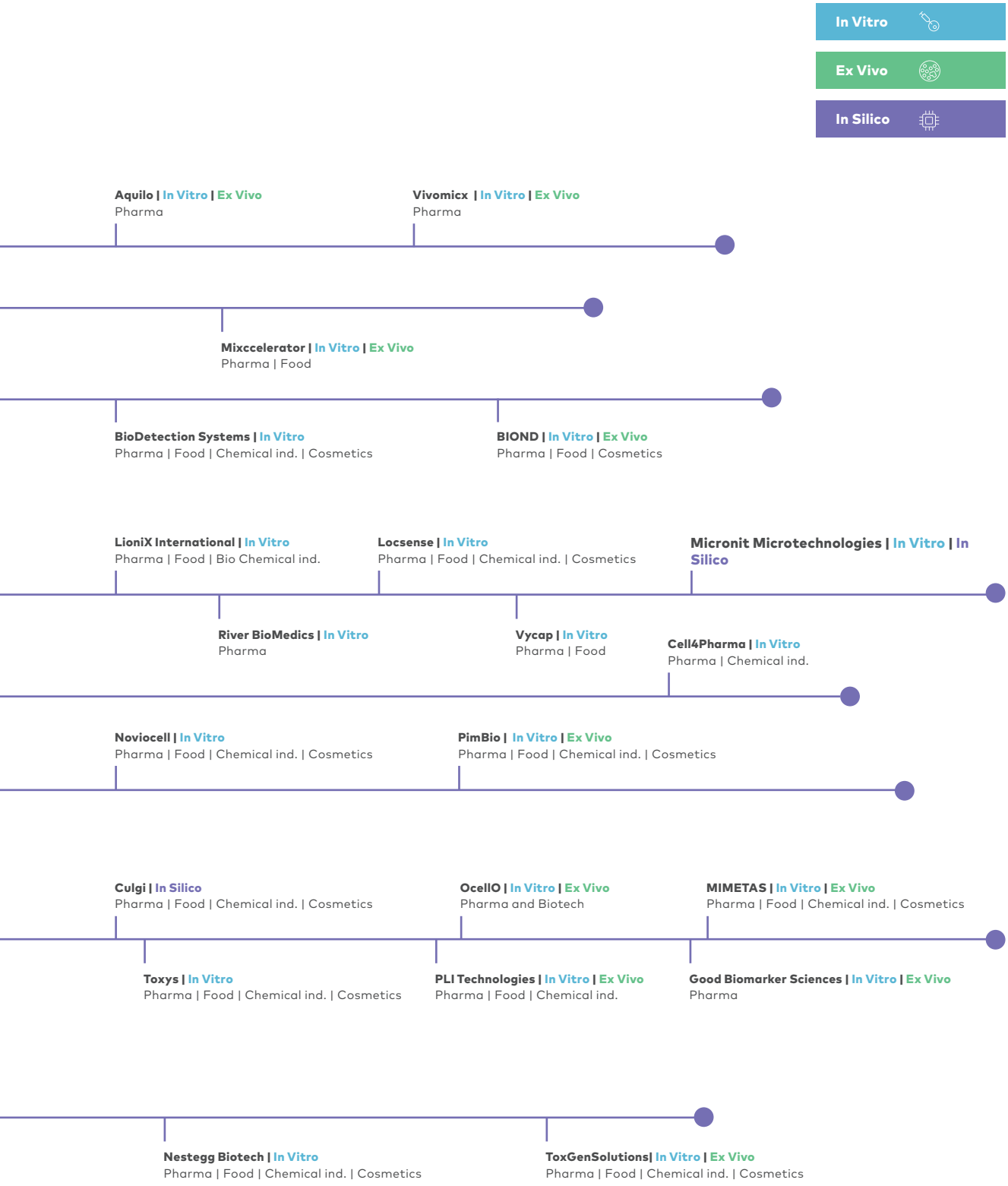
'As the TPI flag is being flown by the national government, it's possible to associate your activities with it. It works the same way as with the qualification for corporate social responsibility. There is better backing now', according to Frieling.

26 x start-up and scale-up

Aquilo
BioDetection Systems
BI/OND
Cell4Pharma
Culgi
Euretos AI Platform
Good Biomarker Sciences
LifeTec Group
LioniX Int.
Locsense
Micronit Microtechnologies
MIMETAS
Mixccelerator
Ncardia
Nestegg Biotech
Noviocell
OcellO
PimBio
PLI Technologies
River BioMedics
Thromboseek
ToxGenSolutions
Toxys
Vivomicx
VSPARTICLE
Vycap

Geographic map




In Vitro
Ex Vivo
In Silico
Aquilo | In Vitro | Ex Vivo
Pharma
Vivomicx | In Vitro | Ex Vivo
Pharma
Mixccelerator | In Vitro | Ex Vivo
Pharma | Food
BioDetection Systems | In Vitro
Pharma | Food | Chemical ind. | Cosmetics
BIOND | In Vitro | Ex Vivo
Pharma | Food | Cosmetics
LioniX International | In Vitro
Pharma | Food | Bio Chemical ind.
Locsense | In Vitro
Pharma | Food | Chemical ind. | Cosmetics
Micronit Microtechnologies | In Vitro | In Silico
River BioMedics | In Vitro
Pharma
Vycap | In Vitro
Pharma | Food
Cell4Pharma | In Vitro
Pharma | Chemical ind.
Noviocell | In Vitro
Pharma | Food | Chemical ind. | Cosmetics
PimBio | In Vitro | Ex Vivo
Pharma | Food | Chemical ind. | Cosmetics
Culgi | In Silico
Pharma | Food | Chemical ind. | Cosmetics
OcellO | In Vitro | Ex Vivo
Pharma and Biotech
MIMETAS | In Vitro | Ex Vivo
Pharma | Food | Chemical ind. | Cosmetics
Toxys | In Vitro
Pharma | Food | Chemical ind. | Cosmetics
PLI Technologies | In Vitro | Ex Vivo
Pharma | Food | Chemical ind.
Good Biomarker Sciences | In Vitro | Ex Vivo
Pharma
Nestegg Biotech | In Vitro
Pharma | Food | Chemical ind. | Cosmetics
ToxGenSolutions| In Vitro | Ex Vivo
Pharma | Food | Chemical ind. | Cosmetics

Aquilo

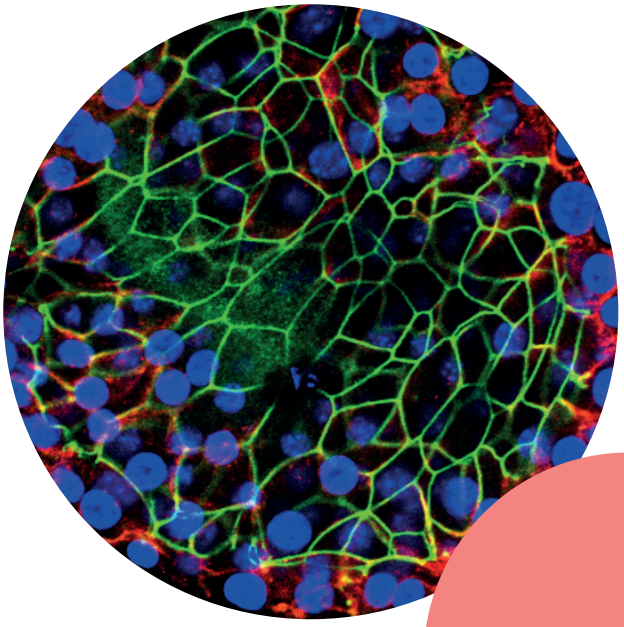
Aquilo is a CRO focused on the respiratory system, founded as a spin-off from Groningen University. We perform efficacy studies on novel compounds and therapies for lung diseases using models of lung fibrosis, COPD, and asthma. For this, we use classical in vivo animal models as well as novel ex vivo lung slice and organoid models, which can be prepared from human tissue or cells. Furthermore, we have in vitro models available with cells of human origin, including diseased cells.

What is your contribution to the transition to animal-free innovation?

We invest in novel models for efficacy testing, thereby aiming to reduce or exclude the use of animals while at the same time increasing the translational value of the data. We do this by direct investments in developing novel models. We are currently working on novel organoid models by validating several disease stimuli and the effect of registered and novel drugs thereon. Furthermore, we participate in research projects that develop novel models including the NEURO-CHIP project from Groningen University, which will be implemented in Aquilo's portfolio.

What is your personal motivation doing this work?

I want to contribute to drug development and recognize the limitation of animal models in this field. Therefore, I feel motivated to invest in novel – human – models with the potential for higher translational value.



A representative picture showing a human organoid (mini-lung).

Target Sector	Pharma
Company size	1 – 10
Contact	Loes Kistemaker | l.e.m.kistemaker@aquilo.nl | +31 50 3636 372 | www.aquilo.nl

AQUILO
RESPIRATORY CONTRACT RESEARCH

BioDetection Systems

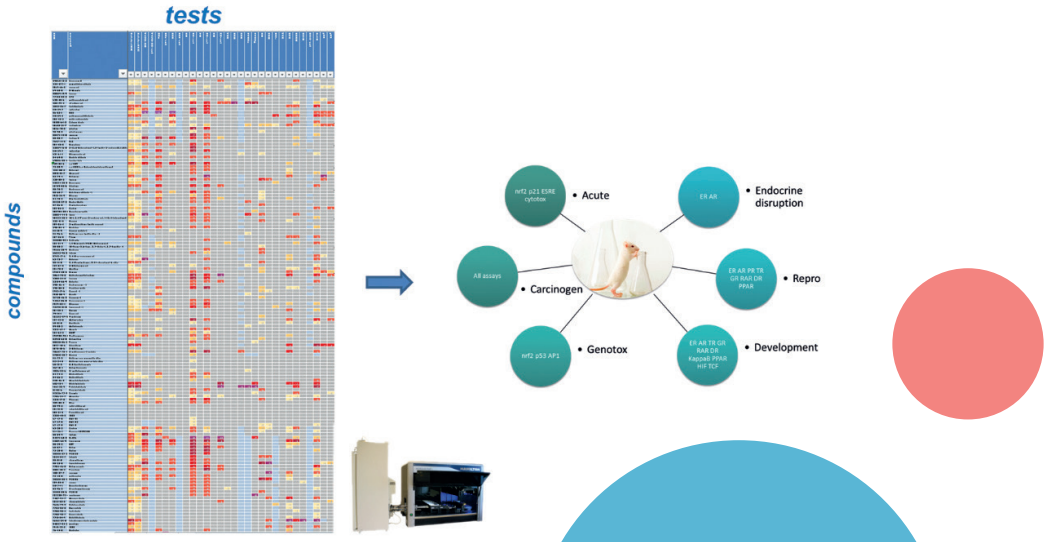
BioDetection Systems (BDS) protects the safety and quality of food, health and the environment by offering sensitive and efficient in vitro test methods, without the use of animal experiments. The proprietary CALUX® methods measure the interaction of compounds with key toxicological targets in human cells and are used as alternatives to animal testing in a range of relevant application areas. BDS has established a platform of these cost-effective high-throughput tests that can rapidly inform on the toxicological properties of single chemicals and chemical mixtures. Methods are disseminated world-wide through licensing and training.

What is your contribution to the transition to animal-free innovation?

From its start in 2001, BDS has been actively engaged in promoting the use of its methods as animal alternatives. This involves new product development, demonstration studies, and successful validation and guideline development together with international organizations like OECD and EURL-ECVAM. The key role of innovative small and medium-sized enterprises (SMEs) in these processes is increasingly acknowledged.

What is your personal motivation doing this work?

To make toxicological assessments more robust and cost-effective while replacing animal testing.



In vitro predictions of animal test results range between 75-100%, which is similar to variation in animal experiments and interspecies extrapolations.

Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	11 – 50			
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BI/OND Solutions

BI/OND supports biologists working in pharmaceutical companies, biotech, and academia in exploring fundamental questions about human health and diseases by providing versatile, dynamic chips for 3D tissue assays. BI/OND provides microfluidic chips on a six-well plate format able to nourish, stimulate, and monitor complex 3D tissues. The microfluidic chips use the fabrication technology of mass-produced computer chips. BI/OND products are versatile as they are qualified for complex 3D tissue (organoids, ex vivo tissue, spheroids, microtissues) cultivation as well as tissue-tissue interface models.

What is your contribution to the transition to animal-free innovation?

Since its incorporation, BI/OND has been enabling and supporting biologists who want to transition from in vivo to in vitro models, in particular those who recognize organ-on-chips as one of the most promising technologies to work towards an animal-free research process. BI/OND eases this transition by providing robust and intuitive products so that biologists can focus on what they do best, without worrying about the technology behind their models.

What is your personal motivation doing this work?

The BI/OND team recognizes the importance animal tests had in the past during the development of life-saving cures. However, at the same time we also believe that by combining our technology with the new developments in biology our customers can achieve better models than those provided by laboratory animals. For this reason, the BI/OND team feels it has the duty to provide new chips to our customers to bridge the gap between in vitro and in vivo, and, eventually, to pave the way towards animal-free solutions.

BI/OND's product supports up to six cultures in parallel, with the option to perfuse compartments with different flow rates, to stimulate mechanically and to image 3D tissues. It is compact, reusable and compatible with any perfusion system.

Target Sector	Pharma	Food	Cosmetics
Company size	1 – 10		
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BI/OND

Cell4Pharma

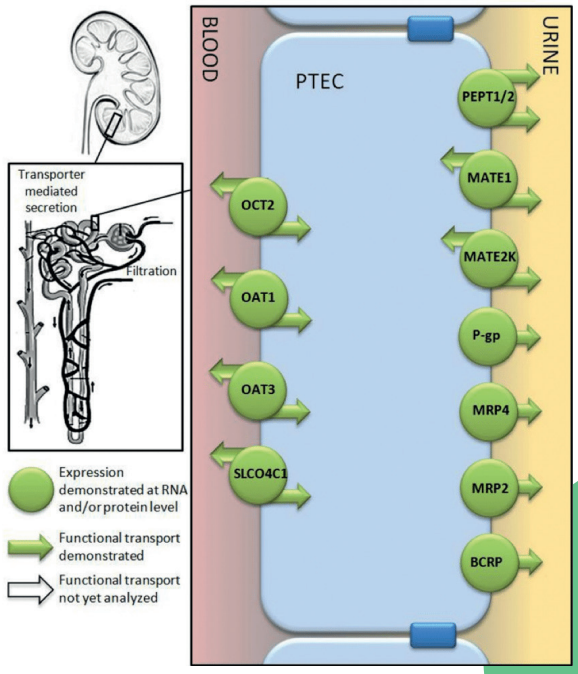
Cell4Pharma offers several tools to (bio)pharmaceutical companies, CROs and academia in the field of drug toxicity screening, drug–drug interaction studies, and kidney-related research, such as an immortalized human renal cell model (ciPTEC model). Furthermore, we produce transport models based on human tissue that we offer as a service to (bio)pharmaceutical companies.

What is your contribution to the transition to animal-free innovation?

All our models are directly derived from human cells and/or tissue. This enables us to show high robustness and predictability for in vitro drug screening. As a result the attrition rate during the expensive clinical stages of drug development decreases. Drug toxicity testing is still being performed on animals. By providing our models to the pharmaceutical industry we offer an alternative to animal testing.

What is your personal motivation doing this work?

Unfortunately, a lot of toxicological testing is performed on animals. Several studies have shown that in vitro models could be an even better alternative than animal testing.
By providing our models to the life sciences industry we intend to contribute to more efficient drug development, decrease animal testing and ultimately develop safer drugs for patients and physicians.



Target Sector	Pharma	Chemical industry
Company size	1 – 10	
Contact	Ron Byron | info@cell4pharma.com | +31 6 223 510 74 | www.cell4pharma.com	

Cell 4 Pharma

Culgi

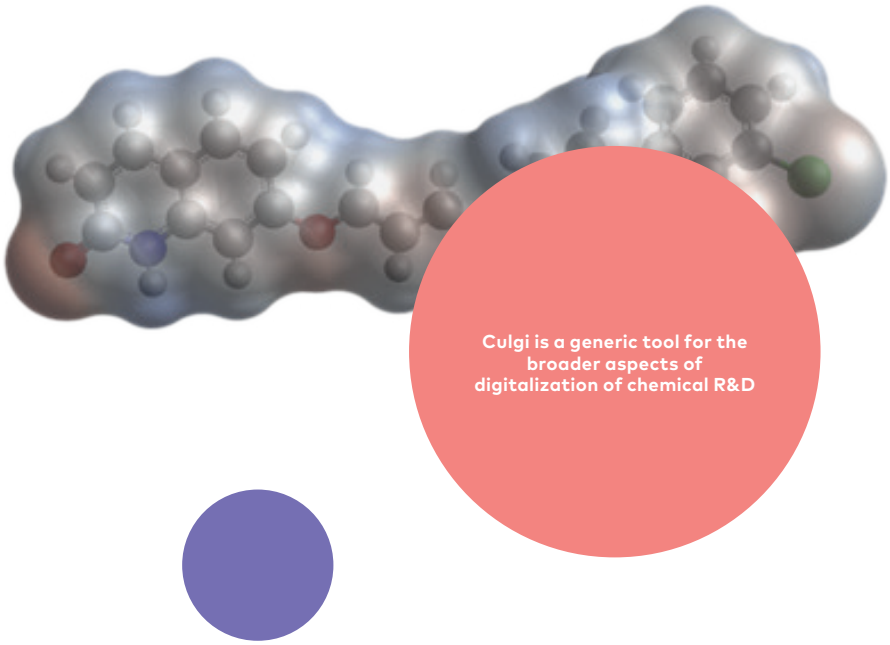
Culgi's core activity is computational chemistry: modeling the properties and the behavior of chemicals in complex mixtures, such as the human body. The main goal is to speed up the discovery of new products. Culgi offers a professional multiscale-modeling software package, in combination with service and contract research. The science behind the Culgi software ranges from quantum chemistry to coarse-grained modeling and from chemical informatics to thermodynamics, machine learning and artificial intelligence

What is your contribution to the transition to animal-free innovation?

Candidates for a new drug to treat a disease might theoretically include 5,000 to 10,000 chemical compounds. On average, about 250 of these compounds show sufficient potential for further evaluation using laboratory tests with mice and other research animals. Culgi predicts the properties of drug candidates, such as toxicity, in a very early stage of drug discovery, even before the materials or candidates themselves exist. Therefore, Culgi reduces the number of lead compounds to be tested on animals in the next stage.

What is your personal motivation doing this work?

We respect all life on earth and prevent unnecessary pain and suffering. The use of Culgi software and computational methods do not cause any damage to the health of humans, animals, or the environment. R&D based on Culgi is a smart way to work on sustainable solutions in chemistry without wasting animal lives, material or energy.



Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	1 – 10			
Contact	Erica Fraaije-van der Stelt | erica@culgi.com | +31 71 3322 055, mob: +31 6 52665017 | www.culgi.com			

CULGI

Euretos AI Platform

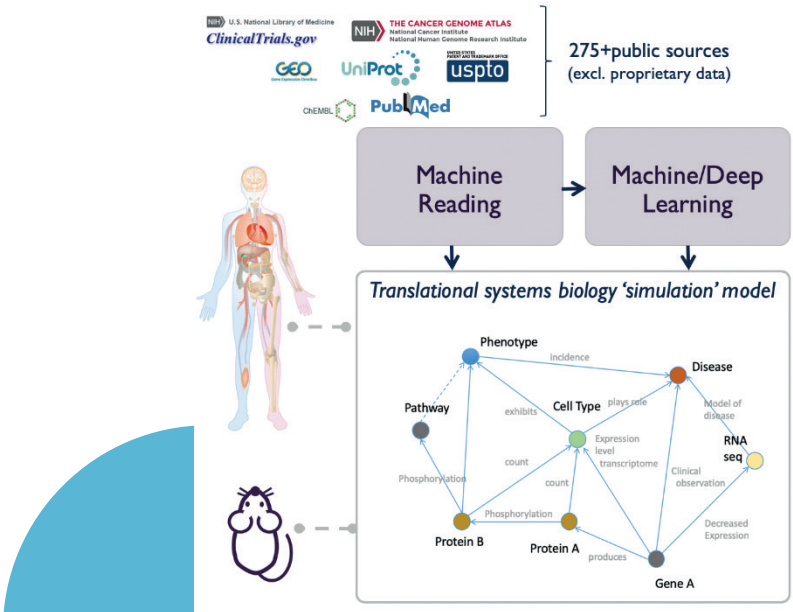
Euretos AI Platform provides AI-driven research support as well as direct access to the Euretos AI Platform to enable in silico discovery and validation of targets, biomarkers and indications. We enable (pre)clinical researchers to take a translational systems biology approach connecting molecular multi-omics interactions – through cellular involvement – to the level of functional and phenotypic characterization that are relevant for a disease or pathology. Inter- and intra-cellular protein networks are identified through deconvolution of bulk expression profiles leveraging Euretos' extensive cell type expression library.

What is your contribution to the transition to animal-free innovation?

The Euretos platform provides a unique 'translational systems biology' model of diseases. This enables in silico simulation analysis to assess drug efficacy, response and toxicity. The platform contains detailed information of many types of animal models as compared to human biology and helps to address the translation gap of moving from the preclinical stages of drug development to the clinic.

What is your personal motivation doing this work?

Our primary motivation has always been to increase the effectiveness of target and biomarker development within the context of drug discovery. By maximizing the use of in silico methods the preclinical stage can be shortened and the translation gap to clinical testing reduced. This, in the end, will reduce the risk and cost of drug development resulting in better and cheaper therapies that enter the market earlier. This is an important benefit to society, which we believe should come at minimal cost for any living organism involved in this process.



Target Sector	Pharma
Company size	11 – 50
Contact	Arie Baak, co-founder | information@euretos.com | +31 6 50245801 | www.euretos.com

EURETOS
AI PLATFORM

Good Biomarker Sciences

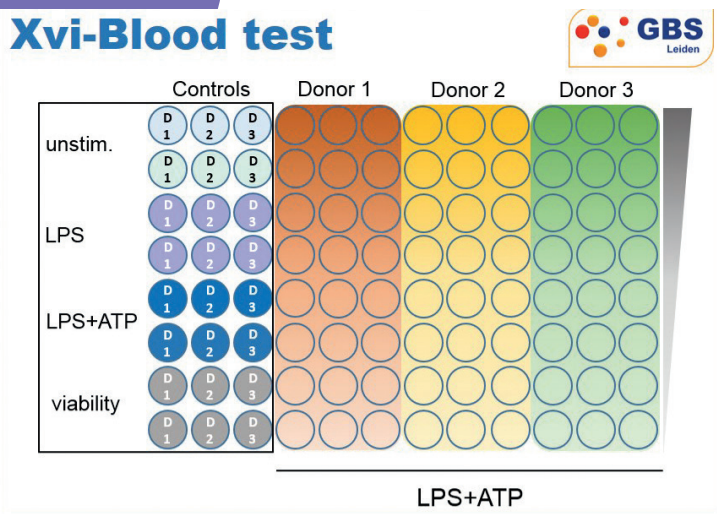
GBS is a Good Clinical Laboratory Practice (GCLP)-certified contract research laboratory specialized in biomarker discovery for late preclinical studies and clinical trials in the field of hemostasis, immunobiology and bioenergetics. We offer biomarker or cell-based platforms that can be used to determine the precise action of drugs or monitor the health of patients. GBS scientists seek to translate scientific findings into new services or products by participating in EU projects together with academia or industry as SME.

What is your contribution to the transition to animal-free innovation?

GBS offers tests to prospective clients to obtain a waiver from FDA or EMA for some in vivo testing. Caco-2 permeability assay to investigate intestinal permeability of new drugs is included in our portfolio of in vitro absorption, distribution, metabolism, excretion (ADME) screening services. Another test is the Xvi-Blood test which is an ex vivo method to assess human cellular immune and inflammasome responses to different challenges in intact human whole blood.

What is your personal motivation doing this work?

My motivation is to reduce the use of animals in biomedical research by replacing the animal models with in vitro/ex vivo testing systems that closely mimic human physiology and pathology. I did my PhD in the field of in vitro vascularization of tissue-engineered constructs in xenogeneic conditions, thus I find a great deal of personal and professional satisfaction in finding scientific solutions that contribute to the reduction and/or replacement of animal testing.



Target Sector	Pharma
Company size	1 – 10
Contact	Dimitar Tasev | d.tasev@gbsleiden.nl | +31 71 7517 175 | www.gbsleiden.com

GBS Leiden

LifeTec Group

LifeTec Group carries out preclinical medical-technical research and technology development by means of different R&D platforms in which ex vivo isolated functional organs obtained from the slaughterhouse are used to mimic the situation in the human or animal.
We support training programs for medical doctors or other end users of medical devices by using our dedicated training platforms. Furthermore, we develop and sell these novel R&D and training platforms. Use of these ex vivo tissue platforms accelerates the R&D path of our clients and it improves training programs for end users.

What is your contribution to the transition to animal-free innovation?

In our platforms we make use of isolated organs that are considered a by-product after slaughtering. Since we can keep these organs functional in our platform technologies, we can very well mimic the situation in the body, thereby reducing the need to perform animal experiments. Our clients significantly reduce the amount of animal studies by working with us and our platforms, or sometimes even replace them altogether.

What is your personal motivation doing this work?

We believe patients deserve meaningful medical solutions and we contribute to this. With our platforms and R&D services we help develop these medical solutions by shortening the time-to-patient.

'Cardiac Biosimulator Platform used to assess the functionality, implantability, and operability of medical devices and to train medical professionals'.

Target Sector	Pharma	Medical devices
Company size	11 – 50	
Contact	Dr. Linda Kock | l.kock@lifetecgroup.com | +31 40 2989 393 | www.lifetecgroup.com	

LifeTec Group

LioniX International

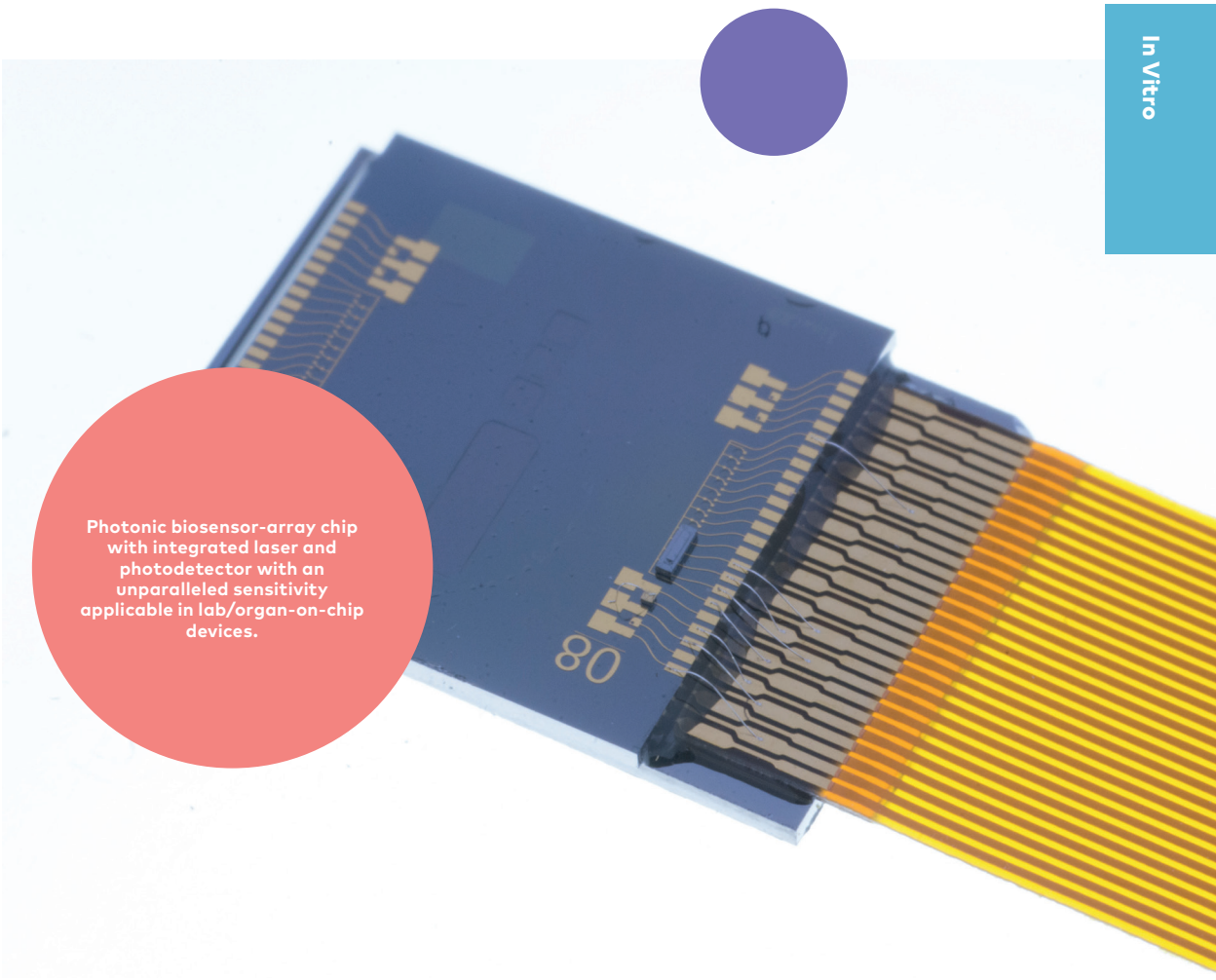
LioniX International B.V. is a global provider of customized microsystem solutions in scalable production volumes. We offer customized solutions for OEMs and system integrators in tele/datacom, life sciences, process control and space: from the design to the full assembly of modules. LioniX focuses on photonic integrated circuits (PIC)- enabled modules based on its proprietary waveguide technology (TriPleX™), in addition to its other core competences micro-fluidics, opto-fluidics and related surface functionalization (sister company Surfix).

What is your contribution to the transition to animal-free innovation?

LioniX has expertise in the area of lab-on-a-chip-based biochemical analysis and processing systems for (molecular) diagnostics, cell/organ characterization tools for drug discovery and development, (companion) diagnostics, and other applications. Lionix projects will result in precursors for the development of high-added value equipment, to be further developed in collaboration with (venture capital) equipment companies.

What is your personal motivation doing this work?

LioniX employees are keen on bringing their integrated photonics technologies to the market in close collaboration with partners who have complementary know-how and technologies. Organ-on-chip is extremely multidisciplinary and a contribution in the paradigm shift of personalized/precision medicine is a highly appreciated area of work.



Photonic biosensor-array chip with integrated laser and photodetector with an unparalleled sensitivity applicable in lab/organ-on-chip devices.

Target Sector	Pharma	Food	(Bio) Chemical industry
Company size	50 – 250		
Contact	Henk Leeuwis | h.leeuwis@lionix-int.com | +31 53 2030 053 | www.lionix-int.com		

LIONIX INTERNATIONAL

Locsense

Locsense enables biologists to automate and standardize their experiments, by developing devices for read-out, stimulation and sensing of cell cultures. An example is the application of the Locsense Artemis for monitoring the heartbeat of cells forming a heart-on-chip. Our intuitive technology lowers the barrier for biologists to include organ-on-chip technology in their routine.

What is your contribution to the transition to animal-free innovation?

Animal testing is costly, considered unethical and, in many cases, not representative for the efficacy of medicines in patients. Organs-on-chip are considered a promising alternative, potentially leading to the development of personalized medicine and treatment.
The number of providers of organ-on-chip platforms has increased accordingly. However, there is a lack of enabling systems for read-out and control. With our expertise in the field of sensors, electronics and microfluidics, Locsense is an excellent partner in cell culture automation. We have already demonstrated this for heart-, lung- and intestine-on-chips.

What is your personal motivation doing this work?

What drives me in this work is the progress we are making in growing a sustainable and innovative company. Through the products and services Locsense delivers, we aim to contribute to a better understanding of disease mechanisms and health(care) improvement. It is very rewarding to collaborate with researchers on a variety of projects.

The Locsense Artemis enables biologists to monitor the integrity and activity of their cells in culture

Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	1 – 10			
Contact	Dr. Susan Roelofs | info@locsense.nl | +31 85 792 1097 | www.locsense.nl			

Locsense

Micronit Microtechnologies

Micronit Microtechnologies is a contract manufacturer for lab-on-a-chip and MEMS devices. With development and manufacturing facilities in the Netherlands and Germany, Micronit is a trusted partner for customers in medical as well as scientific fields. As microfluidics specialist, Micronit can provide devices for DNA sequencing, liquid biopsy or precise spray nozzles.

What is your contribution to the transition to animal-free innovation?

Micronit Microtechnologies develops and produces organ-on-chip devices for customers. On an organ-on-chip platform, cells can be cultured in such a way that they mimic the physiological response of organs. With precisely controlled microfluidic flows, the cells can be nurtured and analyzed to test the effect of e.g. drugs in a biologically relevant context.
An organ-on-chip array mimics in vivo complexity in relatively simple in vitro or in silico devices. The progress in this field shows increasing diagnostic reliability, thus reducing the need for clinical trials on animals and humans.

What is your personal motivation doing this work?

Micronit Microtechnologies provides customers with intelligent and sustainable product solutions. We expect chip technology to become indispensable in healthcare, as it can provide alternatives for the pharmaceutical solutions that are being used at this moment.

Target Sector	Pharma	Cosmetics
Company size	50 – 250	
Contact	info@micronit.com | +31 53 8506 850 | www.micronit.com	

micronit microtechnologies

MIMETAS

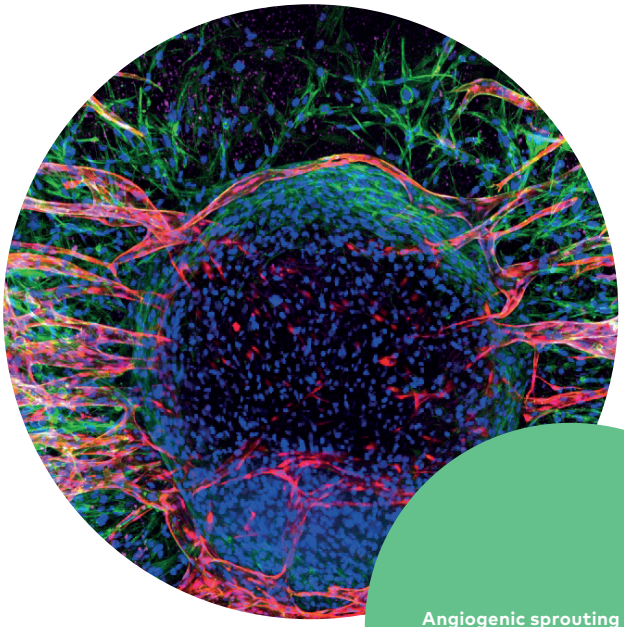
MIMETAS develops human tissue models in organ-on-chip devices for better and safer medicines, chemicals and food. The MIMETAS OrganoPlate® features unsurpassed scalability and ease-of-use to mimic complex physiologies of tissues and diseases, including cancer, inflammatory diseases, and neuronal diseases. MIMETAS offers OrganoPlate® products and innovative tissue model development services to the industry and academic researchers worldwide.

What is your contribution to the transition to animal-free innovation?

The technologies of Mimetas reduce, refine, and replace animal experimentation in medicine and chemical development for discovery, toxicological as well as efficacy and therapy selection studies.

What is your personal motivation doing this work?

For many applications, animal testing lacks predictivity towards people and is therefore not sufficient to develop safe and efficacious compounds. My goal is to provide better tests based on relevant human tissue and disease models that lend itself to fast and affordable testing. In this way, we already prevent unnecessary animal testing, while in the longer run animal testing may become obsolete.



Angiogenic sprouting of HUVEC to a liver spheroid in the OrganoPlate Graft.

Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	50 – 250			
Contact	info@mimetas.com | +31 85 8883 161 | www.mimetas.com			

MIMETAS
the organ-on-a-chip company

Mixccelerator

Medical Innovation Xccelerator (MIX) studies fibrotic renal failure using slaughterhouse porcine kidney perfusion and precision-cut renal slices. Organ fibrosis is the formation of connective tissue in an organ as a response to chronic injury. This response to injury is similar to scarring and can lead to severe changes in architecture and function of the organ.
Laboratory animals and classical in vitro models have shown to be inferior in studying the development of fibrosis. There is a great need for drugs to prevent or repair chronic processes leading to end-stage fibrotic tissue. We developed alternative testing possibilities using waste material from commercial slaughterhouses.

What is your contribution to the transition to animal-free innovation?

MIX uses animal waste products from commercial slaughterhouses, allowing us to study fibrosis in a relevant species resembling humans. With organ preservation techniques from human organ transplantation we maintain high-quality research material. Combining perfusion techniques and precision-cut slices provides the opportunity to study a large range of compounds and conditions on their efficacy to intervene in fibrotic pathways, no longer requiring laboratory animals.

What is your personal motivation doing this work?

To provide innovative relevant research techniques as used in the field of transplantation and fibrotic disease modeling to pharmaceutical drug developers and other interested parties. Traditionally, active compounds are tested in live animals and the effects often do not resemble those observed in humans. We envisioned that with our service, drug testing can be performed quicker and without the use of laboratory animals.
Our motivation is therefore innovation-driven rather than looking for alternatives.

In Vitro

Ex Vivo

Precision-cut tissue slices allow us to test a large number of experimental conditions simultaneously.

Target Sector	Pharma	Food
Company size	1 – 10	
Contact	Henri Leuvenink | info@mixccelerator.com | www.mixccelerator.nl	

Ncardia

Ncardia is a stem cell drug discovery and development company operating worldwide. The company develops and produces highly predictive assay systems based on human induced pluripotent stem cell (hiPSC)-derived cardiac and neuronal (disease) models for safety and efficacy testing. By bringing human biology to the drug discovery and development pipeline, we accelerate and improve drug candidate identification and selection, we reduce animal testing, and, ultimately, we increase drug discovery and development efficiency.

What is your contribution to the transition to animal-free innovation?

Cardiovascular safety liabilities are one of the most common causes of drug attrition. Historically, there has been a heavy dependence on animal models in preclinical (cardiac) safety assessment. Ncardia develops and produces fully functional human iPSC-derived cardiomyocyte models that are routinely used by our pharma partners for efficient and reliable cardiac safety screening.
Predictive human biology in the preclinical phase allows for better decision making and limits animal testing.

What is your personal motivation doing this work?

I love to work at the interface of biology, technology and commercialization. Ncardia was founded with the vision that stem cell technology will help to get better medicines to patients faster by improving the drug discovery process. Translational science, especially in the areas in which we are active – cardiovascular and CNS – is challenging due to large species differences. The opportunity to use human biology for key decisions in drug discovery and development can truly transform the process. At the end of the day every false positive represents wasted resources and every false negative is a missed opportunity. It is extremely rewarding to see that our vision is now becoming reality.

Target Sector	Pharma
Company size	11 – 50
Contact	Stefan Braam, CEO | support@ncardia.com | +31 71 3322 230 | www.ncardia.com

Ncardia
Stem cell experts

Nestegg Biotech

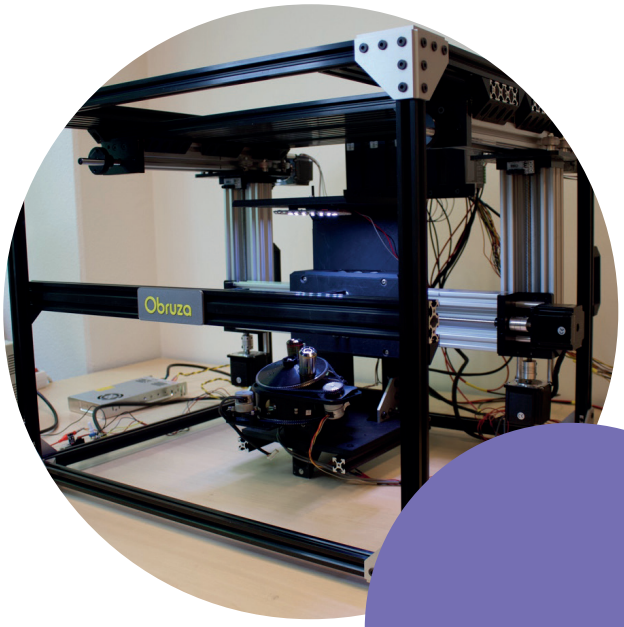
We automate 85% of the work in a typical lab performing in vitro research on human and animal cells. We provide the automated system Obruza which works with our customer's existing workflows and techniques to sustainably increase their productivity through automated imaging, fluid handling, and environmental control. We use 3D-printed parts to make a system that can be tailored to multiple applications, and software to offer smart functionality, allowing our users to monitor their experiments from outside the lab.

What is your contribution to the transition to animal-free innovation?

Obruza is Latin for test. By automating in vitro cell culture testing, we want to contribute to the reduction in animal models for testing pharmaceuticals, therapies, food additives, and cosmetics. We think that by reducing the labor required to perform these in vitro tests, we can reduce the cost per test, thereby increasing their adoption over animal models.
We contribute automated protocols and trial equipment to help TPI participants automate the work they currently perform manually.

What is your personal motivation doing this work?

I grew up on a farm raising free-range, organic hens. My company exists to make an impact using technology, not just on human life but also animal life. A world without animal models would be a better world for humans. I think animals deserve better, and, if we are already capable of doing the same research in more ethical ways, then I would like to increase the spread of those techniques. And that is what a job in automation is perfect for.



Our Obruza prototype.

Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	1 – 10			
Contact	Tanner Carden | tannerc@nesteggbiotech.com | + 31 6 41796209 | Nesteggbiotech.com			

nestegg biotech

Noviocell

Noviocell provides a synthetic matrix for 3D cell culturing, opening up avenues for organoid and precision medicine. It has the only synthetic material that can compete with animal-based material, because it behaves the same way. It is synthetic, therefore, experiments lead to reproducible results. Since it is biocompatible it can be used for regenerative purposes. The gel is thermo reversible and much easier to work with than animal-based matrixes.

What is your contribution to the transition to animal-free innovation?

We are close to curing diseases with self-grown organs. However, many organoids (mini-organs) are grown on animal-derived matrixes, i.e. material derived from mice tumor cells.
This blocks the path to using these organoids for medicine. Noviocell has a solution with a synthetic base, that is better than any other material and that reduces the use of mice for producing animal-derived matrixes.

What is your personal motivation doing this work?

Many new excellent technologies are developed nowadays but not all of them find their way to the patient. Noviocell has a technology platform that many patients worldwide can benefit from. For me, it starts with making technologies available to patients by giving others around the world the opportunity to find new medicines and making tools for better treatment available.

Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	1 – 10			
Contact	Menno de Jong | info@noviocell.com | +31 6 46155064 | www.noviocell.com			

noviocell

OcellO

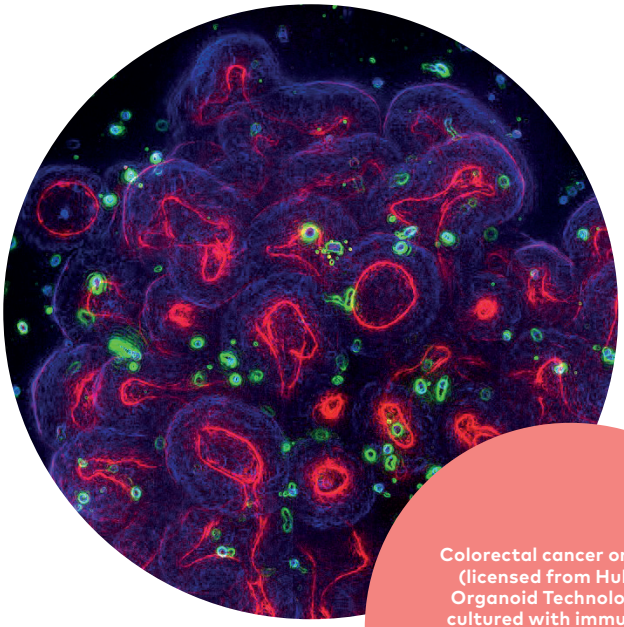
OcellO is an innovative biotech company offering in vitro compound testing services for the drug discovery industry. Core services utilize in vitro and ex vivo 3D cell culture-based assays in immuno-oncology, oncology and polycystic kidney disease. High throughput and automated assays using organoids and patient-derived material are combined with high-content imaging and analysis to evaluate compound activity.

What is your contribution to the transition to animal-free innovation?

OcellO strives to model human biology as realistically as possible, while retaining throughput and reproducibility. This enables drug developers to reduce their dependence on expensive, time-consuming and often poorly translational animal models. OcellO's in vitro clinical trial approach represents a better preparation for clinical studies.

What is your personal motivation doing this work?

It's thrilling to be at the cutting edge of technology development where automated tissue culture, 3D imaging, and image analysis intersect. That this has already helped bring several innovative cancer medicines to the clinic is deeply rewarding.



Colorectal cancer organoids (licensed from Hubrecht Organoid Technology) are cultured with immune cells (green) and immunomodulatory drugs in 384 well plates. Automated image analysis quantifies immune cell infiltration and tumour killing.

Target Sector	Pharma (and biotech)
Company size	11 – 50
Contact	Leo Price | leo.price@ocello.bv | +31 71 3322 875

OcellO
Discover the full potential

PimBio

PimBio BV was founded in 2014 to develop new and promising in vitro devices for bioengineering physiologically relevant living tissue for different applications. The development of a platform technology producing 3D physiologically relevant in vitro models will make it possible to generate living tissue types and organs which can be used in scientific research, regenerative medicine and industry.

What is your contribution to the transition to animal-free innovation?

PimBio develops and manufactures in vitro devices for the bioengineering of physiologically relevant in vitro models for different applications. We offer sustainable solutions that have the potential to improve people's lives.

What is your personal motivation doing this work?

My personal motivation is creating an accurate non-animal based in vitro high-throughput alternative to traditional animal tests that can be used for applications in patients

In Vitro

Ex Vivo

Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	1 – 10			
Contact	Michael Ponomarenko | ponomarenko@pimbio.com | + 31 73 6214 9 17 | www.pimbio.com			

πBio

PLI Technologies

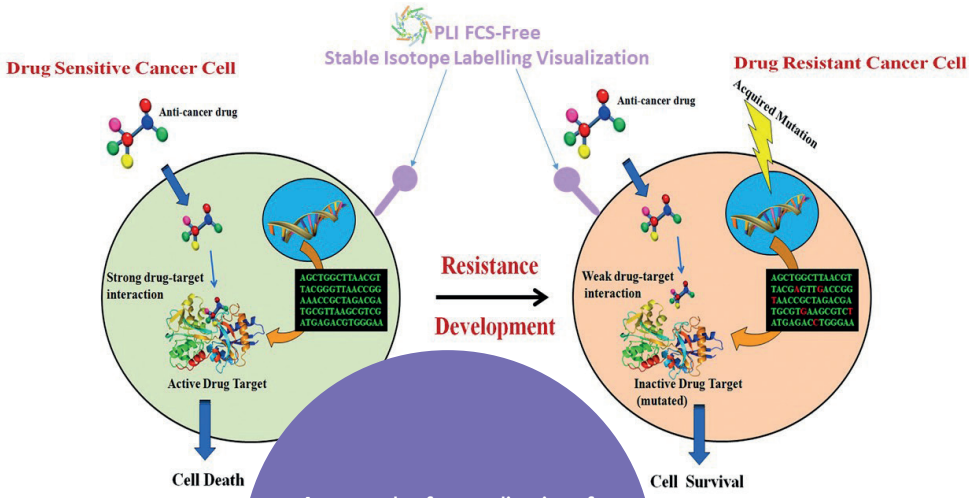
**PLI Technologies has an expertise in:
The biosynthetic preparation of stable-isotope (13C, 15N 2D) labelled molecules with various complexity through cost-effective stable-isotope labelling schemes. This includes the labelling of bacteria, algae, yeast, plants, and FCS-free labelling of insect and mammalian cell lines. The biosynthetic approach enables isolation of high-value compounds that cannot be obtained via chemical synthesis. The non-invasive infra-red analyses for monitoring of cell cultures and screening of new sources of biologically active compounds. Examples include the selection of specific algae with a high protein content and with a polyunsaturated fatty acids (PUFA) profile that can be used as nutrients.**

What is your contribution to the transition to animal-free innovation?

The strategy of PLI is to continue developing animal-free products. The patent 'Compositions and methods for stable isotope labelling of biologically active compounds' has been granted in The Netherlands, Germany, Belgium, France, United Kingdom, Switzerland, Russian Federation, Canada, Australia and Japan. Mammalian cells labelled with stable isotopes could be obtained through specially designed FCS-free cell culture medium. For example, we produce (stable-isotope labelled) histamine 1 receptor for structural studies. Development of new FCS-free products for multiple-disease research is the next challenge.

What is your personal motivation doing this work?

As the CEO and founder of PLI, I aim to develop new products for diagnostics and to further explore the applications of combining the stable-isotope labelling technology with spectrometric (mass spectrometry) and spectroscopic (infra-red, nuclear magnetic resonance) techniques. This multidisciplinary approach will contribute to understanding why certain medicines have effect on some individual patients but are ineffective for others and why the same medicine may cause side-effects in certain patients. PLI develops novel products and technologies with the ambition to contribute to Predictive, Preventive, Personalized and Participatory Medicine (PPPPM) and nutrition strategies.



An example of an application of FCS-free uniform stable isotope labelling [U-SIL] in 'omics technology' for study the mechanisms related to drug resistance in cancer treatments.

Target Sector	Pharma	Food	Chemical industry
Company size	1 – 10		
Contact	Dr. T.A. Egorova-Zachernyuk | t.a.egorova@plitechnologies.com | +31 6 41890594 | www.plitechnologies.com		

PLI Technologies

River BioMedics

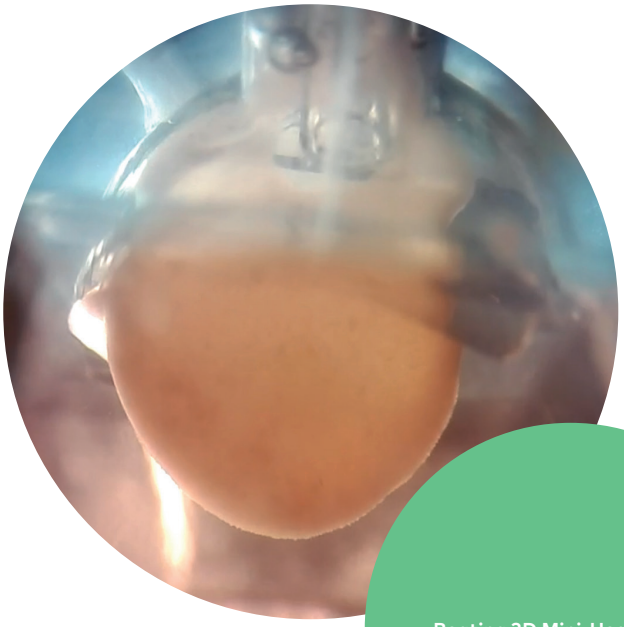
We develop and provide advanced 3D human heart models for disease modeling and drug discovery. River BioMedics is specialized in in vitro platform technology for compound screening based on human induced pluripotent stem cell (iPSC)-derived heart cells. Our platforms can be implemented in the preclinical phases of drug development. Our 3D human Cardiac Strip can be used for high-throughput screens, which can be followed-up by detailed insights in the cardiac performance by testing selected compounds on our human Mini-Heart assay.

What is your contribution to the transition to animal-free innovation?

River BioMedics envisions replacing preclinical animal testing with our 3D human heart models. Our platforms are based on 3D human iPSC-derived heart tissue. Our ambition is to provide in vitro preclinical models that show more predictive outcomes for the real human heart than the currently used animal models. In that way, preclinical animal testing can be strongly reduced.

What is your personal motivation doing this work?

The founders of the company are driven by their motivation to decrease the burden of cardiovascular disease, which is the number one cause of death worldwide. Our team has the ambition to bring this scientific innovation to the commercial market to increase the success rate of cardiac drugs in human clinical trials.



Beating 3D Mini-Heart with a diameter of 6 mm.

Target Sector	Pharma
Company size	1 – 10
Contact	Lisanne Blauw | lisanne.blauw@riverbiomedics.com | www.riverbiomedics.com

Thromboseek

Our core activity is the development human whole blood solutions to determine (side) effects of nutrition, medication or toxics on blood cells (e.g. platelets, white blood cells and erythrocytes). Furthermore, we use these models to investigate the prognosis of patients with inflammatory or inherited chronic diseases, such as cancer and cardiovascular disorders, and inflammatory disorders. All tests will be based on single step methods in human whole blood.

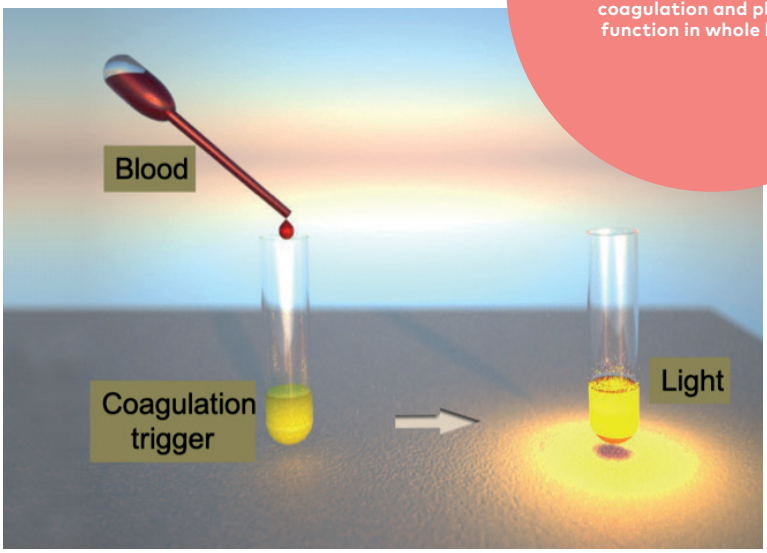
What is your contribution to the transition to animal-free innovation?

We aim to make whole blood testing methods feasible for pharmaceutical testing and clinical applications. We develop models to investigate the response of human blood cells to specific triggers. Using this approach, we can bypass animal experiments.

What is your personal motivation doing this work?

Personally, I am motivated to develop next-generation prognostic methods and models to investigate (side) effects of medication on blood cells and to reduce the number of animal experiments.

Thromboseek develops rapid and accurate tests to measure coagulation and platelet function in whole blood.



Target Sector	Pharma
Company size	1 – 10
Contact	Mark Roest | +31 6 81032534 | thromboseekbv@gmail.com

ToxGenSolutions

ToxGenSolutions works on the application of in vitro and ex vivo methods for testing and assessment of chemicals as well as assessment of the impact of non-genetic and environmental factors on human health. Targeted human health issues are neurotoxicity, immunotoxicity, and carcinogenesis.

What is your contribution to the transition to animal-free innovation?

In spite of all the industrial and regulatory efforts to assure human health and safety, products with adverse effects do appear on the market. Some of these adverse effects (e.g. neurodegeneration, carcinogenesis, immunosuppression) are quite severe and they are a heavy burden on human health and the economy. To address these challenges, I started and co-founded several companies working to promote non-animal testing and assessment. The latest is ToxGenSolutions B.V. (2015, NL), specialized in human relevant peripheral biomarker-based in vitro tools for preventive medicine covering neurotoxicity, carcinogenesis and immunotoxicity. These methods are based on data from novel in vitro methods for toxicity testing linked to human ex vivo data and human cohort studies.

What is your personal motivation doing this work?

The failure rate of current animal models in many areas is too high to be ignored. We can continue to develop yet more animal models of doubtful relevance for human health and safety, or we can explore the power of approaches based on promising in vitro/ex vivo human cell/tissue and artificial intelligence tools.
The currently available data and the fast development of new cutting-edge technologies have motivated me to go all in on the latter. Choosing this new path will significantly contribute to the improvement of animal welfare by eliminating animal experiments that are irrelevant for human safety and health, and thus unethical. Finally, I believe that these new approaches will provide better science, economic advantages, and improved human safety and health..

In Vitro

Ex Vivo

Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	1 – 10			
Contact	Erwin L. Roggen | erwin.roggen@toxgensolutions.eu | +45 3153 8020 | www.toxgensolutions.eu			

ToxGenSolutions
ToxGenSolutions

Toxys

Toxys develops innovative in vitro cell reporter assays for toxicological research and safety assessment of novel medicines, chemicals, cosmetics and food ingredients. We developed the ToxTracker assay for cancer hazard assessment and ReproTracker for animal-free developmental toxicity testing. Our stem cell-based reporter assays not only rapidly and reliably detect toxic compounds but they also have the unique ability to provide insight into the mode-of-action of toxic substances. We support our customers in understanding their compounds and in making informed decisions during R&D of novel products.

What is your contribution to the transition to animal-free innovation?

The majority of test animals are used for toxicological research, despite the fact that in many cases they are not a representative model for humans. Toxys applies stem cell and genome editing technologies to develop cell-based assays for genotoxicity, developmental toxicity and cancer research. These assays are widely used by the pharmaceutical, chemical, cosmetics and food industry to test new products for toxic properties already in an early phase of development. Reliable in vitro safety testing contributes to a significant reduction of animal testing.

What is your personal motivation doing this work?

We strongly believe that technology and excellent science can and should be applied to develop animal-free assays to ensure chemical safety for humans. The future of human safety assessment is not with simple in vitro or in vivo tests that only provide a yes-or-no answer, but advanced in vitro models that provide reliable and relevant insights into the mode-of-action of novel chemicals and materials. We are committed to bringing high-quality information to clients that helps to develop better medicines and reduce animal testing.

Target Sector	Pharma	Food	Chemical industry	Cosmetics
Company size	1 – 50			
Contact	Dr. Giel Hendriks | g.hendriks@toxys.com | +31 71 3322 470 | www.toxys.com			

toxys

Vivomicx

Vivomicx is a tech company that utilizes advanced molecular technologies to analyze the molecular status of subsets of cells in tissues. Our approach improves healthcare as we work with clinically relevant tissues that enable drug target identification, genuine biomarker discovery and development of diagnostic systems. Vivomicx thus makes drug development more efficient by generating valuable information on cell behavior in a pathophysiological context.

What is your contribution to the transition to animal-free innovation?

Vivomicx contributes to Transition Innovation by deriving information directly from patient samples, thereby bypassing the use of animal testing. In addition, our technology can be applied to existing animal tissues that are already available in R&D laboratories of pharma and biotech companies and research centers around the world, thereby limiting the need for new animal experiments to be carried out.

What is your personal motivation doing this work?

We believe it is time to reshape the drug development process for diseases that are difficult to treat, such as cancer and sepsis, by applying recent technological advancements in molecular analyses, including kinome and microRNome profiling, and RNA sequencing. By combining these techniques with laser microdissection of cellular subsets from clinically relevant tissues prior to profiling, our approach will assist in halting the high drug attrition rates for these diseases in clinical trials.

Target Sector	Pharma
Company size	1 – 10
Contact	Jan Zuidema, CBO & co-founder | j.zuidema@vivomicx.eu | +31 6 21124552 | www.vivomicx.eu

Vivomicx
BETTER DRUGS FASTER

VSPARTICLE

VSPARTICLE actively empowers innovators in healthcare technology by making the manufacturing of nanostructured materials as easy as pushing a button, greatly reducing the development time of new materials and products for a sustainable future. Nanoparticles are used for targeted drug delivery, to enhance systemic treatments, to improve imaging and diagnostics for magnetic resonance imaging (MRI) and positron emission tomography (PET) and for anti-microbial coatings for implants. Nanoporous materials are used for sensor array development and novel electrode manufacturing for bio-electronics.

What is your contribution to the transition to animal-free innovation?

VSPARTICLE's tools enable the synthesis of nanoparticles for inhalation toxicology and skin testing. The VSP-G1 is compatible with in vitro exposure machines, so researchers can produce nanoparticles and directly use them for their tests. VSPARTICLE's tools are supporting researchers at the National Institute for Public Health and the Environment (RIVM) and at IUT Duesseldorf in the transition to animal-free testing. In both cases the VSP-G1 is connected to a VITROCELL in vitro exposure machine, allowing the researchers access to a stable, reproducible output of nanoparticles for nanotoxicology studies.

What is your personal motivation doing this work?

We want to empower the acceleration of development within the field of healthcare, risk and safety assessment with pure nanostructured materials, reliable and reproducible output, and open access data that researchers can share using our materials database. VSPARTICLE also plays an important role in accelerating the energy transition by supporting the research in catalysis and clean energy production. We believe that the only way to solve global problems and reduce animal testing is by joining efforts through collaborations between researchers, companies and civil society.

With the VSP-G1, a stable and clean flow of well-defined pure nanoparticles can be generated with the push of a button.

Target Sector	Pharma	Chemical industry
Company size	11 – 50	
Contact	Alessandra Soro | a.soro@vsparticle.com | +31 88 3080 415 | www.vsparticle.com	

vsparticle

Vycap

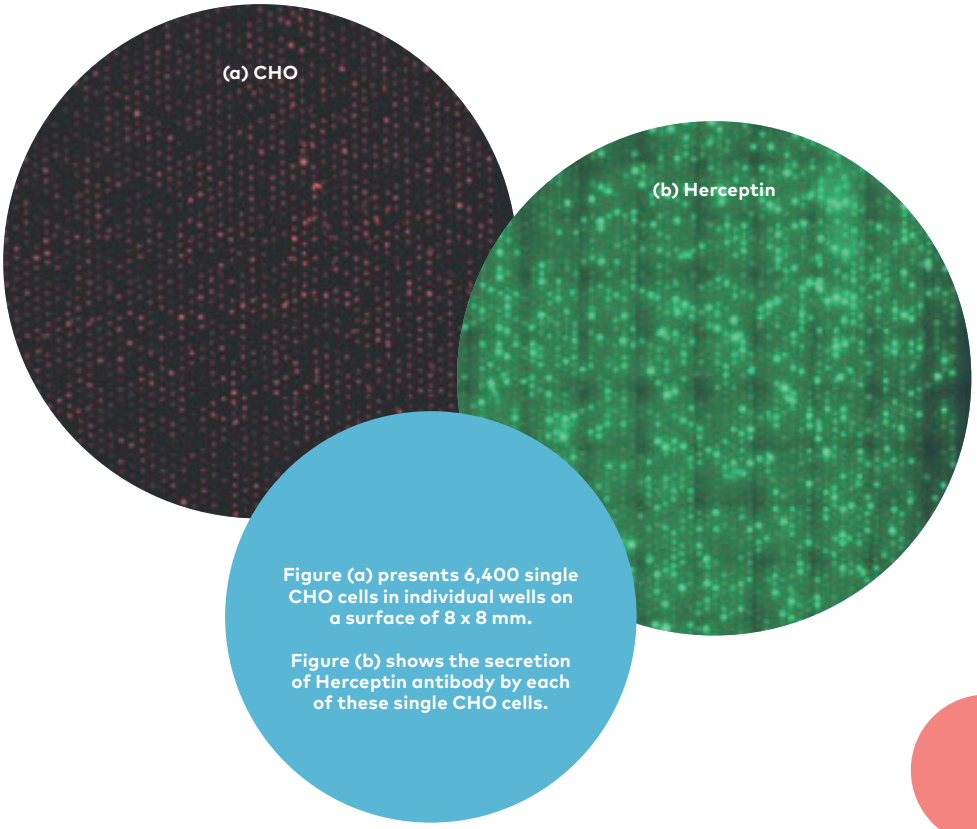
VyCAP has expertise in developing and selling technologies and solutions to determine the influence of compounds at the single cell-level. Based on the cellular response the cell can be clonally expanded or isolated to analyse the DNA or protein contents.

What is your contribution to the transition to animal-free innovation?

The response of cells to different compounds can be tested on 6,400 single cells in parallel. VyCAP technology is easy to combine with organ-on-chip models to obtain additional information on the response of the organ at the single cell-level.

What is your personal motivation doing this work?

Organisms, including humans, all start with a single cell. Our technology aids in understanding the biology at the single cell-level which is necessary to understand the organism as a whole. A further understanding of the biology will reduce the number of animal experiments.



Target Sector	Pharma	Food
Company size	1 – 10	
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VyCAP

Proving that an alternative is safe to use is an international quest.

We can achieve more in an ecosystem

What comes up for discussion when you introduce a scientific innovator looking for business opportunities to a representative from an innovative top sector? This double interview on the position of Dutch start-ups and scale-ups for animal-free innovation in the wider innovation landscape features Pieter Hiemstra, professor of Respiratory Cell Biology and Immunology at Leiden University Medical Center, and Nico van Meeteren, Executive Director of the top sector Life Sciences & Health and a professor at Maastricht University. Such an innovation landscape sees the government, the business sector, scientists and members of the public collaborating in innovation programmes.

Hiemstra: 'Replacing animal studies with better alternatives creates opportunities in health and safety.' Van Meeteren concurs: 'Human measurement models provide humans with a better predictive perspective than animal studies.'

In motion

Van Meeteren outlines the convergence of different developments: 'In the first place, there is a clear demand for better alternatives within the care system, especially given the lack of predictability in animal models. Second, innovative biotechnology offers ample opportunities. For example, we're gaining an ever-increasing insight into organoids, while patients and pharmacists stand to benefit from personalised medicine. Third, we've emerged from a financial crisis, during which knowledge institutions began cooperating more closely as a result of funders avoiding risks and government bodies stepping back. In addition, Dutch parties are increasingly teaming up with each other through sustainable public-private partnerships. Our country is renowned for this type of cooperation.'

Hiemstra: 'Many academics have a strong interest in business activities. One example is the Bio Science Park in Leiden, which also includes incubator buildings. Parties are housed in close proximity, enabling spontaneous, informal development and exchange. Municipal and provincial subsidies for such parks have allowed us to set up a range of successful innovation hubs across the country.'

Van Meeteren claims that it would have been unimaginable 15 years ago for a research group to launch a business supported by external investors. 'Today, annual performance reviews not only cover your scientific work, but also the social and economic contributions made. The entire system is in motion, and public and private parties are no longer fully distinct.'

'At the government level, the Ministry of Economic Affairs and Climate Policy has recently expanded its enterprise policy to include mission-driven top sector and innovation policy,' says Van Meeteren. 'The topic of health and care covers missions where it is essential for us to focus on human models that cater to the unique individual as much as possible. In other words, their predictions on the efficacy and safety of substances and interventions – especially medicines – should be better than those from animal models. This development will provide opportunities for animal-free innovations.'

The Transition to Animal-Free Innovation topic has seen a diverse network of Dutch parties join forces: citizens, scientists, the business sector (including start-ups), research funders, NGOs, regulators and policymakers. Ideally, this network will now expand across the border, as national boundaries do not tend to benefit health innovations.

Future-savvy

Van Meeteren explains that the willingness of foreign universities to cooperate with their Dutch counterparts is thanks to our attractive arrangements for public-private partnerships, our thoroughly progressive and compassionate view of delicate health issues, our take on the business and social side of innovation, and – last but not least – the quality of our research. Despite huge economic pressure, Dutch researchers have never been as highly educated as they are today. 'The life sciences and health sector is making quite a name for itself in the Netherlands and abroad, whether it concerns fundamental research or device development. The relocation of the European Medicines Agency (EMA) will aid in raising our country's profile. Since the Netherlands is highly regarded as a recipient of countless European research grants, it generates revenue for and together with SME partnerships and large research programmes.'

Hiemstra adds: 'Nowadays, you always need consultancy firms when applying for funding from the major European programmes. As a consequence, you have to factor in those costs as well.' There are also advantages though: 'When setting up partnerships with businesses 10 or 15 years ago, I had to discuss both the contents and the conditions. All I have to do now is talk with the researchers, because our technology transfer officers (TTOs) will approach the other party's company lawyers and contract specialists. This way, I won't run into quite as many scientific disputes. Partnerships between academia and the market are also coming up with solutions to issues such as intellectual property. This facilitates rolling out a start-up while based in the university environment. All Dutch universities have their own TTOs to assist enterprising scientists in this matter.'

Van Meeteren highlights the unused potential: 'While real acquisition strategies that are passed on to customers present great opportunities, these chances are not yet commonly known among universities.' He emphasises: 'Given the dynamics of rapid biotechnological developments, we need our rules, regulations and funding to be future-savvy rather than future-proof.'

Hiemstra sets out the dilemma that it is often foreign businesses that are able contribute cash to the co-financing of research, while the Netherlands is mostly home to a range of SMEs in the biomedical and biotechnological sector, which can only contribute in kind. Moreover, he advocates proper support for small businesses, such as a partnership with health funds. Such cooperation would not only enable entrepreneurs to secure a suitable subsidy in conjunction with research organisations, but also to establish a close connection with the target audience. A key element that is gaining traction in our country is to involve the end user or patient in the process.

He adds: 'We require other control mechanisms than the ones known to the research community, as well as people in central laboratories with the upscaling expertise and the helicopter view to take the right decisions. Should you continue to improve dozens of organs-on-a-chip, or should you steadily churn out lower numbers that are consistent in quality?'

Successful cooperation

'Since large pharmaceutical companies have relocated their R&D departments from the Netherlands to abroad, start-ups currently account for most innovations in biomedical research,' Hiemstra explains. As a consequence, large companies are taking an interest in these start-ups. Van Meeteren joins in: 'For example, Philips is involved in the development of medical technology, both for daily care and for high-tech applications. Philips scans young start-ups and scale-ups, occasionally targeting businesses with promising market perspectives to acquire and boost.' While this process may lead to adverse effects if it saps innovative power from the wider business culture, it is usually a herald of success. Hiemstra mentions the sale of access to research and clinical programmes by Galapagos to Gilead as an example of a recent innovative deal that does not involve an acquisition.

The innovations that start-ups are working on are increasingly showing up on the radar of major businesses. Van Meeteren suggests that many start-ups are devising solutions to delineated problems, which he calls point solutions. 'They will come to realise how important it is that the various point solutions jointly accelerate the necessary development. A key role in this process is played by platforms that integrate both the innovations on offer and the needs of end users. In this context, validated products and services should be able to generate revenues as well as volumes. For example, Dutch companies are contemplating the development of multifunctional robots that can produce anything, anywhere in the world, from crash barriers to labs-on-a-chip.' So how do you become the front runner in mass-producing a wide range of technologies? What logistical, operational and financial facilities does this require?

In recent years, competition and cooperation have been increasingly interconnected within our ecosystem, which comprises members of the public, scientists and government bodies, as well as large and small businesses. This trend allows us to shape a unique and appealing vision in which we can achieve more with scarce resources.

Do you want more information about the Dutch topsector Life Science and Health?

Check the website of Health Holland:
www.health-holland.com

And the Lifescience@work accelerator:
www.lifesciencesatwork.nl/#lsw-accelerator

Building blocks of the European Organ-on-Chip roadmap

'An Organ-on-Chip is a fit-for-purpose microfluidic device, containing living engineered organ substructures in a controlled microenvironment, that mimics one or more aspects of the organ's dynamics, functionality and physiological and/or pathophysiological response in vivo under real-time monitoring' (definition by the experts in the ORCHID network).

Emerging at the junction of tissue engineering and microfluidics, Organ-on-Chip (OoC) technology is widely postulated as a promising approach to creating new model systems for healthcare research. OoC models aim to mimic aspects of human anatomy, physiology and pathology for use in drug discovery, efficacy and toxicology, as well as in personalised (or precision) medicine. The goal is to improve existing bioassays and provide insights into the mechanisms underlying the development and progression of diseases in humans. In addition, OoCs are considered to be potential contributors to reducing the need for, cost and ethical burden of animal studies.

In a recent EU-funded Coordination Support Action project called ORCHID (Organ-on-Chip in Development), initiated by the Dutch Organ-on-Chip Consortium hDMT, an inventory was made of current needs that could be addressed by this technology, as well as of its key challenges, barriers and perspectives. This formed the basis for the European Organ-on-Chip roadmap. Six specific building blocks were identified for this roadmap, which includes priorities, methods and targets for each block:

1. **application**
2. **specification**
3. **qualification**
4. **standardisation**
5. **production and upscaling**
6. **adoption.**

In the immediate future, the focus of OoC is expected to be on qualification and standardisation. Limited standardisation, automation and inter-chip compatibility are perceived as hurdles to end users adopting OoC solutions. Much like all computer equipment interfaces use a Universal Serial Bus (USB), the intention is that biologists will be able to use chips from various vendors to obtain an OoC model that answers their specific questions. A new step in this direction is the Translational Organ-on-Chip Platform (TOP), currently under development, which addresses precisely this issue and provides infrastructure for automated

microfluidic chip control. The TOP Platform is available for academic and commercial chip developers to transform their OoCs to 'plug and play' formats. Converging towards component, method and data standardisation requires a collective dialogue among experts, a debate which will be facilitated by the recently established European Organ-on-Chip Society (EUROoCS).

With regard to the characterisation and qualification of OoC models, plans are underway for establishing independent centres for testing their biological relevance and performance. There are many proof-of-concept models, developed by a host of developers, but these are not always as robust and reproducible as end users would usually require. To overcome this problem, a proposal for a European Organ-on-Chip Infrastructure5 is now being prepared to bridge the gap between developers and end users. This infrastructure includes a centre for method development and training, a centre for testing and qualification, and a virtual data centre with publicly available data. This will result in independently qualified and fully characterised fit-for-purpose OoC models with guidelines and standard operating procedures on use and applications. EUROoCS will facilitate the OoC community achieving this goal.

EUROoCS should not only play an important role regarding the specific building blocks of the OoC roadmap, but also with regard to the general aspects, such as regulation, ethics and communication. EUROoCS can mediate contact with all stakeholders and help bring together the necessary experts, facilitate the dialogue, disseminate information on the newest developments and results, create awareness and thus stimulate the adoption of the technology. The economic impact of OoC, new business models and the training needs have also been identified.

the hDMT consortium

hDMT: Netherlands Organ-on-Chip Consortium

The mission of hDMT, established in 2015, is to develop and qualify cell culture models of healthy and diseased human tissues based on Organ-on-Chip (OoC) technology, and to facilitate the valorisation, implementation and availability of these models to end users tailored to their needs. By providing better models of human organs, animal testing is expected to be reduced. The scientists of the hDMT consortium share their expertise, facilities and ideas, and collaborate on single models, such as skin-on-chip, brain-on-chip, cancer-on-chip, or combinations thereof.

The hDMT partners also collaborate with a network of companies in independently funded multidisciplinary projects. One major project that has received a grant from the Dutch Government – the Netherlands Organ-on-Chip Initiative (NOCI) – focuses on brain, heart, and gut-on-chip, and the study of the disease mechanisms of these organs and their interactions. NOCI is a very important incentive for the Organ-on-Chip research in the Netherlands.

The OoC network in Europe was initiated by hDMT, a founder of the European Organ-on-Chip Society (EUROoCS).

Organ-on-Chip In Development (ORCHID)

In 2017, ORCHID started as a Horizon 2020 project aimed at:

- creating a roadmap for OoC technology;
- building a network of academic, research, industrial and regulatory institutions;
- moving OoCs from laboratories into general use to benefit the citizens of Europe and beyond.

The ORCHID Consortium is a collaboration between seven partner organisations from five European countries:

1. Leiden University Medical Center (coordinator, the Netherlands)
2. Institute for Human Organ and Disease Model Technologies (hDMT, the Netherlands)
3. Delft University of Technology (TU Delft, the Netherlands)
4. Commissariat à l'Energie Atomique et aux Energies Alternatives (CEA, France)
5. Imec (Belgium)
6. Fraunhofer Institute for Interfacial Engineering and Biotechnology (Fraunhofer IGB, Germany)
7. University of Zaragoza (Spain)

ORCHID's international advisory board comprises world-renowned experts from the OoC field.

EUROoCS

In 2018, EUROoCS was established as an international independent not-for-profit organisation aiming to encourage and develop Organ-on-Chip research, and to provide opportunities for sharing and advancing knowledge and expertise in the field to ensure better health for all. Membership is open to individual researchers and others with an interest in OoC technology worldwide. With the support of EUROoCS, the OoC community will be building bridges that close the gaps between end users, developers and regulators.

Various point solutions jointly accelerate the necessary development.

Thrilled to support a wonderful initiative

With our foundation 'Proefdiervrij', the Dutch Society for the Replacement of Animal Testing (dsRAT), we are making every effort to create a world without laboratory animals. We are convinced that a world without animal testing is better for both animals and humans. To reach this goal, we have joined forces with the worlds of science, politics and society to enable innovations, and to stimulate the development of animal-free methods that have the potential to make lab animals redundant.

A lot has happened over the past decennia. We witnessed a decrease in the number of laboratory animals in the Netherlands from 1.5 million in 1982 to about 0.5 million in 2017. To aid this decrease, we set up a special fund to finance scientific projects intended to make the use of laboratory animals redundant. So far, we have financed over 25 innovative developments focused on subjects such as tissue models, 3D bioprinters, stem cell technologies and in silico models. Not only can such innovations lead to a significant decrease in the number of laboratory animals, but they can also improve the research possibilities regarding human health. The implementation of these animal testing-free methods, however, appears difficult: the 'valley of death' is a gap that truly needs bridging.

It is our mission to bridge that gap. We aim to do so by using the knowledge within our ever-growing network and offering the needed support, financial and otherwise. This was why we sponsored one of the teams that participated in the Venture Challenge in 2018. The Venture Challenge is a programme run by Health Holland and LifeSciences@Work intended to turn an initial idea – a breakthrough research result – into a solid business case. This is a very important step towards implementation. Take the team from 'River Biomedics' that developed a 3D model of the human heart to use for the development of new medication, completely animal-free. We were thrilled to support such a wonderful initiative.

We are currently collaborating with our partners to develop a 'Proefdiervrij Venture Challenge'. This will be a way to create a bulletproof business set-up for the impressive innovations that we have seen in the past few years. We are committed to helping these great developments towards the necessary market introduction.

We are ready and willing to use our expertise and experience to help start-ups working on a solution that promotes the transition towards a world without animal testing. Do you have an initiative that could use our support, or do you have information that we would be of interest to us? Please feel free to contact me. I am looking forward to your email or call!

dsRAT, the Dutch Society for the Replacement of Animal Testing

'The aim of the Dutch Society for the Replacement of Animal Testing is to replace animal experiments. To achieve this goal, we stimulate the development of animal-free research through positive collaboration with parties including scientists and politicians, and with society. By working together, we can develop animal-free methods that not only replace lab animals, but will also have scientific advantages and will better translate to the human situation. Animal-free research is truly a win-win situation.

Rapid developments are currently taking place in science and technology that allow animals to be replaced in research.
We therefore strongly believe that now is the time to truly make a difference.
Since 1982, a significant decrease in the number of lab animals being used has taken place. In the last decade, however, this decline has stagnated, despite the fact that newly developed technologies form a strong tool to create better models than the animal models currently in use.'

Smarter testing means getting from bench to bedside faster & better

The life sciences and health sector is living up to its promises. Thanks to innovative medicines, vaccines and therapies, we are able to offer patients and others new perspectives. Everybody deserves to participate in society, to pursue a career, to be an active community member and to enjoy family life. The future looks bright, with scientific progress driving innovation to bring new products to those still in need.

It is no secret, however, that the current drug development trajectory from bench to bedside is long, risky and expensive. To provide a solution for the numerous patients around the globe still awaiting effective treatment, the sector will need to do this faster and better. We must step up our game.

Fortunately, there are plenty of opportunities to do so. Scientific breakthroughs have led to a new generation of entrepreneurs that invest heavily in technology. Stem cell technology and tissue engineering are being used to create 3D in vitro models, such as organoids. By combining top-notch biology with state-of-the-art microfluidic technology, we are now able to set up high-throughput screening assays.
In addition, the wide range of 'omics' technologies enable us to measure all aspects of life, using genomics, proteomics, metabolomics, microbiomics, etc. In addition, the booming bioinformatics and artificial intelligence field allows to mine and interpret ever bigger datasets.

This wave of innovation is instrumental to achieving another bold breakthrough as well: phasing out animal testing. Not only because there is a strong societal demand to do so, but also because animal models simply no longer suffice, when tackling the drug development challenges the sector faces. We must test smarter. Therefore, we need better models and testing methods throughout the value chain: with greater accuracy and resolution, better predictability, higher throughput rates and lower costs than today's gold standard.

There is no doubt that these developments will ultimately accelerate and improve both therapy development and clinical practice.
However, there are still plenty of hurdles to overcome before they will. In looking at Dutch biotech companies – many of which are highlighted in this bidbook – HollandBIO identifies three distinctive obstacle categories:

1. **Technological:** technology is limiting objectives being achieved, so additional basic research, other research and development is needed.
2. **Qualification and validation:** the technology is successfully being used in a research-only setting but is not yet qualified and/or validated for commercial use in a drug development or clinical setting.
3. **Implementation:** the innovation is ready to be widely implemented, but somehow has not yet found its way into everyday healthcare practice.

Each category represents its own specific set of hurdles. These range from early-phase funding and tech transfer hiccups to the absence of significant scale-up investments, lack of regulatory clarity, reluctance to change and rigid healthcare procedures.

As a rule of thumb, innovative frontrunners are the first to bump into the boundaries of the current system. HollandBIO will certainly be doing its part to remove hurdles that prevent these game-changers from succeeding.
In addition to putting opportunities and challenges on the public agenda, we will be introducing and advocating win-win solutions to reap the benefits of testing smarter.

But we cannot do it on our own. We will be joining forces with stakeholders who dare to challenge the status quo. Because that's what it will take to speed up developments, to reduce the risks and lower the costs of drug development, and to deliver health and wellbeing in a sustainable and animal-friendly manner. The Dutch life sciences sector is up for the challenge. Are you?

Join us! Let's challenge the status quo together. Today.

HollandBIO

HollandBIO is the Dutch biotech industry association connecting, supporting, and representing over 200 members that fully reflect the biotech sector: from start-ups, small and mid-sized companies, all the way up to major businesses, all active in healthcare, nutrition or the biobased economy. HollandBIO works tirelessly every day to fulfil biotechnology's promise. Because the better the life sciences sector is doing, the greater its contribution to a healthy and sustainable society.

Look for more information about the startups in the Dutch Life science database:
www.hollandbio.nl/business-solutions/dutch-life-science-database

We must step up our game.

Colophon

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We need our rules, regulations and funding to be future-savvy rather than future-proof.

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