Building our Biobased Economy together

BE-Basic Foundation Annual Report 2015

Colophon

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We thank all scientists and parties involved for their cooperation.

BE-Basic Foundation Annual Report 2015

Foreward

2015 was clearly a year of change. The first large-scale lignocellulosic ethanol plants came online, a range of biobased building blocks (lactic acid, succinic acid, FDCA, itaconic acid etc) had their first applications and various biobased feedstocks and products have been shown to have environmental and safety characteristics which are in many cases better than their conventional (often fossil) counterparts. Sustainable biofuels are now broadly accepted in sectors without or with only limited alternatives, such as in aviation and maritime applications. And serious implementation strategies are being embraced by the Netherlands' national and regional governments and other authorities.

Of course we also encountered our first serious challenges, which were both essential and expected for the growing maturity of the biobased sector. Low fossil prices challenged business models and technology problems at the new plants caused by working 24/7 with real feedstocks (sand, mud, stones and metals) needed to be solved. With respect to the latter, we have come to realise that treating crop residues (stover, bagasse etc) as waste is too simplistic and harvesting methods have to be re-thought. And last but not least, the debate around biomass sustainability saw a number of new peaks via interventions in some media and a few professional organisations. Although frustrating at times, the public attention shows that biobased development is maturing and beginning to provide a serious alternative to our still predominantly fossil fuel-based economy.

All of this shows BE-Basic is entering a new phase in its development. Project teams have completed many (but not all!!) of their laboratory proof-of-concepts and piloting. Demonstration plants such as 'our' Bioprocess Pilot Facility in Delft and others are now fully operational. BE-Basic has committed its last FES budgets to these developments and so have companion programmes at European and regional levels. This is why BE-Basic is hosting BioPort Holland, the coordination body of the aviation sector and why we were invited to take part in biobased implementation projects such as the Brazilian Agropolo programme. BE-Basic has also contributed to important strategy documents such as the Dutch Aviation Vision, Action and Implementation plans, and to ambitious global sustainability studies[1] about biomass availability, income distribution and job creation, biodiversity and climate impacts.

All signs show that fossil fading-out has started in financial terms and at high rates that are difficult to match with investments in renewables (the 'carbon bubble'). BE-Basic also changed its communication from relatively distant and neutral towards speaking-up in an insisting and even stronger tone. Change is urgent and all financial as well as human resources need to be focused on investing in a cleaner, more beneficial and profitable world. BE-Basic cannot afford to sit on the side-line and must pro-actively communicate the advantages of our integral strategies such as in the HIP programme, the REDEFINERY, the Dutch fuels mix and the like. If we don't, who will?

As you read this public summary of the BE-Basic annual report, you will find this sense of urgency stressed by all interviewed partners. More products and services are invading the commercial domain but the rate of change and implementation needs to be higher. Please join us on this journey in 2016 towards a sustainable future and beyond – we will get only one chance!

Bram Brouwer and Luuk van der Wielen
Board of Directors of BE-Basic Foundation

1) Such as the Macroeconomic Outlook, SCOPE Report on Bioenergy and Sustainability, Biomass studies of Cie Corbey and others.

BE-Basic objectives

The BE-Basic Foundation is an international public-private partnership that develops industrial biobased solutions to build a sustainable society. As we want to switch from fossil fuels to biomass in the near future, new technologies and insights are required for all industries that provide us with food, chemicals, materials and energy. The BE-Basic Foundation initiates and stimulates collaborations between academia and industry, between scientists and entrepreneurs and between the Netherlands and abroad.

To reach these **objectives**, BE-Basic Foundation coordinates and stimulates RD&I programs for science and technology development, especially –but not exclusively- on environmental and industrial biotechnology. BE-Basic stands for *Biobased, Ecologically BAlanced, sustainable Industrial Consortium.* The focus is on integral and sustainable biobased solutions, that balance and optimise economic value and climate impact for non-energetic (chemicals, materials, food&feed) and energetic (transportation fuels, power/heat) uses. Those balances are reached best by applying cascading and integral biorefinery concepts, and prioritise energetic uses for those sectors without alternatives (aviation, marine and heavy road transport).

Integral sustainability is a key driver. BE-Basic Foundation spends roughly 10% of its budget in societal programs that explore, investigate and communicate sustainability impacts (people, planet, profit) in broad national and global settings and develops sustainable solutions. This includes participation in and contribution to balanced, high level policy briefs and organisations.

International respect. BE-Basic Foundation is headquartered in The Netherlands, but understands the critical role of a global reach for the open Dutch economy. Therefore, BE-Basic Foundation supports hubs/programs in Europe (BIG-C with German and Flemish partners), BBI, and CLIMATE KIC, the America's (Brazil, USA, Canada), and South-East Asia (Malaysia, Vietnam, others) to interact with the local organisations, industries, science and society. Here local solutions are sought and developed for sustainable use of biorenewables for food, feed, fiber, fuels and energy that differ from The Netherlands' and European situation.

With that, BE-Basic Foundation is one of the largest, most active, visible and respected global public-private players targeting responsible and sustainable use of biorenewables for food/feed, materials, and energy/fuels sectors. **The BE-Basic Executive Board and Supervisory Board are fully aligned on these objectives and lines of implementation.**

Prof. dr. ir. Luuk A.M. van der Wielen — **President of the Executive Board**

Prof. dr. Bram Brouwer — **Managing Director**

Dr. Herman van Wechem — **Chairman of Supervisory Board**

BE-Basic Foundation

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Governance
The executive board consists of Bram Brouwer (managing director) and Luuk van der Wielen (chairman). The board's task is to ensure cohesion across the entire BE-Basic programme and to take care of day-to-day business including decisions about funding and the continuation of projects. The board presents its decisions to the supervisory board for its recommendations. The supervisory board monitors the actions taken by the executive board and represents the interests of the BE-Basic partners. In addition, all partner organisations are represented in the Consortium Partners Assembly (CPA). The CPA offers important, non-binding advice to the board.

The actual research takes place in Flagships, each of which focuses on a specific aspect of the biobased economy – from technology development to public acceptance. In total, over 80 projects are ongoing under the auspices of the Flagships. In addition, the BE-Basic Innovation Centre (BE-BIC) stimulates innovative start-ups and entrepreneurship in the field of the biobased economy. Progress in the Flagships and BE-BIC is monitored by the management team, in which all Flagship managers and the board are represented.

BE-Basic also hosts the Dutch EBD (Economy, Policy and Sustainability) programme of TKI-BBE – the Top Consortium for Knowledge and Innovation, Biobased Economy, which is supported by the industry and academic parties as well as the government (Topsector Energy). The EBD programme in Flagship 11 focuses on developing policy to stimulate support for the biobased economy among stakeholders and the general public and is closely related to Flagship 9.

In addition several TKI-BBE projects are governed by the BE-Basic Programme, such as the AMBIC project on microbial-based industrial production of chemicals and biofuels and ISIM on improved stability and productivity of microbes for industrial production. Moreover, the BE-Basic Foundation hosts the EFRO-funded project Isobutanol Platform Rotterdam (IBPR), aiming at pilot scale and industrial production of isobutanol and related chemicals and fuels from biomass.

Accountability
BE-Basic accounts for its results and research to several different bodies.

Financial
BE-Basic's programmes are funded by industrial and academic partners as well as the Dutch government's FES fund and other resources (TKI-BBE, EFRO). The Netherlands Enterprise Agency (RVO.nl) monitors research progress and financial accountability on the basis of deliverables and key performance indicators (such as published papers, the implementation of new methodology by industry and patent applications). The supervisory board has assigned an auditing committee to check the annual accounts of the foundation.

Review and evaluation
All new project proposals are subject to an internal (by the board and management) and external review by the International Peer Review Committee, an independent body of external, distinguished specialists from academe and industrial leaders in the field from the Netherlands and abroad.
The BE-Basic programme is also reviewed by the IPRC on an annual basis. They discuss progress in all projects with the Flagship leaders and draw up a confidential evaluation report.

To stimulate innovation from within the consortium, the Innovation Evaluation Committee reviews all papers prior to their publication on possible protection of foreground knowledge.

On the threshold of transition

Once the transition to a sustainable, biobased society seemed a distant spot on the horizon, now the momentum for change is almost palpable. It is no longer a question of if but of when and how quickly it can be done. BE-Basic's managing directors Bram Brouwer and Luuk van der Wielen have faith in the technological possibilities, but at the same time they feel that now is the time to act. "There is a window of opportunity but that window will not be there for ever. Not everyone is aware of that."

"Upscaling and improving are today's key words," says Brouwer. "Many solutions have reached the demo phase or even the marketplace and that has shown us where the bottlenecks and loopholes are. It's an important part of the process. Some things can't be solved with the existing technology. With the knowledge and experience we gain along the way, we can concentrate on finding alternative solutions. Once we take those final hurdles, we are ready for the marketplace."

Open to new ideas

Brouwer and Van der Wielen look at those hurdles as so many positive new challenges. "As we move from concept to application, we learn new things all the time," Van der Wielen say. "We had a clear view of that spot on the horizon, but we didn't know how to get there. The strength of BE-Basic is that we are always open to new ideas." "That openness is also down to the unique partnership between scientists, technicians, companies and governments," adds Brouwer. "Over the years relationships of trust have been built which have set off a process of cross-pollination that has proved enormously beneficial. It's now becoming clear how successful those alliances have become."

Implementation

A growing number of techniques and biobased solutions are ready to be marketed. Van der Wielen: "BE-Basic is at the forefront of biobased research and infrastructure. At our Bioprocess Pilot Facility the number of industrial requests and indications of interest has been increasing, and our approach is regarded as successful internationally as well. If we want to build on this success we need to be pro-active." Brouwer: "The opportunities are there, we have the technology and we have the people. Much depends on the investment climate and that is not something we have complete control over. It's an important aspect, one that we have to tackle right now."

Partnerships

The transition will require a public-private approach for the foreseeable future. "We need to recognise that we are on the threshold of great changes," Van der Wielen said. "And the laws of transition decree that with transition comes a certain chaos. Investors feel the risk is too big at the moment, increasingly of fossil and less and less in renewables. Governments have a role in mitigating those risks. They can do this by investing but first and foremost they can create the right conditions." At the same time, biobased solutions have to be supported in order to create a level playing field with, for instance, solar energy and wind power. "I sometimes joke about the need for a 'state bio refinery' in Rotterdam," Van der Wielen says. "By that I don't mean it should be 100% state owned, on the contrary I would be fine with just private funding for future projects and so would the BE-Basic partners. But we have to work together to find investors who are prepared to consider the medium and long term possibilities." For Van der Wielen the long term financial success of biobased solutions is not in doubt. "You only have to look at the pension funds. The investments that they had to write off were mainly fossil fuel related. With an investment of 10% of that loss we could have the whole Dutch aviation sector running on biofuel, and that is the future."

Give a boost

The BE-Basic biobased perspective is firmly linked to the present-day situation. Van der Wielen: "The importance of the port of Rotterdam as a transport hub is widely acknowledged. The Netherlands is a rich country and by taking pro-active measures to ensure a clean economy it will remain a rich country. The Macroeconomic Outlook (see page 29) outlines scenarios for an industrial future based partly on the use of biofuel embedded in the existing infrastructure. BE-Basic wants to accelerate that process. It's one of the reasons we are involved in Bioport Holland. It has a clearly defined limited time path which will lend a sense of urgency to the improvements that are needed with regard to, for instance, sustainable feedstocks, and which will boost the development of the product until it can stand alone in the market."

Make choices

Meanwhile, that small spot on the horizon has been growing quite substantially. It's a different perspective which Brouwer and Van der Wielen feel has practical implications. "There is now a continuous pressure to forge ahead with the introduction to market of the latest biobased solutions," they say. "BE-Basic will continue to focus its efforts on the movement towards implementation. We need to make choices, we can't research absolutely everything and anything. 'Benefit scope' must be at the heart of every decision. It's a complex matter, and there is no single right answer. But at some point we have to come up with the best decision for the time and implement it. BE-Basic is unique in its public-private partnership expertise and is happy to provide the platform for a relevant and deliberated discussion on how to go about this."

ECO-BIO

In 2015 BE-Basic and Elsevier took up the organisation of the first edition of the ECO-BIO Conference, which took place from March 6 to 9, 2016 at the World Trade Center in Rotterdam. The conference provided an international platform for industries, scientists, NGOs and governments to discuss the needs of a biobased economy from academic, environmental and societal viewpoints.

During the conference it became apparent that there are economical, societal and technological challenges which need to be solved to achieve definitive breakthroughs for a biobased economy. Delegates also agreed that the use of biomass for biofuels, chemicals and polymers production will be instrumental in reaching CO_2-emission targets (COP21, Paris 2015). The biobased economy, they argued, makes sense from an economic point of view in the long term.

Marcel Wubbolts, chief technology officer at DSM, stressed the importance of using biomass in reducing greenhouse gas emissions and slowing down global warming. "Given the increase in the world population and the rise of the middle classes in emerging economies, we need to develop renewable energy, not only wind and solar, but also biomass for energy and chemicals/materials," he said. "At DSM we have developed several biobased materials which offer unique selling points in terms of functionality and their environmental footprint."

The rise of advanced biofuels

Carlos Henrique de Brito Cruz, Scientific Director at FAPESP, stressed that biomass is needed just as much as wind and solar energy and said all three should have been mentioned at the COP21 in Paris. "The energy share of biomass worldwide is hovering around the 10% mark, most of it being first generation biomass, such as sugar cane," he pointed out. "Currently, the share of advanced - 2nd generation - biofuels is relatively low. However, this share is expected to rise to 70% of the total biomass volume for energy purposes by 2035." The shift towards developing biofuels from non-edible biomass will also have an impact on the sustainability discussion. According to De Brito Cruz, using 2nd generation biomass does not exclude discussions on sustainability issues, such as water and land use, land rights and so on. "We need to develop crops which are less dependent on water and that have higher yields," he said.

During the conference, several speakers stressed that products which are able to offer other functionalities do not necessarily compete on price with fossil-based products. Unfortunately, the producers of one-on-one replacements, so-called drop-in's, are experiencing difficult times because crude oil prices are hovering around the 30-40 dollar level. Therefore, incentives need to be put in place to level the playing field, such as carbon taxing or fiscal measures. This means, speakers said, that firm policies need to be put in place over a longer period of time. Without this, CO_2 reduction targets will not be met, and this will lead to ecological problems and substantial costs in mitigating the effects of climate change. Furthermore, it will setback reviving local economies, which are highly dependent on local biomass.

New business models

Creating new value chains, redefining value. The transition towards a biobased economy requires more than just developing and marketing products, according to DSM's Marcel Wubbolts. "In essence, it is about connecting the renewable (biological) cycle with the non-renewable (technological) cycle, in which renewables increasingly compensate for losses in the technological cycle."

Participants	**380**
Countries represented	**40**
Plenary speakers	**5**
Speakers	**22**
Posters	**over 180**
Company tours	**6**

Second generation carbon-based compounds

*The Flagship **Second generation carbon-based compounds** aims to develop clean, efficient and otherwise sustainable industrial processes for carbon-based chemical building blocks mainly for the chemicals, materials and fuels industries either by fermentative production or by modification of substrates or precursors. The research focuses on the conversion of lignocellulosic materials and other biobased feedstocks, including their contaminants, into relevant products.*

FS1

‘Sugarcane bagasse: a promising feedstock for bioplastics'

Bioplastics, the sustainable alternative to conventional plastics, are made from sugars extracted from vegetable biomass. Can these sugars also be obtained from plants or parts of plants that are not fit for human consumption? One project within Flagship 1, led by Mirjam Kabel of Wageningen University in cooperation with several other groups of Wageningen University and Research, DSM and Corbion, is looking at the potential of sugarcane bagasse.

The project ‘Process development for the production of C3-Acids from ligno-cellulosic feedstocks’ has already resulted in six academic publications, and four more are currently awaiting approval. Wageningen University has awarded two doctorates on the subject and a third PhD student is still researching new strains of lactic acid-producing bacteria. In addition, a patent has been requested for a new discovery making the bacteria which produce lactic acid more accessible to genetic improvements. “Things are beginning to take shape,” says Mirjam Kabel.

Sugarcane bagasse

Kabel’s team has researched how to improve the sugarcane bagasse conversion into sugars, which contributes via lactic acid to the production of poly-lactic acid (PLA), a bioplastic. Bagasse, the fibrous material left after the juice has been extracted from sugarcane, is largely comprised of cellulose and hemicellulose but also contains lignin. Kabel’s team researched which factors play a role in the degradation of bagasse. To a more limited extent, they also researched the role and structure of lignin. Lignin is next to cellulose the most prevalent organic matter on earth, so it may play an important role in the production of sustainable materials. Further research is still needed to better understand its complex chemical structure and what happens when it is broken down. Once that is understood, the number of applications for lignin will be much greater.

Alkaline process

A lot of time has been invested in finding a good way to turn the lignocellulosic biomass into the fermentable sugars that are key for the creation of lactic acid. “At the moment, the state of the art approach involves dilute acid (slightly acidic, high temperature) and hydrothermal pre-treatments (high temperature without the addition of chemicals),” says Kabel. “We have looked into whether an alkaline process with a high pH and relatively low temperatures would also be an option. One advantage of an alkaline-based process is that the lignin is partially broken down and can be separated from the cellulose and hemicellulose. This lignin fraction could be used, for example, to provide the energy needed to carry out the process. Another advantage of the lignin separation is that the conversion of (hemi-)cellulose to sugars proceeds much more smoothly. The presence of lignin slows the enzymatic conversion.” There are also disadvantages. “We have been working with sodium hydroxide which is expensive,” says Kabel. “It is only cost effective if you can reuse it and that is difficult. Sodium carbonate would appear to be a good alternative even if the pH is a little lower.”

New enzyme

Kabel is extremely pleased about the results. “We better understand which enzymes are needed on top of the existing cocktails. We know xylan-degrading enzymes are very important as well as cellulases. We’ve characterized a new enzyme – alpha-glucuronidase, which can contribute to a better conversion. Finally, the research has given us better insight into which components are released alongside sugars when sugarcane bagasse is pretreated and what impact these substances have on the fermentation of lactic acid.”

Nitrogen-based specialties

*The Flagship **Nitrogen-based specialties** develops novel technologies for the production of nitrogen-containing compounds from renewable feedstocks through the use of advanced engineering of micro-organisms. Research within this flagship is focused on the design and optimisation of pathways for the production of compounds that can be used as pharmaceuticals or as building blocks for materials. In addition, this flagship includes high-throughput bio-pharmaceutical process development aiming at the optimisation of protein production.*

FS2

Targeted experiments with a lab-on-a-chip

Medicines used in the treatment of cancer are very often based on proteins. Genetic technology enables mammalian cells to be modified so they produce a tiny amount of human protein. But how do you know what is needed to produce that one specific protein-based drug in large quantities? The answer lies in experimentation, which can be extremely time consuming. The Flagship 2 project Peptides and Proteins: High-Throughput Bio-Pharmaceutical Process Development will enable this to be done more quickly in the future.

"Say you have a protein-based product and you want to know how one can produce it on a large scale, but you only have a small quantity available," says Marcel Ottens from Delft University of Technology. "This means you don't have enough material to perform many experiments. However, we now have the technology in house to carry out these experiments more efficiently and more quickly. This research project is about carrying out many experiments with a very small volume of protein." Ottens' team has looked at how process development can be done more quickly (high-throughput process development) using the tiniest amounts of available protein. Together with the University of Twente, the Karlsruhe Institute of Technology (KIT), DSM and Synthon, they have developed a new approach to process design. "This approach is a combination of robotics, which generates a lot of data, and mechanistic models, which can predict the behavior of proteins," says Ottens. "By linking these two aspects, you can experiment more efficiently. You already have an idea of where you need to focus." In order to automate the process, the team is developing a special lab equipped with robots. The robots may be two metres wide, but the proteins are of nano format. It is now, however, possible to carry out some parts of the process via a lab-on-a-chip device.

Commercialisation

The approaches taken by Ottens' team will allow new medicines to be developed and hit the market more quickly. "The technology we have developed is also available to other parties," Ottens says. "An integral part of this research project was to find out if we could commercialise the results. We've taken the first steps.

A business plan has been put together for a startup to provide this service to interested parties. There is a lot of interest from bio pharmaceutical firms, but it takes more to create a successful and independent company. That is something to look at next." One important part of commercial success is ownership of the discoveries, and a patent is currently pending. "It's just a matter of time," says Ottens. "Patents strengthen the position of a company. We can offer the software and infrastructure we've developed to clients."

International reach

International companies are very interested as well in this approach, which Ottens describes as 'trendsetting'. "TU Delft has a name in terms of high-throughput process development," he points out. "There is a reason why some of the researchers who have worked on this project have found jobs with international companies like Novartis and Novo Nordisk. Within BE-Basic we are part of an international consortium with important partners. For example, we have worked with a German lab that is highly experienced in robotics. By joining forces, we are able to make major advances."

Sustainable soil management and upstream processing

*The Flagship **Sustainable soil management and upstream processing** focuses on developing and testing scenarios for waste management from the perspective of closing cycles and the prevention of negative side effects deriving from a biobased economy (spilling=spoiling). The aim is to prevent potential negative side effects associated with a more biobased economy and to ensure that a biobased economy really results in a more sustainable planet.*

FS3

Assessing the social, environmental and techno-economic impact of jet biofuels and bioplastics

Developing new methodologies and techniques is one aspect of driving forward sustainability in the biobased economy. In the HIP project, however, the team has been looking at the techno-economic, environmental, and social consequences of producing jet biofuels and other renewables from a wide variety of feedstocks. The ultimate aim is to ensure the sustainable regional production of jet biofuels and bioplastics.

The focus of this project is on the production of value added products in key regions in Brazil using different local feedstocks in order to draw up specific, local, sustainable solutions. The first phase of the project involved developing the methodology for a fully integral sustainability analysis of entire value chains, from biomass production to logistics, (bio)chemical conversion and waste management, as well as social quality, and human and environmental health.

Total value chain

Once the most promising sustainable production pathways have been identified, the team carries out detailed due diligence reports for industrial piloting and demonstration projects. These also include an analysis of hazards, opportunities and benefits for local farmers and communities. "There are so many aspects to consider, and the interesting thing about this project is that we look at the total value chain," says professor Patricia Osseweijer of Delft University of Technology. "It is a project which brings together different partners and different Flagships and tries to assess the impact of biofuel production across all aspects of local communities."

Crops and public perception

Take, for example, the use of sugar cane to develop jet biofuel. "You can make jet biofuel from sugar cane, from soy and from lignocellulosic feedstocks, but it has been difficult to determine which is the most interesting crop," she points out. "If you use sugar cane, for example, you have a crop with quite a high yield per hectare, but the process to make fuels is quite different from oil based crops. Public perceptions also play a role, as well as local transport issues and employment. Palm oil, for example, is the most productive oil crop per hectare, but has a negative image. You also need to look at maintaining soil quality, recycling options for nutrients, and how you dispose of the waste. There are so many factors attached to each crop, and no answer as to which is best yet."

Overall picture

Determining which feedstock to use in a given situation requires looking at the overall picture. "For example, you need to look at the social impact or the impact on jobs and the health and safety aspects," Osseweijer says. "And what we consider to be important here in the Netherlands may be different to the people at the grassroots in Brazil. NGOs may criticise the use of food crops for bioproducts, but Brazil has a vast area of land available to grow products, and extension of markets will help rural income. Food security is not really an issue here. Indeed, 40% of food produced in Brazil is exported. However, it does not mean that deforestation has stopped, and we should therefore carefully analyse these social impacts as well. For instance, most areas where sugar cane has been expanded show a higher human development index and higher education levels. For the locals, it means a higher perceived level of well-being. One of our Brazilian students is looking at the actual and perceived impact of sugar cane at a grassroots level."

Data gaps in the value chain

John Posada Duque, also based in TU Delft, is working on the main data gaps in the value chain. The starting point involves more than 25 feedstocks from different locations in Brazil, five conversion technologies for jet biofuel production, and 10 biobased products. "All of these options resulted in a large number of potential combinations for the value chain. So, we screened these multiple options based on techno-economic and environmental criteria, but first we had to harmonise and validate the contradictory information obtained from the literature," he says. "We are now developing a framework to design integral sustainable production scenarios with special attention for social impacts assessment."

*The Flagship **Bioconstruction materials** focuses on the development and testing of microorganism-based solutions to create smart (bio)construction materials which are self-healing.*

FS4

Bioconstruction materials

The last stage before a major market launch

The self-healing concrete developed by Henk Jonkers of Delft University of Technology has been creating a buzz for years, and in 2015, Jonkers was nominated for a European Inventor Award by the European Patent Office. Following the development of the basic idea, Jonkers has been working with Corbion, to develop a fully-fledged product. Companies from all over the world are interested, but a commercial launch remains a challenge.

"We made a major advance from the lab phase to actual projection in 2015," says Henk Jonkers. "We can now produce several thousand kilos of self-healing agent, bacterial spores, nutrients and lactate/polylactic acid-based substrate, which heal the concrete from within – that's enough for 20,000 kilos of concrete. The only problem is we currently need two external companies to produce a ready-to-use product and that is forcing the price up to some €80 extra per cubic metre of concrete. This is too expensive for the construction industry."

Reducing the price

Nothing more can be done to cut the price of the healing agent. "From a scientific perspective, it has been developed. We have the right bacteria, the right product composition and the right processes," says Jonkers. "The price is due to the raw materials and the fact we need outsiders in the production process." The solution would appear to be straightforward: start their own healing agent production line. "That is a serious option," Jonkers says. "It could take the price down to €30 a cubic metre of concrete and that is acceptable to the private sector. But it would require investment of €4M. There are potential investors, but they quite rightly want confirmed orders before they start."

Show it works

Proof that the self-healing agent works is one of the major value adds that Jonkers' research group has. "Concrete often gets damaged warming up after frost. We've been able to speed this process up in the lab to show the positive effects. But commercial companies really want to see the process in reality. So we are doing as many practical tests as we can. For example, the Limburg Water Board has a waste water processing tank which is partly made of self-healing concrete. The tank looks fine at the moment, but of course concrete rot takes a few years to materialise. So we don't know when we will see that the self-healing section is in better condition. The water board has already said that as soon as the process has been proved, they will use the healing agent in all their projects. Then you start to make major advances."

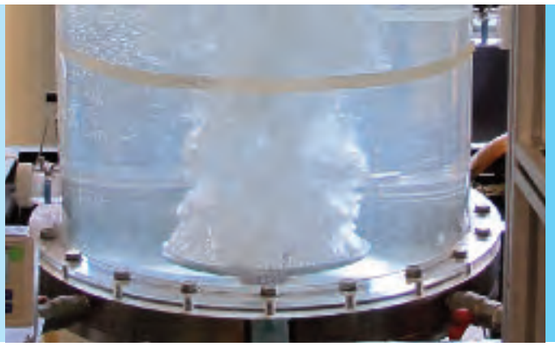
More speed using repair mortar

The healing agent can also be added to the mortar used to repair current damage, and Jonkers is running practical tests to prove this to potential buyers as well. One of these involves a project in Groningen for construction group BAM. "You can show the way the healing agent works in the repair mortar more quickly, and companies are prepared to pay more for it. We expect that the repair mortar will be accepted more readily by the market and that buyers will then be willing to put the healing agent in new concrete. That will take setting up our own production line a step closer."

The self-healing concrete is based on bacteria which produce calcite when fed and activated. The bacteria and its foodstuff (the healing agent) are added to the concrete in tiny capsules that only open when the concrete has hardened and cracked. The capsules are made from bioplastic developed by Corbion.

*The Flagship **Microbial production of biofuels and biorenewables** focuses on the development and optimisation of microbial-based conversion process technologies for the conversion of biomass into biofuels and other biorenewables.*

FS5



Microbial production of biofuels and biorenewables

Upscaling the production of diesel and jet biofuels

Major steps forward have been made within Flagship 5's project to develop an integrated bioreactor for the production of diesel and jet biofuels. The research team has developed technology to directly recover lipids used to produce biofuels, a noteworthy result because both fermentation and separation take place in the same stage. In 2015 the team realized proof of principle for the separation technology on fermentation broth and proof of concept for the reactor design. This has established the fundament to scale up the integrated process and equipment to a prototype of significant 100L scale. In 2016, this three metre bioreactor will be placed in the Bioprocess Pilot Facility (BPF), allowing larger volumes of diesel and jet biofuels to be produced. A successful 100L prototype run in 2017 will be followed up by a pilot reactor of 8m^3 at the BPF in 2018.

"In 2015 we focused on achieving two targets," says Kirsten Steinbusch, managing director of the BE-Basic startup Delft Advanced Biorenewables (DAB). "An engineering post-doc student from Delft University of Technology has worked on engineering and testing of the process and equipment for integrated fermentation and separation of diesel and jetfuel-like biofuels. In addition, we focused on testing the separation technology on real fermentation broth that microbially produces diesel and jet biofuel-like compounds. And the ultimate aim was to integrate both parts and scale up the integrated process and equipment to a 100L bioreactor prototype. It was a terrific moment when we realised the separation technology really worked and when the plastic reactor prototype was given approval. It is fantastic that we now have the green light to build the reactor."

Operational tests at the BPF

The team comprises three different groups working closely together: Delft University researchers within BE-Basic; DAB, the startup which is taking the promising technology to the market and the BPF. "The pilot plant has been specifically designed to enable the transition from laboratory to industrial scale," says Peter Flippo, business development manager at the BPF. "Over the past year DAB has carried out operational tests with model emulsions containing two prototypes from the DAB reactor. Being able to carry out fermentation and separation in one step is unique and reduces the scale of the process, so in the end you can produce diesel and jet biofuels more cheaply. This is extremely important because of the pricing pressure in the biofuels market."

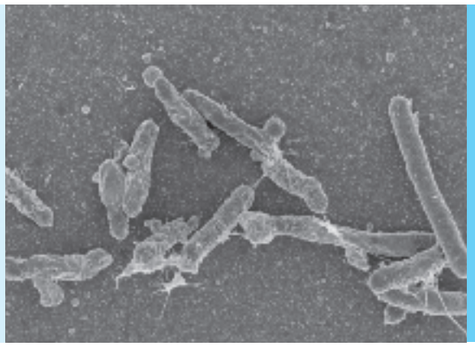
Full scale production in 2020

The further upscaling steps that are planned are large scale production at 1000L scale in a fermenter at the BPF. That reactor run will allow production of up to 1000L of fuel. "By using larger volumes, we can carry out more tests to validate our models," says Steinbusch. "In addition, we can use the principle of fermentation separation to carry out tests using other organisms. At DAB, we will also do this on behalf of third parties, who will also be able to upscale using a reactor installed at the BPF." The development is good news for the production of diesel and jet biofuel in general. "Once the upscaling phase has been completed at the BPF by validation of a second scale-up step to 8000L by 2018, by 2019 it should be possible to build a factory," says Steinbusch. "Industry itself will have to actually set up a full-scale plant, but the fuel could be produced on a commercial scale from 2021."

Synthetic biology

*The Flagship **Synthetic biology** develops tools and techniques for the improvement of micro-organisms. The design and optimisation of novel pathways to desired products are complemented by unique cell membrane engineering aiming for efficient product export and improved robustness of the production organisms.*

FS6



Helping cells to survive in more extreme conditions

Can cell membranes be engineered to become more robust and survive in more extreme conditions, such as cold and heat, and can they be made tolerant to organic solvents or byproducts during industrial processes? "Archaea are single cell organisms that can withstand really difficult environments such as hot springs or extremely cold habitats," says Groningen University researcher Antonella Caforio, who has been working on one of the projects in this Flagship for nearly four years together with a team in Wageningen. "If we can introduce this ability to other organisms such as bacteria, we may be able to make them withstand stressful conditions and, in turn, increase cell productivity during industrial processes."

New form of life

The idea behind the Flagship's work is to make *E.coli* bacteria more robust. Every cell's membrane is composed of lipids and the lipids, in Archaea are thought to be responsible, at least in part, for the organism's ability to live in such extreme conditions. "So if we can introduce the Archaea ether lipids into the *E.coli* membrane, we should be able to improve the bacteria's robustness," says Caforio. Once this has been achieved, the team will have developed an *E.coli* bacteria which should have a higher tolerance to toxic products, organic solvents and byproducts without loss of productivity. Such an organism with a mixed membrane will be a new form of life. "The existence of a last universal common ancestor (LUCA) with a mixed membrane is one of the hypotheses at the basis of the differentiation between Archaea and bacteria," says Caforio. "The development of a viable bacterial cell with a mixed membrane will help us understand the molecular basis of evolution."

Methodology to engineer lipid species

In 2015, the team succeeded in identifying all the key enzymes involved in the ether lipid pathway and the pathway, was introduced into *E.coli* via metabolic engineering. The development can be seen as a general methodology to engineer lipid species that can be applied to other micro-organisms which have industrial relevance. In other words, it has opened the door to further improving the process and proving a direct correlation between the introduction of the ether lipids and the robustness of the *E.coli* membrane. "We could detect the presence of the archaeal lipids in the *E.coli* but not in sufficient amounts," Caforio says. "We are now improving the strain and optimising the processes to try to produce higher production of lipids and really determine if the process has improved the robustness of the cells. So far, our efforts are paying off."

Actual applications

"In previous years the focus was on the production of ether lipids in the *E.coli* membrane to try to affect the properties of the bacteria. Now the robustness tests are being performed on the evolved bacteria strain and, depending on the results, will be used to develop actual applications," says Caforio. Eventually, the technique could be applied to other industrially relevant microorganisms to increase high temperature or pressure stability. The robustness of the constructed strain could also support developments in lipid-based drug delivery systems. For example, if the carrier is made more resistant to the acidic environment of the gastro intestinal tract, drugs could be delivered to the targets without being compromised.

High-throughput experimentation and metagenomic mining

FS7

*The Flagship **High-throughput experimentation and metagenomic mining** develops and applies high-throughput approaches and tools to explore and mine the metagenome, genetic material that comes directly from our natural ecosystem. In addition, this flagship aims to engineer and screen enzymes and other products for improved properties.*

'As there is an immense societal demand for new bioactive compounds such as antibiotics and novel enzymes to be used in biobased production processes, it is fantastic to identify a novel microbial compound which becomes a concrete product.'

The hunt for new and improved enzymes and bioactive compounds continues to deliver surprises. Take, for example, the discovery that two different bacteria growing in association produce a compound active against fungi and pathogenic bacteria, which is not formed when the organisms are grown separately. Such compounds could be used as antibiotics. High-throughput technology makes it possible to rapidly test different combinations of bacteria.

Competition between bacteria

"When they are in pure culture, many bacteria do nothing but when they notice another strain, they start to compete and for this often produce bioactive compounds" says Flagship manager professor Hans van Veen of the Netherlands Institute for Ecology, NIOO-KNAW, which is based in Wageningen. "We've discovered that bacteria turn different groups of genes on and off to produce various substances, depending on the neighbouring bacterial species. High-throughput screening is helping researcher Olaf Tyc to identify interesting combinations of bacterial species capable of producing novel bioactives."

The project is part of Flagship 7 and aims to identify promising new compounds. "We have also looked at rotting wood because we expected to find useful antioxidants which pose less of a risk to eukaryotic cells and therefore ultimately to humans," says Van Veen. "The theory did not entirely work out, but we did find a completely new family of bacteria which are closely related to the commonly used antibiotic-producing Streptomyces. We've managed to map the genomes of several species of this family so that in the future we can screen for the relevant characteristics more quickly and accurately. That research is now being continued in close collaboration with Leiden University."

Towards the market

The search for new compounds within Flagship 7 will end mid-2017. "Finding the substance is only the first step," says Van Veen. "After that, we face the challenge of obtaining the pure compound from the bacteria and building up a file of useful information for the market." Van Veen sees his mission as to bridge the gap between science and the market. "Scientists no longer sit in ivory towers," he says. "Everyone who works here is aware of the need for practical applications. Of course, it would be great if my research led to the launch of a new antibiotic or if the novel antioxidants were used in cosmetic products. But here at this institute, whose core activity is fundamental ecological research, we cannot carry out thousands of tests if they don't contribute to improving our fundamental knowledge and to our main products: our publications and theses. And the market needs those tests before they will invest. We are trying to close that gap with start-ups such as MicroLife Solutions (MLS), and we are increasingly talking to industry at an earlier stage in the research process. This is how we try to encourage researchers to become more market-oriented and to interest industry in investing in highly promising research. For example, Dick Janssen's research on modelling enzymes in another Flagship 7 cluster involves intensive contact with industry and has generated patent applications."

Towards the future

Interesting discoveries continue to be made, even though the project is nearing its end. "We've found Acido bacteria which produce new forms of PHA and EPS, both of which are bioplastic components and non-toxic in these forms. They offer real commercial opportunities," says Van Veen. Such discoveries, illustrate the added value provided by BE-Basic. "The charm of a big project like this is that you can carry out broad-based research. BE-Basic has given metagenomic mining an enormous boost and shown which research angles and methods have the best chance of success. There is an incredible amount to discover in nature, and high-throughput genomic research makes those opportunities more visible. I'm convinced it will lead to the delivery of many more commercially interesting concepts and products."

Environmental impact of chemicals, biobased molecules and processes

*The Flagship **Environmental impact of chemicals, biobased molecules and processes** develops novel and efficient biobased monitoring tools for the evaluation and improvement of chemical safety in the biobased economy. Research is focused on the environmental and human safety issues arising from the transition to and implementation of a biobased economy, as compared to existing industrial activities.*

FS8

From monitoring chemical safety to creating added value

Flagship 8 focuses on developing tools and methods to measure whether biobased building blocks are safe for mankind and nature and how to map the risks associated with soil exhaustion. Now more results are being evaluated, this risk analysis has become the starting point for adding value across the chain.

Professor Wim van der Putten of the Netherlands Institute for Ecology NIOO-KNAW, Flagship manager professor Hauke Smidt of Wageningen University, and doctor Bart van der Burg from BDS have been looking back together at the results booked by Flagship 8 in 2015. “After all,” says Van der Putten, project leader within FS8 and manager of FS3, “it is the variation of expertise within BE-Basic and the willingness to cooperate across disciplines and flagships that are key to our success. For example, FS3 is able to use techniques and tools that have been developed in FS8 and that are now being tested and integrated into decision support systems.”
“It has also helped in the way we think,” adds Smidt. “The starting point for this flagship was ‘end of pipe’ – to warn about and clean up dangerous substances. Now we have a different perspective. Perhaps we could create something new and sustainable by seeing waste as a resource instead.”

Variety and precision in farming

Take recent research by Van der Putten and colleagues, for example, which establishes that willow can improve soil. “By rotating between maize and willow you actually improve impoverished soil and produce raw materials to make bioethanol at the same time,” says Van der Burg. “The knowledge we have now enables us to look two to three steps ahead,” says Van der Putten. “That is necessary in order to design an entire production chain, including bringing value to the waste products.”
Scientific advances have also been made in remote sensing, which is key, for example, to developing a decision support system for farmers. Remote sensing allows farmers to decide how to manage crop health by anticipating future problems. “We have established proof of principle that a different microbial make-up in the soil can be detected by hyperspectral imaging of the plant itself, by measuring wavelengths that cannot be seen by us humans,” says Van der Putten. “This offers great perspectives for precision farming, for example by helping farmers to decide where on their land they can make use of which type of waste.” It will still take some time before this becomes a common practice. “A lot of research still has to be done, and a market launch takes time,” says Smidt. “But it is an important development for the decision support tool.”
“These discoveries,” says Van der Putten, “could have a great impact on the sustainability of human society.”

Screening

In the meantime, BDS has won its spurs with the CALUX screening panels that highlight toxic substances by illuminating cells. “We can rapidly identify biobased compounds with low toxicity,” says Van der Burg. "We have recently shown that biobased FDCA (furan-2,5-dicarboxylic acid) is an interesting new 'green' alternative to plastic building blocks as it is devoid of endocrine and other activities often associated with these molecules. In addition, we are trying to adapt the technique to increasingly complex blends. In the end, you want to be able to test biobased waste streams quickly, and by definition these streams contain biological activity. The screening panel should make it possible to separate the beneficial biological activities from the harmful. Behind the scenes we are making great steps forward in this.”
The team’s vision for screening tools has also changed. “The tools focus on the point at which a substance becomes toxic,” says Van der Burg. “But before that point is reached, the substance might be beneficial in smaller quantities.” Smidt adds, “Our perspective has shifted from warning about dangers to identifying economically valuable molecules in biomass. This is essential to make the biobased economy a real option.”

Societal embedding of a biobased economy

*The Flagship **Societal embedding of a biobased economy** optimises the societal embedding of the products and processes developed by BE-Basic. The Flagship focuses on the identification of socio-economic aspects and sustainability issues and the development of adequate systems to monitor and model them. The Flagship develops effective and efficient education, communication and societal valorisation programmes.*

Flagship 9 and Flagship 11 both focus on societal aspects of importance for the transition to a biobased economy.

FS9
FS11

‘Availability of land is not a limiting factor: will this finally bring the biobased economy closer to reality?’

In 2015, BE-Basic booked its best ever results in the field of embedding the biobased economy in society at large. It was the year the SCOPE report on Bioenergy and Sustainability, which offers a positive perspective on the realisation of a global bioeconomy, was published. The 800-page report by the Scientific Committee on Problems of the Environment reviews scientific evidence on the benefits of sustainable energy to society. “The report is already being called the ‘Bible of sustainable bioenergy’,” says Patricia Osseweijer, chairwoman of the Economy, Policy and Sustainability (EBD) programme. “The peer-reviewed report is a collective effort with contributions from 137 researchers at 82 institutions in 24 countries, and we are proud that BE-Basic experts contributed to nine of the 21 chapters. The impact is immense because the results give countries and companies a license to move forward.”

“The conclusions of the peer reviewed report can be called spectacular,” says Osseweijer. “It concludes that land availability is not a limiting factor and that bioenergy can contribute to sustainable energy and food supplies even with increasing food demands, the preservation of forests, protected lands, and rising urbanisation.” The report was launched in São Paulo, Brussels and at the World Bank in Washington. “Such extensive communication is crucial, and it is good to see so many people who are involved in bioenergy innovation use the report. A policy paper based on it was presented during the European launch at the Green Energy Week in Brussels.”

New tools to boost cooperation

The SCOPE report also reviews studies on sustainability impacts and modelling, including those carried out within the confines of BE-Basic. “Our programme is crucial to help innovation succeed,” says Osseweijer. “And with the results now being presented, we see increasing attention for the subject, from industry as well. This year a number of sustainability studies led by the Copernicus Institute were finalised, providing models for sustainable land use for biobased production. The programme takes a very broad approach and looks at the influence of land use changes, the socio-economic aspects and smart monitoring tools. Such tools should help stakeholders throughout the value chain to decide on the best practices for crop management, transport, and biobased production. This is unique and necessary for the transition from a fossil-based to a biobased economy because society demands this be sustainable. Also, situations are radically different in a biobased economy. For example, the chemicals industry needs to link with farmers for feedstocks – and that requires different tools for cooperation and agreements to ensure a reliable supply of feedstocks.”

Biorefineries, the harmonisation of certification and education

More is needed to support this transition, including ensuring that the new insights land on the right desks and that future engineers and entrepreneurs are well educated and trained. For example, BE-Basic has provided input for the ‘redefinery’ – a blueprint for building a biorefinery in the Netherlands which incorporates the impact of socio-economic factors. The harmonisation of European rules for certifying solid biomass is another aspect which BE-Basic contributed to. This is key to organisations which issue sustainability certificates. Furthermore, extensive efforts have been made to boost both professionalisation and digitalisation in education. “We want to learn from our success with the MOOC and digitalise educational elements that can be used in different settings, and for large audiences, such as preparatory material for an advanced Master or PhD course,” says Osseweijer. “Our second MOOC

EBD Programme: Economy, Policy and Sustainability

Flagship 11 ***EBD Programme: Economy, Policy and Sustainability*** *focuses on providing insight into the societal preconditions for the economic and sustainable introduction of bio-renewable chemicals, materials, fuel and energy production. It provides policy recommendations on the likely macro-economic impact of the large-scale use of biomass in the Netherlands (including imports) and aspects of sustainability and contributes to (inter)national committees.*

Flagship 9 and Flagship 11 both focus on societal aspects of importance for the transition to a biobased economy.

FS9
FS11

'Industrial Biotechnology' was followed by 10,000 students. And in Brazil, many courses have been developed which we offer to a wider public using different forums."

Focus on communication
In the meantime, a broad discussion about the biobased economy is under way in society at large, helped by publications such as the SCOPE report. BE-Basic has been instrumental in driving the debate forward by, for example, publishing a weighty reaction to the Dutch Economic Affairs Ministry's new energy policy. "There are many new insights," says Osseweijer. "We know more about the critical points in the chain and which technologies are feasible. And we've debunked several myths. One of the most stand-out facts is that we do have enough land to feed the growing population and that the global food versus fuel discussion is history in terms of facts. For example, it has been established that the use of land to grow biomass for fuel production actually can improve local food production and quality. Growing raw materials for bioenergy induces sustainable agriculture and that means people get better access to food. So there are improvements across the entire chain. We need to communicate these insights to a much broader public to give the biobased economy a real chance of success. So in 2016, we are going to enlarge our focus on communication."

Developing policy
Making the biobased economy a reality also demands a change in official policies. Within BE-Basic, Flagship 11 has developed various models and tools to calculate variables such as emissions and to predict the economic impact of different scenarios. The Macroeconomic Outlook was published in 2015. BE-Basic also contributed to the Corbey Committee report on the availability of biomass. "The combined projects of our Flagships are accumulating a better understanding of how novel technology can land in society in a sustainable way and how we could help accelerate positive impacts," concludes Osseweijer.

Corbey Committee
The Corbey Committee called on the Dutch government to make developing a biobased economy a much higher priority with the publication of its vision document 'Naar een duurzame bio-economie' ('Towards a sustainable bioeconomy') in October 2015. The document points out the advantages of a bioeconomy in which biomass is a resource: fewer CO_2-emissions, less dependency on fossil fuels, and more employment opportunities. It explains that the biobased economy would be lucrative for the Netherlands, but that it requires ambitious integral policymaking and a stronger government role to drive it forward. The results of two BE-Basic research projects on the availability of national biomass and the import of biomass into the Netherlands were included in the report.

International Energy Agency
BE-Basic supports the Dutch membership of the International Energy Agency (IEA). IEA Bioenergy's strategic plan envisions biomass as making a substantive contribution to future global energy demands by accelerating the production and use of environmentally sound, socially accepted and cost-competitive bioenergy on a sustainable basis. This would provide increased security of supply and reduce greenhouse gas emissions from energy use. Dutch industry and research institutes are involved via an implementing agreement, financed by the TKI-BBE.

Five questions about the Macroeconomic Outlook II

BE-Basic's Macroeconomic outlook of sustainable energy and biorenewables innovations (MEV II) was completed in 2015. The extensive study offers guidance for Dutch energy and bioeconomy strategy. Research leader Hans van Meijl from LEI Wageningen UR discusses the main findings.

1. What is the Macroeconomic Outlook II?
The study looks at the impact of a Dutch biobased economy in which biomass is used on a major scale, both at a system and a macroeconomic level. System-level impacts include renewable energy deployment, fossil fuel reduction, and greenhouse gas (GHG) mitigation. Impacts at the macroeconomic level include gross domestic product (GDP), value added, employment and trade balance.

2. What are the most important findings?
The study shows that the biobased economy can make a positive contribution to the Dutch economy in general and will help cut greenhouse gas emissions as well as cutting the cost of achieving that reduction. The macroeconomic impact depends on fast technological change, high fossil energy prices, a worldwide trading system and low biomass prices. A biobased economy which is driven by fast technological change and cheap, easily available biomass, will cut the cost of reducing CO_2-emissions and will make biobased options more attractive. But the bioeconomy will not become a reality while oil prices are at their current level. Intervention in the form of a tax on CO_2 or changes in R&D strategies would have an impact on this.

3. What are the main factors influencing the transition to a biobased economy?
There are a number of issues which need to be taken into account in achieving the above-mentioned results and switching to a biobased economy. Major technological advances, high fossil energy prices and the low worldwide prices for biomass are essential elements for a successful transition. At the same time, low fossil fuel prices dampen the macroeconomic advantages.

4. What more can be done to drive these developments forward?
The study shows that a strategy of stimulation – such as CO_2 taxes or R&D policy – is key to realising the macroeconomic benefits and a reduction in CO_2-emissions. For example, the Netherlands supports electricity production using wind and thermal energy and that has made a considerable contribution to meeting targets on renewable energy sources. In addition, technological developments are needed within biobased sectors to make bioenergy and biochemicals cost competitive. Biorefineries can play a crucial role here. A high tax on CO_2-emissions can also be an effective policy instrument. Low feedstock prices and good access to international sources of biomass are also essential. So stable international biomass markets will need to be established as well.

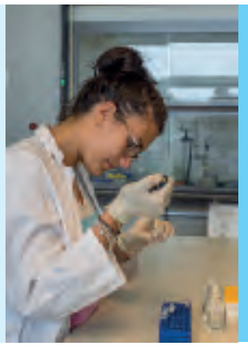
5. How do the BE-Basic findings impact the realisation of a biobased economy?
BE-Basic stimulates the development of fundamental and applied technological knowledge to make biobased technologies a competitive reality. This is essential in the transition to a biobased economy. In addition, BE-Basic focuses on driving forward social acceptance of the changes. This is crucial, as the debate on GMOs within Europe has shown.

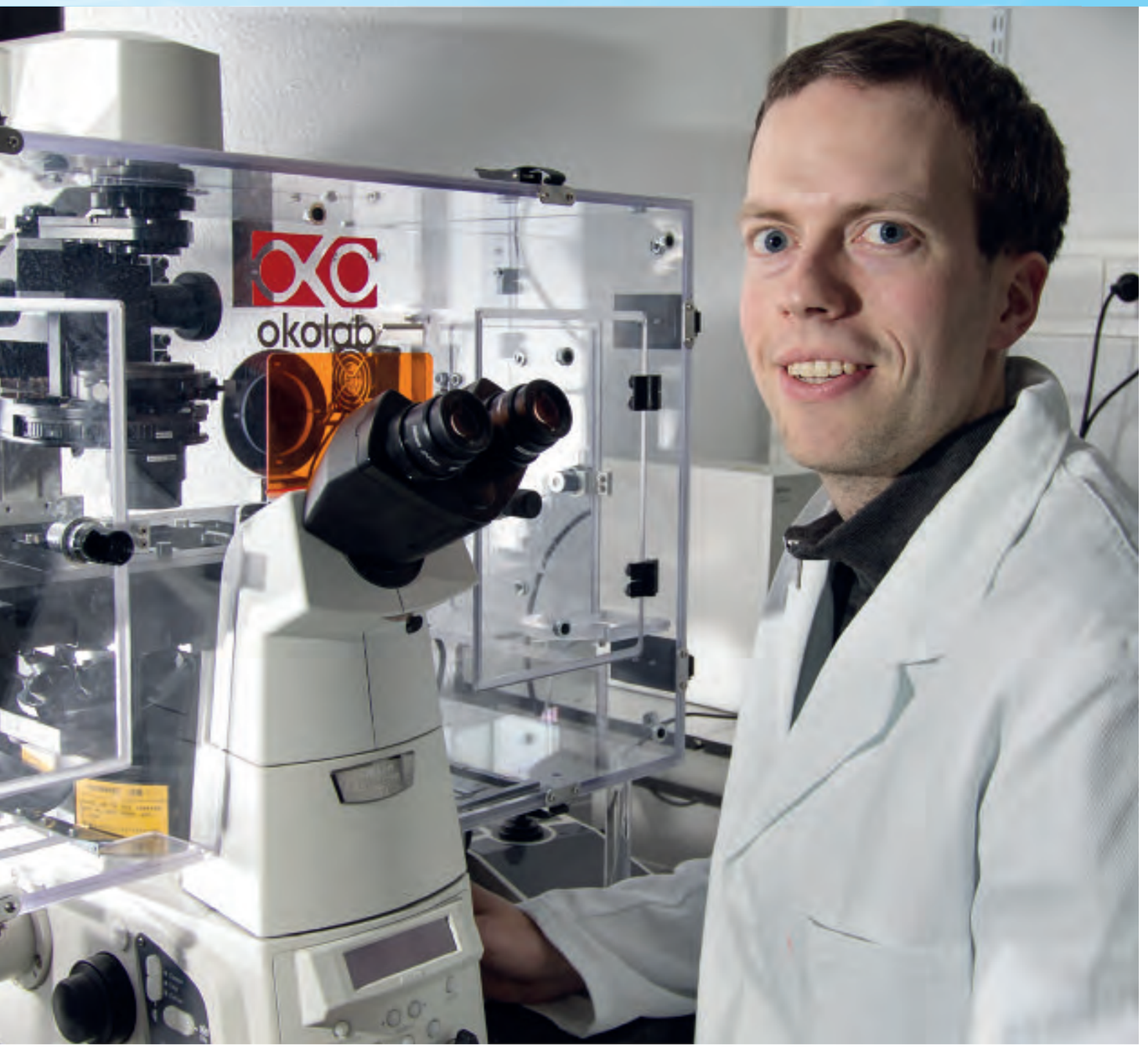
Partners
The research was carried out by LEI Wageningen UR and the Copernicus Institute at the University of Utrecht. Project partners Essent, DSM and Corbion also contributed to the economic and technical aspects of the report. The public version of the impact study and the full scientific report can be downloaded for free from: http://www.be-basic.org/downloads.html.

Genomics for industrial fermentation

*The Flagship **Genomics for industrial fermentation** aims to deliver improved fermentation processes for bioconversions in the food industry, focussing on the selection of natural strains or strains resulting from directed evolution or (non)-genetic modification.*

FS10





Seeking a natural way to improve lactic acid bacteria

Is it possible to improve strains of lactic acid bacteria using methods that also occur in nature? This question is at the heart of the novel strain improvement project within Flagship 10, led by Oscar Kuipers at the University of Groningen in close cooperation with several industrial partners. "The project has been running for under two years," says Kuipers. "We have looked at three natural methods for transferring lactic acid bacteria DNA and have developed new methods to achieve strain improvement in the laboratory. In time, this will help industry to develop new flavours and boost the shelf life of dairy products."

The novel strain improvement project is very much driven by industry. "Lactic acid bacteria determine the taste, texture and preservation of dairy products," Kuipers says. "The food industry is interested in other flavour compounds and improving anti-bacterial activity to, for example, increase the shelf life of a product. The food industry would be extremely pleased if we can adapt transfer processes that occur naturally." Four PhD research projects are now underway which focus on three of the bacteria which occur in cheese, yoghurt or other food: Lactococcus lactis, Streptococcus thermophiles and Bacillus subtilis.

Mapping the transfer of genes

The researchers have looked into three ways by which genes are transferred horizontally in nature, and Kuipers and his team are now developing the technological methodology to do this in the laboratory. "First of all, bacteria can transfer DNA material via a process known as conjugation. Then there are bacteria which take up DNA out of the environment in a process which we call competence. This happens naturally, for example, during decomposition in soil. Thirdly, there is phage transduction, a natural process in which foreign DNA is introduced into a cell. Phages are bacterial viruses that infect bacteria and take over part of the DNA – this is also something which happens in soil. To carry out this research, we have access to a large collection of phages capable of transferring DNA. This is a process we can mimic in the lab and stimulate."

Selecting characteristics

Further development is needed to ensure the technology can be used by industry. "Transferring DNA is not the problem," says Kuipers. "The challenge now lies in developing ways to select the characteristics which you want to obtain. We want to develop natural methodologies, so we want to carry out this screening process in a natural way as well. These characteristics can be captured, for example, by screening for phenotypical markers. We could for instance make selections based on polysaccharides, which can be easily identified because they create slimy colonies. But we would rather hone in directly on DNA, which is why we are researching the use of specific probes."

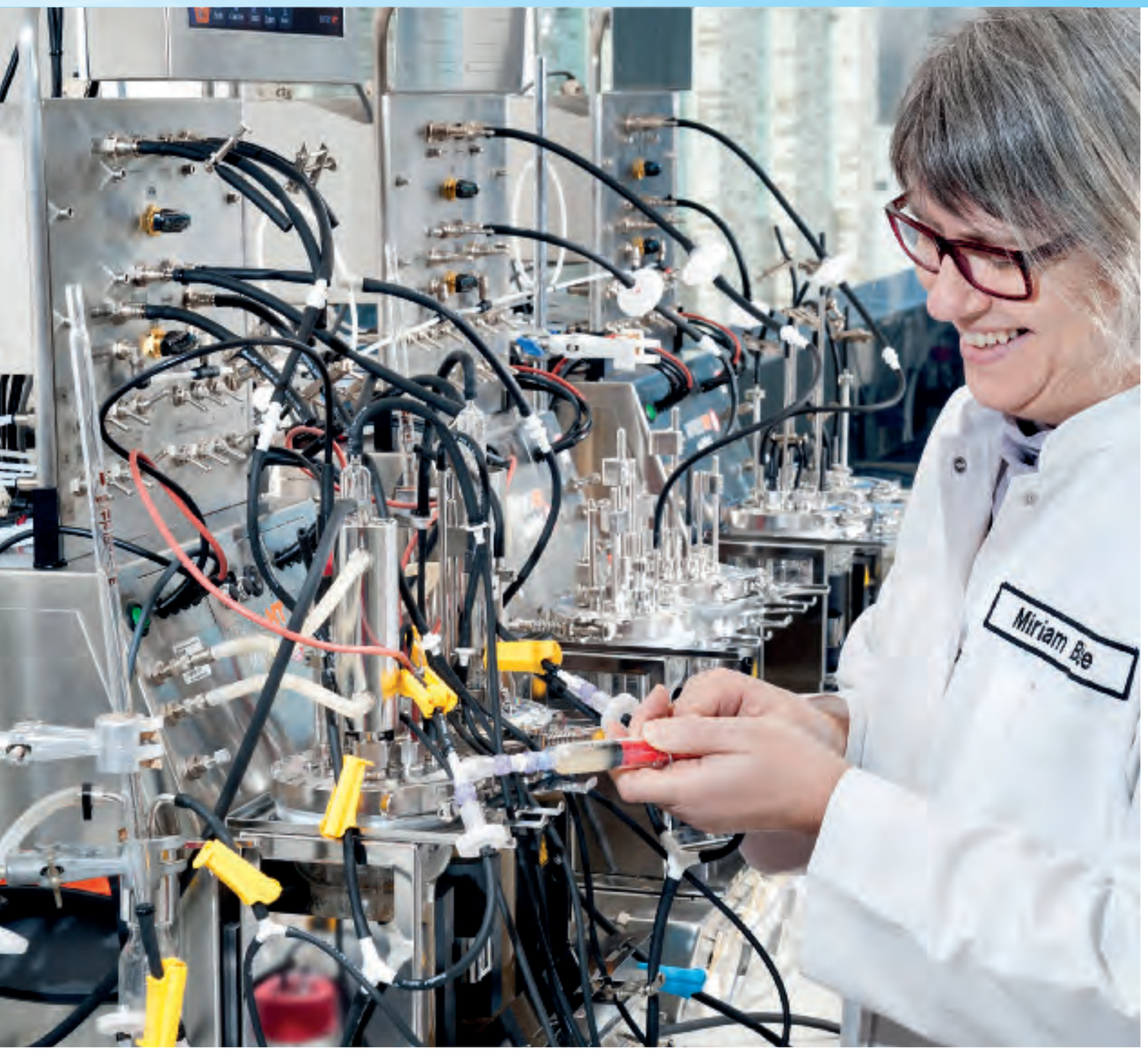
Possible industrial and environmental applications

Developments in this field are being closely followed by the Flagship's industrial partners. "We only take our results to the outside world once they have been cleared by industry because they could create major shifts in the market. The technology we are developing could also be used for other applications. For example, certain bacteria and fungi could contribute to clearing up pollution. It is quite amazing what natural methodology makes possible."

Iso-Butanol Platform Rotterdam (IBPR)

*The Flagship **Iso-Butanol Platform Rotterdam (IBPR)** explores a biobased value chain for producing commodity chemicals and fuels from woody biomass using an improved Organosolv pretreatment and is based in the Rotterdam region.*

FS12



Technical feasibility biorefinery demonstrated

Flagship 12's main project focuses on the cascading conversion of lignocellulosic feedstock into isobutanol and the further valorisation of its derivatives as well as developing high-value applications of the lignin fraction. In 2015, the team was able to demonstrate the technical feasibility of a biorefinery in the Rotterdam area based on the platform molecule isobutanol. The project encompassed the entire value chain from lignocellulosic biomass up to and including the high-value end-products.

Researchers Jaap van Hal, innovation manager at ECN, and Ana López-Contreras, senior scientist in food biobased research at Wageningen UR, say they are pleased with the results so far. "The results show the importance of isobutanol as a platform molecule," confirms Van Hal. "In this project all the individual process steps of the entire value chain of the biorefinery have been proven on lab scale. And the economics of the full-scale biorefinery were estimated in detail based on a dedicated process design."

Three main fractions

During the conversion process, the biomass is fractionated into three main fractions: cellulose pulp, hemicellulose, and lignin. Isobutanol is produced by fermenting the fractions which contain carbohydrates. The end products studied in the project are GTBE, isobutyl acetate and isobutanol-acetone condensate, as well as the purified lignin that results from the ECN-patented, ketone-based Organosolv pre-treatment process.

The best case plant design shows a feasible pay-out time of six years. The life cycle assessment shows the advantages of the biobased isobutanol platform in comparison to the petrochemical isobutanol platform. The 'non-renewable energy use' is approximately 45% lower when compared to its petrochemical counterpart. The GHG emissions are up to 25% lower for the biorefinery when compared to their equivalent fossil systems. For fresh water depletion, savings can even be up to 58% over their petrochemical counterparts.

Room for further optimisation

"The project was successful," says López-Contreras. "We've got a good hydrolysis and fermentation process for isobutanol. The fermentation can be optimised still further for the use of highly concentrated sugar solutions, because of the toxic components for the micro-organisms in these solutions."

The economic viability hinges on developing high-value applications of lignin. This lignin fraction is currently burned in most pretreatment processes, but scientists are also looking at whether it is possible to give the high-purity lignin of this process added value so that it can be used, for example, in coatings or bunker oil. The next step is the development of a pilot plant based on a business plan for a world-scale plant in the port of Rotterdam.

The Flagship 12 consortium members are: BE-Basic Foundation, AVR, Corbion, Deltalinqs, ECN, GEVO, Sweco (formerly Grontmij), Port of Rotterdam, Procede, Delft University of Technology, Utrecht University, Food and Biobased Products Wageningen UR, BDS and Zirk©Technology. In addition, the IPBR project was supported by EFRO (Europees Fonds voor Regionale Ontwikkeling).

Investing in your future
The IBPR project is partly financed by the European Development Fund of the European Union

International alliances: seizing opportunities

A breakthrough in enzyme research in Vietnam, concrete feasibility studies in Brazil, broader cooperation within BIG-C, and over 25 dual degree students working on projects or preparing to do so: 2015 has been a good year for international alliances.

Vietnam
The research into intelligent mining in Vietnam has brought into focus various enzymes capable of breaking down cellulose and lignin. These enzymes contribute to the pre-treatment of biomass for biofuel, a process which is necessary to make the production process faster and more profitable. "We have demonstrated proof of principle in the laboratory, a breakthrough I'm very happy about," says Bram Brouwer, general director at MicroLife Solutions and managing director at BE-Basic. The enzymes were found in hot springs and mud pools in a remote, almost uninhabited area of Vietnam. "Nature has had its way there undisturbed for years, allowing the rotting leaves of the trees to create a special microbial environment in the mud pools. We think we will be able to find similar enzymes in the hot springs, with the additional advantage that these enzymes are active at temperatures of 60° to 90° Celsius. This means they will be able to withstand comparable temperatures in the pre-treatment reactors. We are also looking at enzyme genetics which can help determine evidence of clusters of properties in new microorganisms in order to speed up discovery."

Sustainable research
The breakthrough has been welcomed both by Vietnam and the Netherlands. "Now we need to work towards a pilot and a production environment, but we need to act carefully and respect nature," says Brouwer. "You can't just rip out lots of plants, or sample many mud pools for microorganisms because before you know it, you will have destroyed a unique environment. We are talking about setting up a system for growing plants and microorganisms on location in a national park which we think could be operative by the end of 2016 or in 2017. BE-Basic rates sustainability highly, a fact much appreciated by our Vietnamese partners. We are even held up as examples to neighbouring countries."

Europe
Cooperation between the Netherlands (BE-Basic), Flanders (FISCH) and North Rhine-Westphalia (CLIB2021) in the BioInnovation Growth Cluster (BIG-C) has become more concrete in 2015. BE-Basic Managing Director Luuk van der Wielen is closely involved in BIG-C. "There is a lot of industrial activity in this region, much of it dependent on fossil fuels," he says. "The better you can tap into the existing infrastructure, the easier and more successful the transition to a biobased way of working will be. Is it possible to extract feedstock from fossils, or use carbon as a raw material for new processes? These are the kinds of questions we need to find answers to, and technological and stakeholder analyses are already being made to determine the role of carbon in this area as well as the extraction of aromates from wood biomass." The project is very much an international endeavour. "European cooperation is essential," says Van der Wielen. "Many of the BIG-C projects are developed along European Union research lines. And that research base is being broadened continuously. Recently, we have entered into a partnership with Toulouse White Biotech so we can share knowledge and facilities. We have also agreed with CLIB to initiate innovative partnerships with Brazilian organisations in order to speed up developments in Europe."

Brazil
Opportunities for the development and implementation of biobased solutions continue to present themselves in Brazil, even if the economy is not growing as fast as it has been. The 2015 public-private partnership Agropolo, modelled on a French initiative, is just one of the many innovative ventures initiated here. Agropolo is not only about science but also looks at the social implications of the agro-industry. "The Brazilians have come to the conclusion that the industry needs reforming. At the moment it is all about end products, such as citrus juice or meat for consumption. Now they want to look into ways of making waste flows profitable as well," Van der Wielen says. The first phase of the Agropolo project consists partly of workshops explaining what might be done. BE-Basic has ample experience in public-private partnerships in this area and is closely involved in this part of the project. "We help develop ideas from step one. The process is similar to that involved in the Macroeconomic Outlook (see page 29) in the Netherlands. If you want a biobased economy with a certain GDP, a certain level of employment and certain emission standard, how do you go about it? What links are missing in the value chain? Opportunities become feasible if you back them up with figures, and that is what is happening, for the first time, in the region of São Paulo. Eventually, it will happen in the whole of Brazil." Van der Wielen thinks Dutch industry could benefit from the developments in Brazil. "Together with the Netherlands Enterprise Agency (RVO.nl) we are looking into the instruments needed to help companies wanting to work there, such as subsidies and practical support." BE-Basic has had an office in Brazil for a number of years, and that is a great advantage, too. "We have our own networks as well as the ones provided by the Dutch government," he says.

Dual degrees
One of the key objects of BE-Basic Brazil is to put in place a dual degree structure which will see people take PhD degrees both in Brazil and the Netherlands. The hard work is beginning to bear fruit. "Many people are very interested indeed," says Van der Wielen. "High level education is a critical priority for the future of Brazil." This was underlined by over 30 Brazilian and Dutch academic leaders during a recent visit to Brazil by Dutch Education Minister Jet Bussemaker. "The minister was very enthusiastic about the programme," says Van der Wielen. "We have now agreed to extend the dual degree programme from 20 places in 2020 to 100 by 2025. At this moment only TU Delft and the University of Campinas UNICAMP offer a dual degree route but there is room for expansion and others will follow. The added value of a dual degree construction is being recognised more widely. It would be nice if the University of Wageningen would agree to come in as well. Most biomass is found outside of the Netherlands, that we know. So it is up to us to go out there and take advantage of that fact to develop a bright, biobased future."

Activities

BE-BIC
The BE-Basic Innovation Centre (BE-BIC) stimulates and supports all the innovation activities taking place within the BE-Basic research programme. In 2015 BE-BIC organised the fifth and final Ideation Workshop for postdocs and PhD candidates to raise awareness of how technological know-how can be turned into business. In September 2015, the first Action Lab took place: five teams of researchers developed a business plan and presented the result to the management team. The winning team from Wageningen University presented a business case for their new technology to discover plant enzymes that can be used to produce natural flavours by fermentation. Their prize was €20,000 to further develop their ideas within their spin-off Radix Botanicals. Two other teams, MicroLife Solutions and DAB (Delft Advanced Biorenewables), each won an incentive prize of €10,000.

One participant, Bart Pieterse (Green Waste Support) explains: "The Action Lab was very valuable for me. Without the right focus, you can easily waste a year of research."

MOOC
In 2015, BE-Basic's Massive Open Online Course (MOOC) on 'Industrial Biotechnology' (formerly 'Technology for biobased products') was run for the second time through the EdX platform. In the MOOC, biotechnology, bioprocess design and sustainability assessment are integrated into 66 video lectures by course leaders from TU Delft and guest lectures from industry and UNICAMP. The second edition attracted about 10,000 participants – in line with the first edition in 2014. In total, 100 of the participants received an ID-verified certificate and 225 received a (free) honorary certificate.

Holland Biotech Pavilion in Montreal
BE-Basic again coordinated the Holland Biotech Pavilion at the BIO World Congress on Industrial Biotechnology, which took place in Montreal between July 19 and 22. It is the third time in a row that BE-Basic has overseen the coordination. The pavilion included 12 Dutch organisations and companies with a focus on biotechnology, biochemistry, energy, feedstock production, transport and logistics. The Holland Biotech Pavilion is financially supported by the Topsector Chemie via the Strategic Conferences Program coordinated by RVO.nl.

With more than 1,200 visitors from some 725 organisations from around the world, the congress was well attended and offered an excellent opportunity to explore mutual interests for international partnerships through one-on-one partnering meetings and network receptions. Furthermore, BE-Basic organised a partnering workshop to give Canadian and Dutch organisations an opportunity to pitch their business. The bike raffle, presented by Rochus Pronk, Deputy Head of Mission at the Dutch Embassy in Canada, was sponsored by the Rabobank and proved a great success.

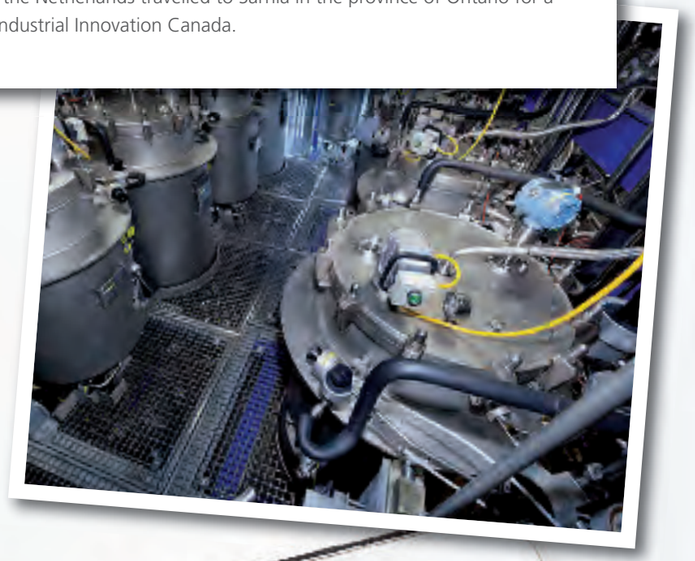
After the BIO World Congress, a delegation from the Netherlands travelled to Sarnia in the province of Ontario for a workshop and a company tour, organised by Bioindustrial Innovation Canada.

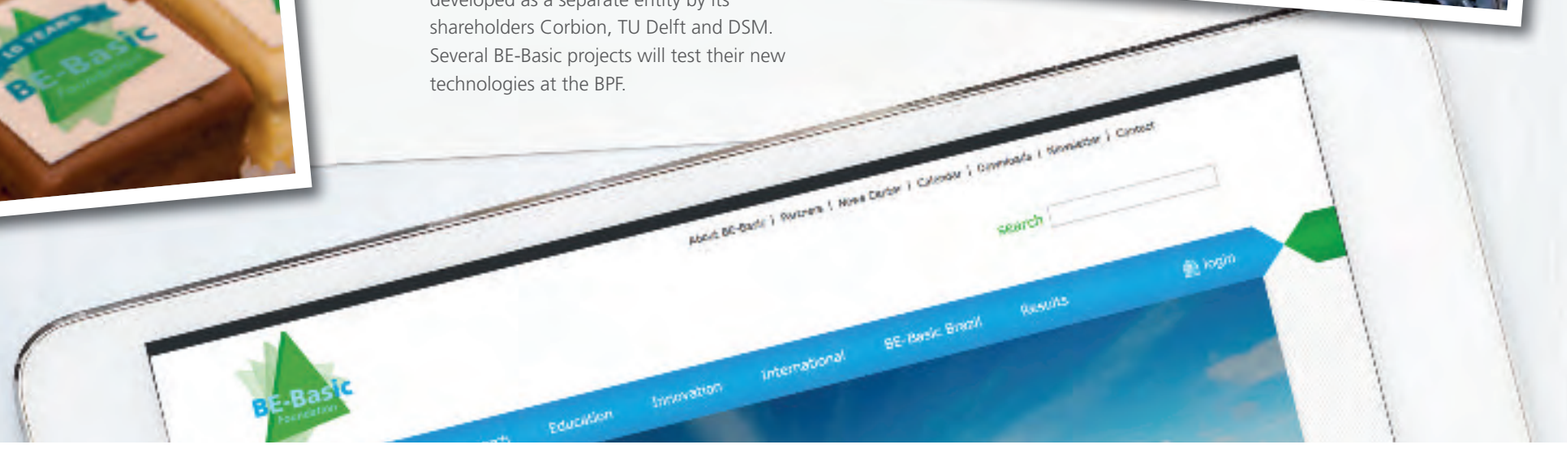
BE-Basic Annual Meeting
This year the BE-Basic Foundation celebrated its 10th anniversary. In recognition of this, a special edition of the public Annual Report with a video highlighting biobased product, process and company development over the last 10 years was launched at the annual general meeting. The event at the Leeuwenhorst conference centre in Noordwijkerhout, was attended by some 250 guests. It focused on the consortium's recent developments and on the next steps needed to implement biobased technology into society.

Guest speaker Erick Fernandes (World Bank) reflected on the rapidly growing world population and the increasing demand for meat, (bio)fuels, food and energy. Sean Simpson (LanzaTech) and Niels van Stralen (ChainCraft) focussed their presentations on how to bridge scientific knowledge and concrete entrepreneurship.

This year's winners of the Poster Pitch and Poster Award were Youri van Nuland and Willem Dijkman, respectively.

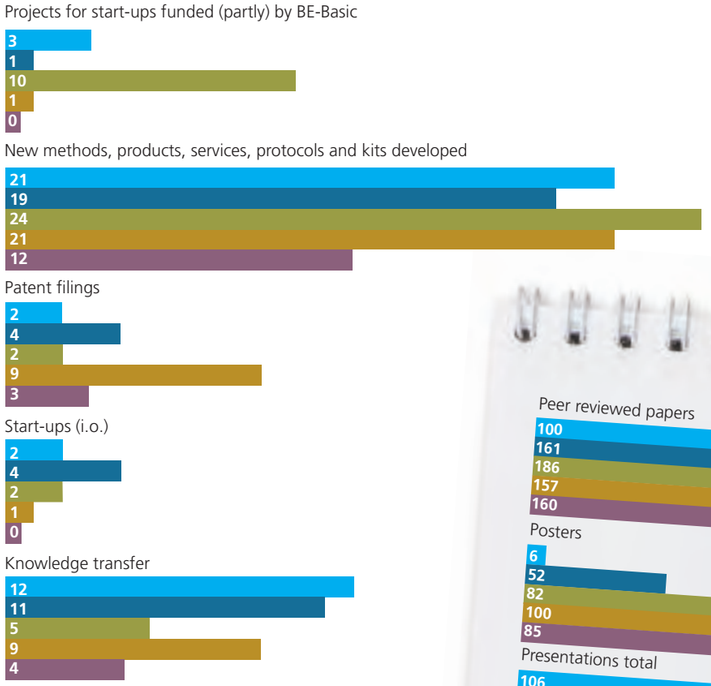
Bioprocess Pilot Facility opened
The Bioprocess Pilot Facility (BPF) was officially opened in March 2015. The BPF is a unique multi-purpose facility for bioprocesses. Universities, companies and institutions from all over the world can use this open access facility to investigate how production processes can be scaled up. The BPF is located at the Biotech Campus Delft and is allied with BE-Basic Foundation (see also Flagship 5). In the early plans, the pilot plant was part of the BE-Basic programme, but has since been developed as a separate entity by its shareholders Corbion, TU Delft and DSM. Several BE-Basic projects will test their new technologies at the BPF.



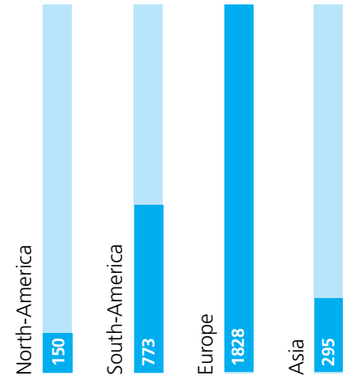


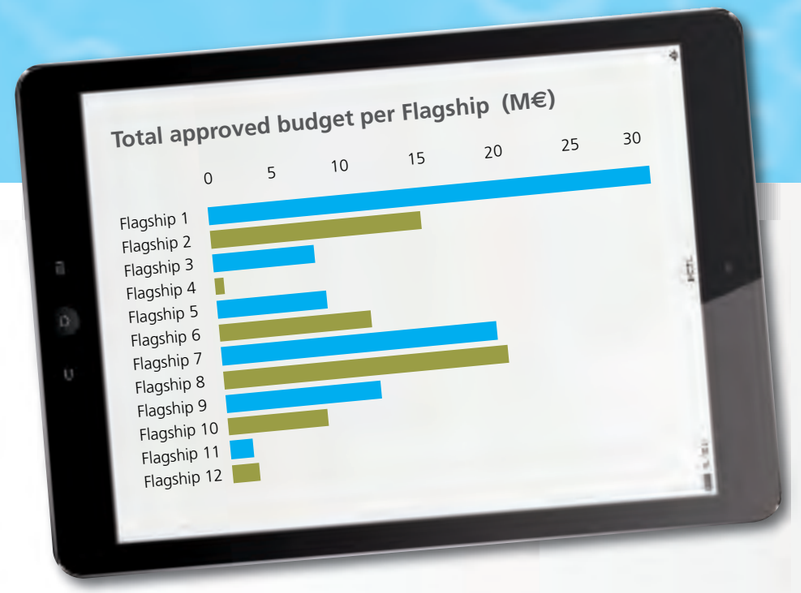
Facts and figures

Valorisation output



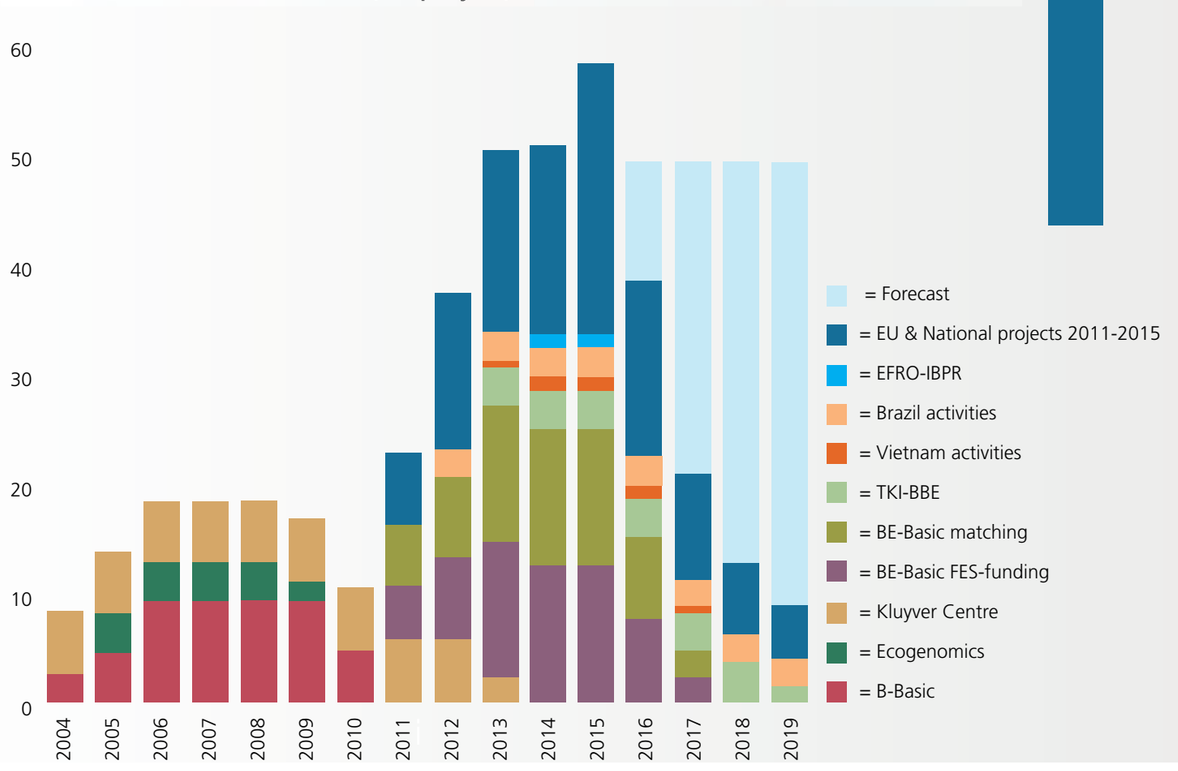
Participants international workshops (2010-2015)





Distribution of BE-Basic funds (%)

Size of different funds BE-Basic (M€ per year)



BE-Basic Foundation

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