

interACTS

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interACTS is the official newsletter of Advanced Chemical Technologies for Sustainability (ACTS)



New chairman Teun Graafland

Highlight: the ABC of penicillin production

Chemistry excels as key area

ACTS



Facing the Future

ACTS is currently considering its future. With several programmes drawing to a close over the next few years we need to consider which programmes can be continued and whether new programmes can join the ACTS portfolio. Another important question is how we define a programme's success with due consideration to the aspect of sustainability. And in a rapidly changing world, what should we be looking for in public-private partnerships? ACTS is developing a vision document that will answer these questions but will also consider the relationship with the Regiegroep Chemie (Steering Group Chemistry), which has been given a directive role by the government in such areas as PPP initiatives. Our new ACTS chair Teun Graafland, who like me is a member of Regiegroep Chemie, introduces himself in this issue of interACTS and sets out his vision for ACTS' future.

Besides ACTS' plans for the future, this issue also highlights a research project from one of the ACTS' programmes. After all ACTS' focus is on the fantastic research that takes place within its programmes. This time postdoc Andriy Kovalchuk tells us about the highly promising research he is carrying out within the B-Basic programme.

With our Executive Board back up to full strength I look forward to the future of ACTS with confidence and yet also a good dose of healthy tension. Our future depends on us doing our utmost to be the 'preferred partner for public private partnership'. And with your commitment and understanding I am confident that we shall achieve that goal.

Dr. Louis B.J. Vertegaal
DIRECTOR ACTS, NWO DIVISIONS FOR CHEMISTRY
AND THE PHYSICAL SCIENCES

The greatest challenge facing the new chair of the ACTS Executive Board, dr. Teun Graafland (55), is realising a robust structure for the cooperation between ACTS and the Regiegroep Chemie (Steering Group Chemistry). He has been a member of the Regiegroep for many years and wants to involve all relevant parties in this process.

Graafland has had a summer break to think about his next step. When he was invited to become chair of ACTS he had just become Manager European Science & Education Programmes at Shell. A large part of his time is devoted to the extramural research of Shell. The wealth of contacts he therefore has with universities and with colleagues from the private sector will prove very useful during his chairmanship of ACTS. Graafland has worked for Shell since 1981 and his links with ACTS also go back a long way. For example, he was involved in setting up the ASPECT programme for sustainable bulk chemistry.

Graafland gained his degree (cum laude) in physical organic chemistry from the University of Groningen where he later obtained his doctorate (cum laude) for his work on 'intramolecular carboxyl catalysed hydrolysis of sulphonamides', or in plain English: looking at factors that can speed up the chemical process. He has worked for Shell in Amsterdam, America, and Belgium and he is now located in The Hague. He describes himself as 'highly involved in exploratory research and having a lot of university contacts'. In the 1990s he helped to produce the catalysis roadmap.

Fireworks

His passion for chemistry developed during his high school days says Graafland. "I got into making my own fireworks. Firecrackers but also smoke bombs. We found the recipes in books and I can remember us shrouding the school in all different colours of smoke". He subsequently turned chemistry into his profession and is the owner of several patents, for example, polymers that swell up in water and which are used in baby's nappies and in synthetic rubbers. Shell is no longer involved in polymers and nowadays his work scarcely brings him into a laboratory. "I worked in a lab for years and some people even do it for their entire working lives. I much prefer using my chemistry outside of the lab and so being behind the bench is not something I miss. However, I still enter a lab occasionally and I also visit other companies on a regular basis albeit that such visits rarely entail a look in the labs".

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'I prefer to work with the consensus model'



Graafland is married and has a daughter aged 22 and a son aged 23. His daughter is studying history and his son medicine. "They should do what they enjoy", says Graafland. He is not disappointed that they did not choose a career in chemistry, even though he has spent a lot of time promoting chemistry in education. For example, during his years as coordinator of Jongeren en Technologie Netwerk Nederland (Dutch Network for Young People and Technology), Jet-Net, whilst at Shell. This became a five year break from research and development during which Graafland focussed on promoting chemistry in education. That fits in with one of the lines of action of Regiegroep Chemie, namely improving the image of chemistry in cooperation with the Association of the Dutch Chemical Industry and the private sector.

Consensus model

Graafland wants to be a chair who brings together the different parties involved in ACTS. He considers his greatest challenge to be providing a robust structure for the cooperation between Regiegroep Chemie and ACTS. "I want to involve all interested

parties in this process. I am somebody who believes in using the consensus model to get everyone on-board". He finds it difficult to say what he would do differently from his predecessor Colja Laane. "Cooperation with Regiegroep Chemie and determining the future of ACTS were not really part of Laane's remit", says Graafland.

ACTS is now facing an important period in its history. Some programmes will cease to receive funding in 2011 and if these are to continue then new funding will have to be obtained from the public and private sectors. Moreover, the success factors and sustainability of each of the five programmes will become clear. "Undoubtedly some of the programmes will not be continued. Then the question is 'what next?'" To answer this Graafland and the ACTS Executive Board are writing a vision document. This must clearly state who will be responsible for setting up new programmes, ACTS or Regiegroep Chemie. "Some of the initiatives shall come from the Regiegroep, not everything can come from ACTS, but plans could also be put forward by external parties. We should seek to support such initiatives", says Graafland. In his opinion, ACTS does not always have to hold the strings but can instead choose to support good ideas from other parties.

Just four months into his job Graafland is confident that he will complete his mission successfully. According to plan, he aims to implement ACTS' vision document over the next year. The document must clarify ACTS' new position with respect to the Regiegroep Chemie. After all, the Regiegroep is the leading party that determines policy and forms the first point of contact with the government. To realise his goal he is making use of his involvement in several initiatives from Regiegroep Chemie such as the Sector Plan Physics and Chemistry, his involvement with the public-private partnership via ACTS in the DSTI (Dutch Separation Technology Institute) and with the Centres for Open Chemical Innovation (COCIs) located in the vicinity of large industrial research complexes. He mentions Chemelot at DSM in Geleen as one example and New Energy Docks in Amsterdam, close to the Shell Technology Centre, as another.

Sports

Graafland, who at the time of the interview had just returned from a skiing holiday in Austria, is a keen sportsman with tennis, golf or jogging being his favourites. On top of that he sings in a choir and is an active member of the Rotary Club. In principle he has agreed to be chair for a year. In October he shall review the feasibility of continuing to combine both jobs with his employer, Shell. "To date it has been a busy period but also a challenging one. And I like that combination."



B-Basic highlight

The ABC of penicillin production

A semisynthetic antibiotic based on penicillin can be produced more efficiently than is currently the case. If researchers succeed in modifying the metabolism of the fungus *Penicillium chrysogenum* then a chemical step in the production process will become redundant. Yet to realise this goal the researchers need to know more about that metabolism. Postdoc Andriy Kovalchuk is therefore trying to map the ABC transport proteins of *P. chrysogenum*.

P. chrysogenum is used for the production of penicillin. Two types of penicillin, penicillin G and V, act as the building blocks for semisynthetic antibiotics. After the usual penicillin production process by means of fermentation a further chemical refinement takes place. Without this chemical step penicillins are no longer effective as many bacteria have now become resistant to them. Postdoc at the Microbiology Research Group of the University of Groningen Andriy Kovalchuk: "Manufacturers of semisynthetic antibiotics based on penicillin use organic solvents for that mechanical refinement. This method is expensive and incredibly energy intensive. Our aim is to integrate this chemical step into the metabolism of *P. chrysogenum*. Then the antibiotic can be produced using just the fermentation process."

Unfortunately we still know little about the metabolic processes that the fungus uses to produce penicillin. Kovalchuk: "For example, we need to know far more about the transport proteins that play a role in the metabolism of *P. chrysogenum*. My research focuses on identifying these proteins. In particular, I have set my sights on the class of ATP-binding cassette transporters, the so-called ABC transport proteins. These proteins are present in all organisms from bacteria and plants through to humans and animals. They play an important role in the excretion of substances."

Valuable

Several years ago, chemistry and biotech concern DSM unravelled the entire genome of the fungus in question. It published the genome sequence but divulged this knowledge in advance to the microbiologists at Groningen. DSM had already been cooperating with the research group for a long time. Kovalchuk: "It is quite unusual for us to be working with an industrial fungus type instead of a model organism. Industrial organisms are usually too close to the company's core technology to be released to outside parties."

Kovalchuk started his research by screening the genome of the fungus: "Using bioinformatic tools we identified the ABC proteins in *P. chrysogenum*. We know the function of some of these and in certain other cases we can make an educated guess. Yet there are still a lot of proteins for which we do not know the function yet." Kovalchuk used fluorescence microscopy to determine the location of various transport proteins. Kovalchuk: "The location of a protein in the cell says something about its function. The next step in the research was producing various mutant cells and examining how they affected the protein production." The purpose of this trial-and-error method is to bring the researchers a step closer to unravelling the proteins and their functions.

DSM already uses genetically modified fungi to produce cephalosporins. These are antibiotics that are chemically related to penicillin but which can also combat other infections. Cephalosporins are still only produced in Western countries. Kovalchuk: "Yet that is definitely not the case for semisynthetic penicillin. These are produced on such a large scale in China and India that European manufacturers have had to cease production over the last few decades. If we can contribute to a new, more efficient production process then Europe will be able to re-enter the race." Moreover a non-synthetic production would also improve the sustainability of the production process as the solvents currently used shall become redundant.

Arms race

Knowledge about ABC transport proteins in *P. chrysogenum* should eventually lead to a targeted modification to the metabolism of the fungus. Kovalchuk: "The fungus might well contain the proteins needed to carry out the chemical conversion. Another possibility is incorporating a gene from a different organism into the genome of the fungus."

The semisynthetic penicillin is not the only possibility for this research says Kovalchuk: "The more we know about the intracellular metabolism of the fungus, the more possibilities we have to modify it. We can probably use *P. chrysogenum* for the production of a wide range of materials."

To date Kovalchuk has not found any transport proteins that are involved in penicillin production: "With this type of research it is difficult to predict how quickly you will achieve your objective. This project has just six months to go. You never know, by that time we might have identified several ABC proteins. Yet on the other hand more research might be needed to realise this goal." There is a continuous arms race between bacteria and antibiotics says Kovalchuk: "One day we might devise a completely new way of controlling bacterial infections, but until that time we continuously need to develop new antibiotics. And that means we must continue to extend our knowledge about fungi such as *P. chrysogenum*."

News on the ACTS programmes



IBOS

The IBOS programme (Integration of Biosynthesis & Organic Synthesis) aims to realise a change of strategy in synthetic chemistry by integrating organic chemistry, modern biochemistry and biotechnology.

The 7th IBOS (closed) conference will be held on 1 and 2 October 2009 in Lunteren. During this conference Monique Quelle of Schering-Plough will organise a workshop on intellectual property. Professor Anton Glieder from Graz University of Technology (Austria) will give a guest lecture on molecular biotechnology. The research fields of prof. Glieder are protein engineering, heterologous yeast-based expression systems, directed evolution of enzymes and host systems, industrial biocatalysis, and yeast metabolic engineering.

Development of conditional protein-ligand exchange applied to immune technology

In this project the fields of (bio)organic synthesis and immunology merge with the aim of developing immune technology for diagnostic and therapeutic applications. Therefore, project leaders Huib Ovaa, Boris Rodenko (Chemical Biology, Netherlands Cancer Institute) and Ton Schumacher (Immune technology, Netherlands Cancer Institute) have joined forces with industrial partners Schering-Plough (Oss), Sanquin (Amsterdam) and Chiralix (Nijmegen). Enantioselective enzymatic reactions are used to synthesise chemocleavable amino acids that can be built into peptides. In turn, these 'conditional' peptide ligands can be triggered to dissociate from their binding partners by means of a chemical stimulus. This methodology can, for example, be used to generate intrinsically unstable, empty antigen-presenting proteins in situ. The researchers will be able to use the protein ligand exchange technology they have developed to screen libraries of drug-like small molecules to identify novel stabilisers of the antigen-presenting complex. Such molecules may function as selective immunosuppressives that can form the foundation for a novel class of pharmacological agents to treat autoimmune disease and solid organ transplant rejection.

ASPECT

The ASPECT programme focuses on enhancing the sustainability of catalytic chemical processes in bulk chemistry. Many of the 21 ASPECT projects presented their results at the 10th Netherlands Catalysis and Chemistry Conference that took place from 2 to 4 March 2009. Some of the results presented are highlighted below.

Gacia Boyadjian (Lefferts group, University of Twente) presented her results on catalytic oxi-cracking as a route to

olefins. Oxidative catalytic cracking of naphtha-range hydrocarbons is a conceptually promising alternative to steam cracking for the production of light olefins. Efforts in recent years to develop efficient oxidation catalysts have not shown any promise; the rates and selectivities achieved are not enough for commercialisation. Recent work has demonstrated that sol-gel synthesised, Li-promoted magnesia (Li/MgO) are promising catalysts for the oxidative conversion of propane to propylene. The authors have now shown that promoting Li/MgO with a 5% monolayer coverage of Mo oxide leads to an increase in hexane conversions while maintaining good selectivities for olefins. Higher olefin yields were therefore achieved. Further, with the addition of the promoter, improved stability of the catalyst was observed.

Andrei Parvulescu (Weckhuysen group, Utrecht University) reported high catalytic activity for the telomerisation of 1,3-butadienes with different diols using the Pd/TOMPP catalyst. Polyols and diols recently attracted considerable interest due to their high availability from bio-based sources and from bio-diesel production. Telomerisation of 1,3-butadiene with nucleophiles produces useful intermediates for fine and bulk chemistry and - in the case of polyols - compounds with interesting applications, like surfactants, could be produced.

Bart Hamers (Vogt group, Eindhoven University of Technology) studied hydroaminomethylation (HAM) – a transition metal catalysed cascade reaction, leading to a linear amine product. The more successful ligands in this perspective are xantphos and its derivatives. Recently, the group demonstrated efficient catalyst recovery combined with excellent activity and selectivity when the reaction was carried out in ionic liquids. The authors have now shown that activity can be improved by modifying the xanthene backbone of the ligand with several amino-functionalised phosphines as this improves the pi acceptor character. These ligands showed high activities and regioselectivities were generally very good at 99% conversion of the substrate.

Sustainable Hydrogen

The Sustainable Hydrogen Programme aims to develop the knowledge and technology concepts needed to facilitate the transition from fossil fuels to renewable sources (clean fuel). For further information see: www.nwo.nl/acts/hz

One of the ten projects in the first phase of the Sustainable Hydrogen programme is "Pure hydrogen production out of biomass-derived fuel". This project is a collaboration between Biomass Conversion Technology group (headed by prof. W.P.M. van Swaaij and prof. H.J. Veringa) and Catalytic



Processes and Materials (headed by prof. L. Lefferts) of the University of Twente. This project is divided into two parts. The first part involves the production of pure hydrogen from biomass-derived pyrolysis oil, based on a cycle including oxidation of a catalyst (iron/nickel/molybdenum) with steam and its reduction with pyrolysis oil. This part of the project is being carried out by Mariken Bleeker. The second part focuses on the steam reforming of biomass-derived pyrolysis oil for hydrogen production. Two PhD students are working on this part of the project: Guus van Rossum is working on optimising the steam reforming process and Berta Matas Güell is developing new catalysts for such process.

New catalysts

Berta Matas Güell showed the latest results of her research in a poster presentation at the 10th NCCC conference in March. She reported on the steam reforming of acetic acid (major model compound in pyrolysis oil) over Platinum-based catalysts (Pt/ZrO₂ and Pt/CeO₂). She observed that the Pt/ZrO₂-catalyst was active but it deactivated rapidly due to coking. Pt/CeO₂ had a better catalytic performance than Pt/ZrO₂ in terms of catalyst stability. This can be explained by (i) Pt/CeO₂ shows excellent activity and stability of a main coke precursor (acetone) and (ii) coke deposition over Pt/ZrO₂ occurred to lesser extent. Unfortunately, Pt/CeO₂ still suffered from deactivation. However, small additions of oxygen in the steam reforming feed resulted in no deactivation of Pt/CeO₂ on the steam reforming of acetic acid. She concluded that the combination of small amounts of oxygen and catalysts with redox properties are key aspects of the excellent catalytic performance of Pt/CeO₂. She suggests the use of Pt/CeO₂ catalyst for the steam reforming of more complex biomass-derived oxygenates.

PoaC

The PoaC programme (Process on a Chip) aims to support new topological concepts that are being developed for the initiation of novel production processes in the areas of food technology, chemistry and life sciences. For further information see www.nwo.nl/acts/poac.

The PoaC programme held its third closed symposium on 30 and 31 March 2009. On the first day of the symposium a discussion was held about the future of PoaC in its second phase. On the second day PhD students presented and discussed their results with other researchers and experts from industry.

One of the six projects in the first phase of the PoaC programme is "Multi-Phase Microreactors as a basis for Process Intensification", a Delft University of Technology

collaboration between dr. Guido Mul from Catalysis Engineering and prof. Michiel Kreutzer from Product and Process Engineering. In this project, a microreactor integrated with attenuated total reflection IR spectroscopy is being developed for operando transient studies of multi-phase catalytic systems. Several tools for transient analysis of gas-phase catalytic systems are already available, but such tools are still missing for gas-liquid and liquid systems. A key hurdle in liquid-phase transient analysis is the long diffusion time. Miniaturised channels, combined with segmented flow and on-chip liquid pulse generation will ensure that diffusional effects do not dominate the transient signals, thus allowing excellent control of the conditions the catalyst is exposed to. It is expected that the device developed will provide a better understanding of how the catalytic systems work, which will allow optimal use of current catalysts and improved design of next-generation catalysts.

B-Basic

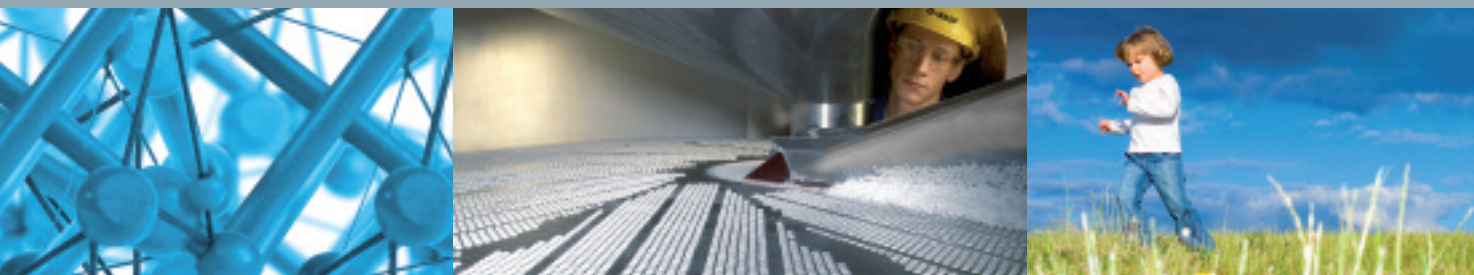
B-Basic (Bio-based Sustainable Industrial Chemistry) is an NWO-ACTS research consortium in which Dutch Universities, research institutes and industry are working together on the development of new biobased production concepts for the chemical and energy industry. For further information see www.b-basic.nl.

B-Basic will establish a Global Network on Bioenergy Science (GNBES). This was decided on 15 November 2008 during a transatlantic EU-US workshop on bioenergy in Chicago. GNBES will serve as a global scientific network of bioenergy research centres to provide insights in what drives and restricts the development of the biobased economy worldwide. By combining scientific excellence across a broad set of disciplines and involving developing countries as well, the network wants to focus on a long-term agenda for governments and science foundations. The launch workshop of GNBES will take place from 17-19 May 2009 in Lisbon. See also: www.ethanolproducer.com/article.jsp?article_id=5087

Bio-based Innovation

As of 2009, B-basic has opened up its Leo Petrus Innovation Trophy for people outside of B-Basic. Anybody with an idea for a green (bio-based) raw material, process or product can submit an entry and compete for the award of 100,000 euros. On 12 December 2008 the launch workshop was held at the WTC Rotterdam, in collaboration with students of the Rotterdam School of Management (RSM). In the morning different points of view on innovation were presented by RSM (Wietze vd Aa) and Shell (Peter Lednor). In the





afternoon George Brouwer spoke about innovation at the Rotterdam Climate Initiative and last year's LPIT winner Wouter van der Star from Deltares told the participants about his experiences with the Leo Petrus Innovation Trophy. At the end of the day small groups of participants, assisted by RSM students, explored the business potential of their ideas. In the second workshop, held on 19 March 2009, several ideas were presented by the teams that had submitted a preproposal. In teams with RSM students, participants elaborated on the ideas and worked on their elevator pitch. The teams then had a few more weeks to further elaborate their idea into a final proposal. The deadline for submission of the final proposal was 15 April 2009.

For more information: www.lpit.nl.

BE-Basic

From 2010 onwards, B-Basic and the Ecogenomics consortium will continue as one public-private partnership under the name BE-Basic: Biobased Ecologically Balanced Sustainable Industrial Chemistry. BE-Basic will build on the proven breakthroughs of both consortia and will include a pilot plant facility and a socioeconomic programme.

ACENET

The ACENET ERA-NET (Applied Catalysis European Network) has been set up with the aim of improving the structure and enhancing the coordination and cooperation between eleven national funding and research management organisations in ten European countries, who are involved with research programmes in the European research area of Applied Catalysis and related sustainable chemical research.

For further information see: www.acenet.net

Initially, ACENET would run till the end of August 2008. However, the European Commission has approved a request from ACENET to prolong its collaboration between the ACENET partners for two more years. No additional funding will be received, but the original granted budget will be sufficient for this prolongation period. In the final two years ACENET will focus on the evaluation of the management and assessment procedures of the first call. Furthermore, the ACENET partners aim to organise a second call for transnational research projects. However, time constraints and a limitation on funding commitments in the current economic situation might make this a real challenge.

Other focus activities for the coming years are related to the network's education programme. From 24 to 29 May 2009,

the Summer School in Catalysis "Catalysis Lectures for Environmental Applications and Renewables (CLEAR)" will be organised in Greece. Please see the website www.clear.certh.gr for more information.

Finally, ACENET will work on a joint roadmapping initiative aimed at further strengthening the collaboration between the national ministries and funding agencies, even after the prolonged operating period of the ACENET project has expired.

ERA-IB

Nineteen research organisations from thirteen European countries have joined forces to form the ERA Industrial Biotechnology network (ERA-IB). This cooperation aims to harmonise the currently fragmented national research policies, to implement a joint strategy, and to coordinate new transnational research programmes in the area of industrial biotechnology. ACTS is one of the founders of ERA-IB and is also the coordinator of the network. For further information see: www.era-ib.net

Eight transnational research projects within the ERA-IB first joint call for proposals have recently been honoured. The theme of the call was 'Industrial biotechnology for Europe: an integrated approach'. In all, 51 research groups in academia and industry were funded, and an additional 7 partners will fund their own work. ACTS, together with the Netherlands Genomics Initiative (NGI), was able to fund the research of four Dutch academic research groups in the ERA-IB projects. A total of five projects have partners from the Netherlands. These are listed in the section of ACTS Allocations. The call was funded by organisations from the Netherlands, Spain, France, Portugal, Poland, Denmark, Belgium, Finland, Germany and the German federal state of Saxony. The participating ERA-IB funding organisations allocated a total of M€ 9.7 to the eight projects.

On 28 April 2009 ERA-IB held a launch meeting for the projects honoured in Helsinki, Finland. During that meeting all honoured projects gave a presentation and the participants had the opportunity to meet the ERA-IB organisation and each other and thus to enhance their network. On 29 April 2009 the participants were invited to attend the satellite meeting SymBio – Industrial Biotechnology and BioRefine programmes Networking Day, which was being organised by the Finnish Funding Organisation for Technology and Innovation, Tekes.

Articles

IBOS

- Doctoral Thesis, 6 maart 2009, Suzanne Wolterink-van Loo: 'Synthesizing Nitrogen-heterocycles in biosynthetic routes' (Wageningen University and Research Centre). Promotoren: Prof. dr. John van der Oost, Prof. dr. Willem de Vos



ASPECT

- P.O. Graf and L. Lefferts; 'Reactive separation of ethylene from the effluent gas of methane oxidative coupling via alkylation of benzene to ethylbenzene on ZSM-5'; *Chemical Engineering Science*, in press
- Doctoral thesis, 23 January 2009, P.O. Graf: 'Combining oxidative coupling and reforming of methane Vision or Utopia?' (Twente University)

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- Doctoral thesis, 31 maart 2009, P. Vermeulen: 'Hydrogen storage in Mg-Ti thin film alloys. An in situ characterization study' (Eindhoven University of Technology)

PoaC

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ACTS Allocations

IBOS

SME-projects 4th tender

Prof. dr. ir. M.W. Fraaije (RUG)
A biotechnological process for the production of (+)-carvone

Dr. ir. L.H. de Graaff (WUR)
Novel laccases and their enhanced expression in *Aspergillus niger*

SPS – Bilateral Joint Seminar

4th Gratama workshop 'Sustainability in chemistry, chemical technology and biotechnology'
Professor dr. I.W.C.E. Arends (TUD)

agenda

28 April 2009

ERA-IB

ERA-IB (closed) Kick-off meeting for granted projects of the 1st call for proposals in Helsinki

24-29 May 2009

ACENET

Summer School in Catalysis 2009 "Catalysis Lectures for Environmental Applications and Renewables (CLEAR)" in Greece.

4 June 2009

ERA-IB

ERA-IB 2nd Platform meeting of Industrial Biotechnology related ERA-Nets (closed), Dresden

13-16 September 2009

GRATAMA

4th Gratama Workshop "Sustainability in Chemistry, chemical technology and biotechnology" (TU Delft).

30 September-1 October 2009

ASPECT

8th ASPECT (closed) conference
At the confidential ASPECT programme meetings, all Ph.D students and postdocs present their progress and discuss their results with other researchers and experts from industry.

1-2 October 2009

IBOS

7th IBOS (closed) conference (conference resort "De Werelt", Lunteren), including IP workshop Schering-Plough

4-5 November 2009

Sust. Hydrogen

6th Sustainable Hydrogen (closed) conference (conference resort De Reehorst, Ede).



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