Summary of the Plenary Sessions

Sixth Annual World Congress on Industrial Biotechnology and Bioprocessing

Linking Biotechnology, Chemistry and Agriculture to Create New Value Chains

Montreal, Canada, July 19–22, 2009

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Not for Sale

Preface and Acknowledgments

Under the leadership and guidance of Brent Erickson [Biotechnology Industry Organization (BIO)] the *Sixth Annual World Congress on Industrial Biotechnology and Bioprocessing* convened in Montreal, Canada, July 19-21, 2009, with organizational input from the American Chemical Society (ACS), the National Agricultural Biotechnology Council, BIOTECanada, and the province of Quebec. Some 200 presentations were made in six plenary and six parallel "break-out" sessions; sixty presentations were made as posters, and three workshops were held. There were 1,100 attendees.

The organizers are grateful to the following supporting organizations, CIC, EuropaBio, GreenPower, OCRI, the Russian Biofuels Association, and the Russian Society of Biotechnologists, to their media partners, *Biofuels Digest*, *BiobasedNews.com*, *Canadian Biomass*, *F+L Asia*, *Industrial Biotechnology*, *Industrial Biotech Innovation* and *Garbrook Knowledge Resources*, and to the many conference sponsors.

Particular thanks are due to the program committee for their hard work and dedication in screening submissions, locating speakers and organizing an excellent program: Georg Anderl, Roland Andersson, Stan Blade, Rich Burlingame, Bruce Dale, Allen Dines, Larry Drumm, Raymond Drymalski, Steve Eury, Steve Fabijanski, John Finley, Caroline Fritz, John Frost, Randy Goodfellow, Kevin Grey, Richard Gross, Jack Grushcow, Ralph Hardy, Richard Howlett, Serge Huppe, Jack Huttner, David Hyndman, James Iademarco, Bob Ingratta, John Kabel, Birgit Kamm, Ron Kehrig, Manoj Kumar, Mike Ladisch, James Lalonde, Sophie Laurie, Dave Lee, Gerson Santos Leon, Eric Mathur, Blaine Metting, Jim Millis, Ramani Narayan, Glenn Nedwin, Erin O'Driscoll, Stephen O'Leary, Adrien Pilon, David Poon, William Provine, John Ranieri, Maria Rapoza, Anna Rath, Manfred Ringpfeil, Kareen Saad, Christophe Schilling, Nathan Schock, Philip Schwab, Garrett Screws, James Seiber, Andy Shafer, James Stoppert, Mark Stowers, Spencer Swayze, Joy Titus-Young, Brian Tockman, David Turner, Larry Walker, David Ward, Roger Wyse, Corinne Young, James Zhang and Paul Zorner.

The unflagging efforts and careful organizational oversight of Matthew Carr, Amy Ehlers, Jocelyn Modine, Courtney Murray and Kimberly Scherr (all of BIO) were vital to the success of the conference.

This *Summary of the Plenary Sessions* provides broad coverage of the plenary presentations. Thanks are due to Susanne Lipari (NABC) for her excellent page-layout/design work.

Allan Eaglesham
Executive Director, NABC
Summary Editor
November, 2009

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How Can Industrial Biotechnology Thrive in the Current Global Economy?

Moderator: Bill Caesar (McKinsey & Company)

Panelists: Stephen Gatto (Myriant), K'Lynne Johnson (Elevance Renewable Sciences), Christophe Schilling (Genomatica), Alan Shaw (Codexis), Marc Verbruggen (NatureWorks)[1]

Bill Caesar opened with an apology for being less optimistic than some bankers. At McKinsey, he and his colleagues see four scenarios for how the economy will play out over the next two or three years: it could be bad, or it could be very bad. "Battered but resilient" and "stalled globalization," are what 75% of corporate executives believe are most likely, ranging from a severe global recession to a very severe global recession. Over the next four to five years, GDP levels will fall precipitously. Declines from peak GDP levels in the United States will be between 5.6 and 7.5%; return to peak levels will occur in late 2011 or later. For a period of 18 to 24 months, we will struggle to return to the GDP levels seen in mid-2008.

A significant slowdown in venture-capital activity is occurring. Money is still being spent, but not nearly at recent levels. Possibly related to funding issues, patent-filing activity is also slowing.

Although the industry may, at this time, feel resilient, there is reason to believe that funding issues will have a significant impact over the next couple of years.

The good news is that the key drivers—which brought us into this industry in the first place, have kept us here and have allowed some, even at this early date, to make money—are still there. The economics of biobased industries are expected to improve as petroleum prices recover; it may take a couple of years, but the long-term expectation is that expensive oil will return. Also, there is growing popular demand for green solutions, because of carbon taxes and increasing environmental awareness. He suggested that the desire to reduce dependence on foreign oil by governments will continue, whether it is being used to produce transportation fuel or something else. And lastly, the agriculture and biomass lobbies remain vocal.

These drivers are applicable as much for biochemicals as for biofuels and will prevail through the recession and beyond. The challenge is in terms of how we manage ourselves through this difficult period.

Caesar initiated the discussion by asking the panel of CEOs, "How are you dealing with the current economy? What has changed in your business? What's different from a year ago?"

Stephen Gatto suggested that the big issue is capital investment. There will be a weaning out of venture capitalists who made extraordinary levels of investment over the past few years with extraordinarily high multiples. VC companies that had cash for six to twelve months will have to go back to the marketplace, which will put more pressure on the existing base and make it more and more difficult.

K'Lynne Johnson didn't know of any companies, small or large, that had not been affected by capital shortage. Nevertheless, she saw emerging opportunities, from government stimulus funding, for example.

Christophe Schilling said that the current environment was a particular challenge to small companies. Restricted access to capital is affecting small businesses like his. They are focusing on advanced programs that are nearest to market. On the other hand, he agreed that this environment holds opportunities. As Bill Caesar mentioned, the key drivers that led to new company formation are still there, and that's

[1] The panellists wore lapel microphones with less-than-optimal audio delivery. Although every effort has been expended to provide comprehensive representation of their comments, some content has been, by necessity, deleted and some may have been misunderstood.

where the focus, the drive, and the optimism have to come from. The fittest will survive, provided there is confidence in the technologies and the products.

Alan Shaw expressed concern at the slowdown in VC activity mentioned by Caesar, and suggested that it resulted not solely because of the economic downturn, but also because the VC model is broken. It is broken, he suggested, because back-end capital investments are so high in this space that it's unlikely that a VC investor will see returns, by the time they have diluted out all the stock over a million times to build a single biorefinery. Their only hope is that someone with deep pockets buys the company and saves them from the undesirable end-game. Since VC is great for innovation, he is concerned that loss of innovation will result, and that rapid consolidation will result from lack of financing. People with deep pockets will be able to buy out companies that need money. He sees parallels with the biotech boom of the 1990s.

The situation at NatureWorks is different, suggested **Marc Verbruggen**, because they have assets in place. They actually doubled capacity during the economic downturn—interesting timing. Their biggest issue over the previous 12 months was markets. In December 2008 and January 2009, their competition, the traditional platforms, saw tremendous decreases in pricing, more than the decrease in oil. On top of that came the credit crisis. Thankfully, these occurred over a relatively short period of time. Their second quarter for 2009 was better than that for 2008, and next December and January are looking good.

Bill Caesar: What will be the roles of big petrochemical, big oil and big ag in this space?

K'Lynne Johnson envisions emergence of more partnerships and collaborations with such companies. These companies understand the market thoroughly, and, at this time, they have a lot more money than many others. Ultimately this space will look like biotech in the pharma world where there was back and forth between innovation in smaller companies, a period of maturation, then commercialization being handed off to, or completed in partnership with, larger companies.

Although Genomatica is at an earlier stage of development than Elevance, **Christophe Schilling** agreed with K'Lynne Johnson that partnerships with larger companies are critical, in order to bring the technology they are developing to the market place. Regarding VC challenges, his company will look at whether exit strategies will be similar to those during the biotech boom. Typically, VC investors in a drug-development company will not hang around until the drug is on the market. We will see new trends in this space and it's up to us to develop examples to show what that model looks like to attract investment.

Marc Verbruggen made the observation that although biopolymers will be produced on a scale less than biofuels, the future market of 15 billion pounds globally will require dozens of NatureWorks and investment of billions of dollars to get there. He expressed difficulty in figuring out who will put up that capital other than big oil or big agriculture.

Stephen Gatto suggested that a distinction should be drawn between industrial biotech and traditional biotech. The former requires a tremendous amount of capital in the bank. Additionally, partnering becomes critical for vertical integration of existing processes, also partnering with companies interested in downstream profits is needed.

Alan Shaw stated that Codexis's relationship with Royal Dutch Shell would be three years old in October of 2009. He expressed satisfaction that maturity has come into this industry, and, three years on, others are forging similar deals. Their program with Shell is huge, and they may be first to market. A product of that will be massive, multi-billion-dollar biorefineries around the world. Codexis won't build them. Shell will. These biorefineries will produce the cheapest source of sugar, which will be converted into multiple fuels. Many companies can leverage that situation to their advantage. Shaw believes that this industry is maturing. Difficult years lie ahead, but we need to talk to each other more than we ever did. Egos will have to be buried and some CEOs will lose their positions, but our technologies will survive and shareholders will see returns. By consolidation, we will get our technologies and products to market. The industry will be driven and the infrastructure built by big oil and big ag, and we can all take advantage of that.

Bill Caesar: What role do you see governments playing in how this industry evolves?

Christophe Schilling sees opportunities to leverage government funds. But he cautioned that long-term business plans should not be built around government policies. Business models must make sense without the requirement of government intervention as subsidies, cap and trade, *etc*. As a small company, they are looking to commercialize products in three to five years; the question is, what will production costs be at that point?

Marc Verbruggen suggested that because customers demand cost competitiveness, whether by cap and trade, grants or tax credits, the government may help a company to take the first step from the economy-of-scale point of view and ensure survival. Without that first step, competing in the marketplace may not be achieved.

One of the areas in which **Alan Shaw**'s company has entered a public/private partnership is climate change. Achieving objectives will take years of investment. They are committed to it, because if they fail the world we bequeath won't be worth living in. Most intellectuals get it, as do most industry leaders. The government has a very important role to play, particularly in something that is ten years out.

Those developing technologies and trying to launch businesses often find themselves—said **Stephen Gatto**—in the "valley of death," having made significant investments, but not yet having bridged the gap into commercialization. Thinking again about industrial biotech versus traditional biotech, hundreds of millions of dollars are needed in investment, and government must play a role in creating impetus for making that investment, with grant programs. Also, loan guarantees can derisk investments that have to be made. We talk in terms of the government being here today and gone tomorrow, but Gatto suggested that there has been a sea-change in current policy. Certainly cap and trade will not only affect the chemical industry as a whole but our lives. More importantly, government needs sustained policies so that we do not lose sight of the fact that this will be a continuing environment requiring innovation. We must cover all aspects of the capital spectrum. The Departments of Energy and Agriculture have helped companies emerge from the "valley of death" by bringing hard capital to the market, and by effectively allowing those of us who have a clear path to commercializing products that did not require subsidy but for derisking access to capital. Government will continue to play a major role.

For many of the emerging technologies, particularly those nearing commercialization, **K'Lynne Johnson** emphasized the importance of regulatory policies. Understanding sustainability, the balance between food and fuel, carbon taxes, *etc*., are new issues for government. These will be increasingly important issues, with impact for industry. While we are figuring out how to pay for the next round of investments we will also be figuring out how to cope with a complex set of policy and regulatory requirements that may change from year to year as government viewpoint stabilizes.

Bill Caesar: How will concerns over intellectual property affect this industry? How important are small companies to creating innovation that large companies later put to use?

Alan Shaw stated that small companies in general have little cash. On the other hand, intellectual property is the one thing they have going for them, whereas IP is often what large companies lack. Working for a large chemical company for seventeen years, it wasn't his job to invest in intellectual property; his job was to find small companies for purchase. The problem is that the model is broken, because if you are too small you cannot invest in getting proper IP coverage in the first place. If you haven't run enough experiments and don't have the appropriate claim coverage, then your IP can be worthless and you may not realize it until it's too late. This critical aspect brought Shaw back to the issue of consolidation. Many of us are doing great stuff but, it may not be worth having. If a small company has thirty patents, half of them may not be worth having because they weren't prepared by the right IP agents; they weren't being paid the going rate of $600 per day, because the company couldn't afford it. Major companies respect IP; it's the one thing that should be fully invested in.

Approaching this from a different perspective, **Marc Verbruggen** stated that he has seen what he calls "anti-patents." Sometimes the whole value chain has to be in place to successfully bring a product to market, and the last thing they need is for progress to be blocked by companies sitting on patents, preventing NatureWorks, or one of their customers, from going to market, ultimately slowing technology adoption.

Freedom to operate is crucial for any company in this space, **Stephen Gatto** suggested. Protection of IP is vital. The number of patents being filed is rapidly increasing and sometimes it's hard to ascertain who possesses what. The situation is complex and a consolidation may be needed over the next three to five years. The issue is not just about freedom to operate. IP is a benchmark. It's about making sure that you can make your products, day in a day out, inexpensively, while addressing any volatility issues. An integrated approach is necessary. There are toolkit players versus integrated players. New players are coming to the market every week with new toolkits. Negotiating that minefield and being assured that you have a robust set of patents or IP—and freedom to operate—are critical. Gatto opined that a significant shakedown will occur within a few years.

For an emerging company, IP is, albeit important, just one source of competitive advantage, suggested **K'Lynne Johnson.** Filing a global patent is extremely expensive, and the trade-off that is made is often in terms of being broader. This sets up the eventual need for partnerships and collaborations to strengthen the claim, and to build in preparation for the next generation of counter claims. Johnson said that she anticipates fewer claims followed by a wave of fast-followers indentifying where they can make money by filling holes.

Christophe Schilling expressed the view that the biotech industry's value lies in its IP. For small companies in this space, IP is of considerable value. Genomatica spends more money on protecting their IP than do most companies of similar size; their technology platform allows this.

Bill Caesar: What will this group be talking about in five years, after the recession is over?

Marc Verbruggen suggested that if we get high oil prices on a sustained basis, biopolymers will become more and more important. Biopolymers will be about 5% to 10% of the plastics market, not just in North America, but globally. The preventive scenario will be oil remaining at $40 per barrel for the foreseeable future. It's very important to get oil back up to $80 to $100 per barrel.

Stephen Gatto said that, at Myriant, they have already commercialized their first products with a partnership signed with PURAC, very much in the same space as NatureWorks—plastics. Launching of their second product is slated for the first quarter of 2010. With the drive towards cheap sugar platforms will come vertical integration. Multi-cut refineries worked for the oil industry because it diversified the revenue platform, and Gatto shares the belief that to be successful in this space, similar diversification will be needed. Many of the players can be "agnostic" regarding the source of cheap sugar, whether it's from corn or cane or cellulose. It's advantageous to have a diversity of raw-material inputs that lead to the same fundamental outputs. It's more important today to focus on chemical intermediates as building blocks, because in that space market-generated revenues are possible, rather than coming up with a new molecule for which a market has to be found. That distinction will yield successes in this space that are essential to all involved, whether it's access to capital or acceptance by the consumer. The products have to be cost-effective, not relying on subsidies. They have to be able to compete when oil is at $50 per barrel. Otherwise, the capital markets will not be accessible. Gatto expressed optimism regarding the next five years.

K'Lynne Johnson predicted two major trends. First, the initial wave of these technologies will be commercialized by companies like Elevance. Some advanced fuels will come to scale within 5 years. Secondly, after early consolidation, greater diversification and proliferation of technologies will occur. Major countries that are not yet "playing" in this space will begin to participate as the realities and drivers strengthen.

Over the next 2 to 3 years, **Christophe Schilling** expects to see many more products moving towards commercialization and some will go onto the market. On the other hand, mere commercialization will be insufficient. Truly transformative breakthrough technologies will be needed to deliver value to shareholders. This will require the partnerships that have been talked about, with large companies getting involved. Current challenges—such as access to capital and oil price—may be mitigated by a couple of blockbuster breakthroughs demonstrating how to make money in this space.

Alan Shaw said that the next 5 years will be more exciting than the past 5 years. He expressed confidence that oil would return to more than $100 per barrel within this timeframe. Within the next couple of years, he predicted that the current US administration will shape the landscape. The macro-economic and geopolitical backdrops are positive. Within 5 years, Codexis's partner, Royal Dutch Shell, will be in the market with commercial-scale, next-generation fuels. Biogasoline as well as biodiesel will contribute within 5 years. This will be hugely important; instead of electric cars, we can focus on maintaining the current infrastructure which will be much less expensive. The next-generation fuel will be the blockbuster that Christophe Schilling asked for, because, then, the government will believe us. Despite the recession, the entrepreneurial strength in North America will develop markets for new products.

Sustainability Issues in Biofuels Production

Moderator: John Sheehan (Institute on the Environment)

Joseph Skurla (DuPont Danisco Cellulosic Ethanol),

Lars Hansen (Novozymes North America),

Jacques Beaudry-Losique (Department of Energy), Lee Lynd (Dartmouth College)

John Sheehan reminded the audience that it was the fortieth anniversary of the moon landing, which not only refocused attention back to planet Earth and the reason for involvement in biofuels, but it also served as a reminder of what can be achieved through technology when we put our minds to it.

Joseph Skurla said that we are on the verge of commercializing a technology that has been worked on for several decades. In Washington are an administration and Congress that are committed to the emergence of a low-carbon economy. Everyone is watching us and expectations are high. There are many good policy initiatives and there is much special-interest-group competition. With change comes opportunity.

DuPont Danisco Cellulosic Ethanol (DDCE) was founded in 2008 to create a completely integrated, robust, low-cost biochemical solution to the cellulosic-ethanol market, uniting technologies provided by the parent companies. Initially, corn cobs and switchgrass will serve as feedstocks, which offer a market potential of 20 billion gallons of ethanol per year in the United States. Progress has ben excellent. Construction of a demonstration plant in Vonore, Tennessee—in conjunction the University of Tennessee's Genera Energy, LLC—is on schedule and budget, and expected to be in production by the end of 2009.

Progress is also being made in achieving commercially viable economics in the production of cellulosic ethanol. Skurla predicted that the technical hurdles to cost-effective cellulosic ethanol will be overcome, and the signs of a vibrant and strategically important industry are now in view.

When they were struggling to scale up from laboratory production, many anticipated the successful transition from R&D to full deployment. After that initial enthusiasm, people started to analyze the risks associated with a fully realized biobased economy. Most attendees at this conference have a strong belief that the science of genetics, rational agricultural and land-use policies, and constantly improved agronomics will enable a steady-state supply of food, fiber and fuel for the growing needs of society; however, this is not obvious to all of the stakeholders. We must expect that everyone with an interest in land and environmental stewardship will be intensely interested in what we do, and how we do it. How do we manage this intense interest? First and foremost, Skurla suggested, we need to deliver technologies that reach for the highest standards of environmental performance, best practices, life-cycle assessment and sustainability management. Also, we need to engage our fellow citizens through on-going conversations with policymakers, the media, and, most importantly, our critics. And we need to realize that, unlike the incumbent industry that we mean to join, our industry is emerging in an age of widespread awareness of climate change, social justice and concern over politicized science.

With regard to reaching for the highest standards of environmental performance, DDCE has several life-cycle assessment (LCA) experts who work with the technical team doing real-time LCA modeling of design options. Based on data generated in a DuPont study that was funded by the US Department of Energy, they know that an 80% reduction in greenhouse gases in emissions—versus gasoline—is possible. They intend to solicit issues of concern from stakeholders and engage them in on-going discussions on appropriate means of response. With that in hand, they will consider the metrics, set their goals and monitor their progress towards meeting them.

This industry needs to be seen as progressive, not just in terms of profit but how profit is made. For example, we should be at the forefront of implementing industrial ecology. This well regarded view of pollution-prevention uses an ecosystem as a metaphor for industrial sustainability. In simplest terms, it is exemplified by an industrial park where the byproduct of one producer is the feeedstock for another; the field of industrial ecology has grown rapidly over the past decade. It is likely that biorefineries will be dispersed throughout the rural landscape, presenting opportunities for innovation to that model for high-performance industrial systems.

What better way is there to attract media and policymaker interest than with excellent technologies, environmental performance, and by implementing the most progressive industrial practices? Will this guarantee a safe haven from critics? Probably not. But it presents the possibility of raising the dialog beyond the level of bilateral debate involving forced positioning and partisanship to the level of collaborative partnership wherein invested allies can play a role in creating sustainable solutions to our national energy needs. With its recent "billion gallon challenge" to the biofuels industry, the National Resources Defense Council has stated that it will lobby the US government to deliver a coherent and powerful incentive system if the industry will demonstrate the potential for a sustainable biorefinery system. NRDC and other environmental organizations want to help us demonstrate sustainable biofuels production. To put that first billion gallons into production, NRDC is willing to be an ally in our effort to elicit policy action from the federal government. The biggest problem presented by the challenge is the need to look beyond the typical boundaries of the biorefinery LCA to a broader boundary. DDCE's LCA is defined in terms of plant performance, and also of soil conditions, biomass yield and carbon emissions from our farmer supply chain. In most contexts, these would be more than sufficient—even ambitious—but NRDC and other opinion leaders in the environmental community seek assurance that the expansion of a biofuels industry will not accelerate deforestation. For them the system boundary is the planet, which has been translated into a regulatory requirement that calls for international or indirect land-use change. The problem that this creates is that the EPA has a draft rule based on economic aspects of international trade flows in agricultural products and combines with international land-use patterns. Industry has been complaining that the inaccuracies of this model have existed for a long time. Many members of the professional environmental movement share concerns over the rigor of the computer models and would like to better understand the correlations between the models and real-world data.

Skurla suggested supporting and participating in this effort. How might this work? If the system boundary is expanded beyond the biorefinery to the biomass basin in which it will operate, new insights will be gained into broader changes brought about by the facility. Baseline data will be generated for the four metrics: water quality, soil quality, wildlife habitat and diversity, and agricultural productivity. Such raw data are currently lacking. Filling those gaps, working in cooperation with stakeholders and experts in academia, a more rigorous understanding of wider impacts will be gained by industry. This approach takes the concept of industrial ecology to the next level, with the production agricultural system optimized for sustainable food, fiber and fuel production.

Is this vision of a biobased economy achievable? The challenge will be in getting ourselves aligned while we simultaneously engage the various stakeholders who have intense interest in what we are doing. Now that we are transitioning from the development to the deployment stage, we have a responsibility to anticipate the very real issues and concerns that our industry brings into focus for society. Our responsibility is clear, but so is the promise of our industry.

In Skurla's opinion, a low-carbon fuel will be delivered. It will be cost effective and it will be made sustainably.

Lars Hansen reminded the audience that corn yields have risen steadily since 1960 and are expected to continue to rise. The current average is ~150 bu/acre, whereas scientists at Pioneer and Monsanto are predicting yields of 200 bu/acre and 300 bu/acre eventually. Combined with improved agricultural practices, the need for fertilizers has also been reduced drastically, and may be reduced further.

Energy requirement for the synthesis of biofuels was reduced from about 35 GJ/m^3 in 1983 to about 10 GJ/m^3 in 2005. Various methods of producing first-generation corn ethanol provide substantial reductions in greenhouse-gas production. Modern corn-ethanol systems have significantly better net-energy yields and greenhouse-gas (GHG) reductions than older coal-fired plants. The most common corn-ethanol plants reduce GHGs by 48–59% compared to gasoline. The latest factories are, of course, the most efficient. Plants built since 2005 represent 75% of ethanol production today.

Another input is water. Although the main input of water is for growing the corn crop, 95% of which is rain-fed, efforts to improve efficiency within biorefineries have led to 20% reductions in within-plant water usage over the past 10 years.

Regarding the total energy balance, it is important to examine not only the absolute numbers that show an advantage for corn ethanol over gasoline, but the trend reveals that, as it becomes increasingly difficult to remove oil from the ground, then the energy balance will deteriorate for gasoline. Furthermore, since biofuel-production technology is in its infancy, it will improve in efficiency, whereas the long-established petrochemical industry has less similar potential.

The GHG footprint is significantly better for first-generation ethanol than for gasoline, and this improvement will be further increased for second-generation processes; in 2015 it is expected that CO_2 emissions from cellulosic ethanol will be 80–90% less than from gasoline.

Since 1973, Novozymes's objectives for their various production systems have included:

- lower energy and water requirements
- improved process efficiencies
- lower capital costs
- less use of chemicals.

In conclusion, Hansen suggested that the key issue should not be a matter of being for or against bioethanol, but to ensure that the potential benefits are realized in a sustainable way.

Growing up north of the border, **Jacques Beaudry-Losique** has long realized that biomass is a hugely important resource, bearing in mind that there are many more trees than people in Canada. Also being familiar with the sustainability requirements of the forest-products industry, it has always been clear to him that biomass must be grown sustainably.

The Obama administration is investing billions of dollars via the American Recovery and Reinvestment Act (the "Recovery Act") to help create hundreds of thousands of jobs. One of the goals is to help double the renewable energy supply in the short term. Almost $800 million of Recovery Act funding will be invested in accelerating R&D in advanced biofuels, in four main areas:

- pilot, demonstration and commercial-scale biorefineries
- fundamental research
- advance biofuels research
- infrastructure and market development.

An announcement was expected the following week[1] from the US Department of Energy (DOE) that $85 million would be made available under the Recovery Act for work on algal and other advanced biofuels, to unite the efforts of leading scientists and engineers from universities, the private sector and national labs to bring new technologies and fuels to market in an accelerated time frame. This approach is based on the belief that diversity of options will be key to meeting the US Renewable Fuel Standard.

The primary emphasis of the DOE is on biofuel development, cost reduction, and support of the Renewable Fuel Standard target, *i.e.* production of 21 billion gallons per year of cellulosic and other advanced biofuels by 2022, or approximately 15% of the nation's liquid transportation fuel needs for light-duty vehicles. The priorities and goals of the program are tied to presidential objectives for energy:

- development and demonstration of multiple pathways of cellulosic and advanced biofuels at scale
- reduction of greenhouse-gas (GHG) emissions by up to 90% for biofuels versus gasoline
- connecting basic and applied bioscience as well as conducting breakthrough R&D to overcome barriers to commercialization
- cost-competitive cellulosic ethanol by 2012.

To be successful, we must ensure that the biofuels industry does not emerge at the expense of negative environmental impacts. Therefore, DOE emphasizes sustainable development of biofuel-related indus-

[1] http://apps1.eere.energy.gov/news/progress_alerts.cfm/pa_id=210/.

tries, from the farm to the end-use in vehicles. The program promotes biofuels that do not compete with food crops, and their analyses are continuously enhanced and refined to improve ability to understand potential impacts on the environment, both direct and indirect. DOE funds field-based research and participates in a partnership led by universities in five major regions. DOE also works in partnerships on impact of climatic conditions on feedstocks, soil type, nutrient cycling, water quality and GHG emissions. DOE's Biomass Program continues to work with the national labs, conducting life-cycle analyses on GHG production and water usage in biofuel production. Pioneering work on life-cycle analysis has been done at the national labs.

Recovery-Act funds are being used to expand work on sustainability in critical areas, including land-use-change forecasting as a result of growing biomass crops as feedstocks for biofuel production. Beaudry-Losique opined that indirect land-use change has been the major sustainability issue of the past year. The DOE has assumed the role of trying to deflect the inherent emotion by focusing on science, with life-cycle analyses aimed at making recommendations for land-use changes. The DOE Office of Energy Efficiency and Renewable Energy, in combination with national labs and universities, is collecting and analyzing data that may be used to inform sound regulations related to the effects of production of biofuels. Some of the models that have been developed have been fed into the US Environmental Protection Agency's rule-making process.

They have been working with the Argonne National Lab and Purdue University to build models to simulate impact on land use, and have gathered experts from academia and industry to review the science, develop protocols for collaboration, and prioritize research needs with respect to land-use change. Two issues emerged from this 18-month effort. First, current models are inadequate to address all of the social, political and economic forces that influence the indirect effects of land-use change. It may be years before all such forces are accommodated, if ever. Second, if we ignore these forces, satellite data and past pictures of land-use change, and use basic economics to build models for land use, assuming that the cheapest means of compensating for lost production is to increase yields or to plant crops on marginal land to minimize the impact of land-use changes on GHG production, then, although other forces are at work, the huge land-use change impacts—as suggested in some publications—would not apply.

At DOE, there has been increased emphasis on sustainability over the past couple of years. Currently, some fifteen projects have an emphasis on sustainability. The Biomass Program is increasing collaboration with stakeholders and key partners, domestically and globally.

Beaudry-Losique asked, "How can we go where we need to go? How can we create a sustainable biofuels industry?" He suggested that we need a comprehensive approach that transcends controversies like those that have emerged recently. We will need:

- biomass crops with minimal requirements for water and nutrients, and work is already in progress in this regard
- to continue to increase yields while minimizing the land-use footprint
- conversion technologies that minimize water consumption with negative air pollution, biorefineries that are integrated and monitored to improve the carbon footprint of future similar facilities
- to promote co-product utilization in fully integrated systems
- infrastructure that minimizes GHG emissions, such as pipelines rather than trucks and trains for fuel transportation
- to avoid negative impacts on human health and safety.

At the DOE they are working hard to address these needs and challenges.

Lee Lynd opened his remarks with the observation that the global transition to a sustainable resource base is arguably the defining challenge of our time. Land-use issues will have a dominant impact on the biofuel industry. The perceived merit of biofuels will be determined to a significant degree by the conclusions that the public and policymakers draw, which, therefore, will affect policy support. Of concern to those involved in commercialization investment, in the future, these same land-use issues will be dominant determinants of the scale and sustainability benefits that will be attained.

To say the least, divergent opinions exist, with little consensus on the feasibility—or even desirability—of biofuel production on a scale sufficient to meaningfully affect sustainability and energy-security challenges, *e.g.* 25% of global mobility. It has been suggested that we, as a society, should forego the biofuel option because of land-use challenges. Lynd suggested that a dispassionate response entails asking:

- What are the alternatives?
- What benefits would be missed?
- What are the prospects for resolving these challenges otherwise?

Currently in the United States, 63% of mobility-energy expenditure is on light-duty vehicles (cars, SUVs, light trucks, *etc*.) and 37% on heavy-duty vehicles (trucks, planes, ships, trains and buses). A not-too-large collection of potentially sustainable sources of energy is available to provide mobility—sunlight, wind, ocean/hydro, geothermal, nuclear—for which the primary intermediates are biomass and electricity. Of particular importance for this discussion, these provide just three chief methods for storing energy:

- organic fuels
- hydrogen
- batteries.

Some vehicle/energy-storage combinations are more feasible than others. For example, electrification—using batteries for energy storage—is impractical for most heavy-duty applications. Similarly, hydrogen faces many challenges, particularly if generated from low-carbon sources. Even with extensive electrification—*e.g.* half of the fleet being 100% electric vehicles and half being plug-in hybrids—organic fuels would still provide at least 50% of overall mobility for light-duty vehicles.

Benefits missed if we forego the biofuel options include:

- energy security
- rural economic development
- environmental
  - — greenhouse-gas emission reduction
  - — reduced demand for unconventional petroleum (shale oil, tar sands)
  - — increased use of low-carbon electricity to displace coal if less electricity is needed for transportation.

Without biofuels, achieving a sustainable transportation sector is substantially more difficult and substantially less likely.

Therefore, since sustainability challenges are pressing and alternatives to biofuels are few, limited and uncertain, and because biofuels offer multiple benefits, bearing in mind that all sustainable mobility options require innovation and change, Lynd suggested that it makes sense to approach the following question with urgency: "Can biofuel land-use challenges be resolved gracefully?" The dimensions of innovation and change that would impact biofuel-feedstock availability include a host of options associated with integrating feedstock production into managed lands without affecting food production. Options are associated also with producing food more land-efficiently. We can alter the amount and kinds of animal products in our diet, and we can decrease demand for fuel. Furthermore, we may anticipate mature feedstock technologies and mature conversion technologies, and although this may seem optimistic or improbable, it would be unrealistic to expect to meet these challenges without both.

This thinking has motivated a project that was initiated in June, 2009—*Global Sustainable Bioenergy: Feasibility and Implementation Paths*. An international organizing committee has been formed, a joint statement published in *Issues in Science and Technology*[2], and a website launched[3]. The key issue being addressed is: *Is it physically possible for bioenergy to meet a substantial fraction of future world mobility and/or electricity demand while our global society also meets other important needs?: feeding humanity, providing fiber, maintaining and, where possible, improving soil fertility, air and water quality and wildlife habitat, and achieving very large greenhouse-gas emission reductions that are not substantially negated by land-use changes.*

Lynd closed by suggesting that biofuels are likely an obligatory part of a sustainable transportation sector and that very-large-scale production of biofuels can be gracefully reconciled with food production and preservation of habitat and environmental quality. On the other hand, the world has somehow gotten this far without a widely accepted consensus and clear understanding with respect to these issues; it would be useful if this were to change.

[2] http://engineering.dartmouth.edu/gsbproject/letter.html.
[3] http://engineering.dartmouth.edu/gsbproject/.

Better Living Through Biotechnology: Innovation in Biobased Materials

Moderator: Doug Cameron (Piper Jaffrey Investment Management)

Volkert Claassen (DSM), Paul Dalby (University College London),
Glenn Nedwin (Genencor)

According to **Volkert Claassen**, it is fundamentally important to make products that fill real needs. This, of course, involves choices and careful selection of life-science and material-science products that address important current trends:

- climate and energy
- health and wellness
- functionality and performance
- emerging economies.

DSM was early to enter the biobased-product field, and it was early to initiate work with emphasis on emerging economies. China is second only to the Netherlands in importance to DSM in terms of planning, people and revenue.

Long-term growth at DSM is envisaged as resulting from innovations in:

- biomedical materials
- “white” biotechnology
- specialty packaging
- personalized nutrition
- biomaterial products
- climate change.

For now, a chief focus is on the interaction between the life sciences and the material sciences. In the health and wellness field, for example, several products were commercialized in the past few years: Trancerta® microparticles for administration of new treatments for diseases of the eye, Dyneema Purity® polyethylene fibers, which help connect hard and soft tissues to alleviate ligament problems, and, in the life sciences, InsuVital™ is a functional food ingredient that enables manufacturers to create products that are clinically proven to help type-2 diabetics manage blood-glucose (sugar) levels after meals, and BioActive™ MTP is a peptide formulation that smoothes and softens skin.

Much of DSM’s innovation results from partnerships of various kinds, particularly so over recent years. Another factor critical to successfully commercializing products resulting from open innovation is careful management of intellectual property. They are on course to realize an objective set out in 2005 to reach $1 billion in sales by October 2010, in spite of the global economic downturn. Pharma sales provide important support for their industrial biotech efforts, comprising biocatalysts that are used to create conversions in pharmaceutical synthesis. They have a unique set of capabilities to address a broad variety of opportunities. Many enzyme platforms have been developed, typically involving enzymes produced in-house that are available for sale as well as used for synthesis of pharmaceuticals and rapid realization of new biotech targets.

Biotech is now making significant inroads in the chemical industry, providing alternatives to petroleum-based chemical synthesis. However, although it is certain that novel biobased alternatives will reduce consumption of petroleum, it should not be assumed that every biobased approach has a smaller environmental footprint than “ordinary” chemical methods. Not all chemical processes will be replaced by biobased alternatives. Biobased methods will be successful only if equal product quality is delivered at substantially lower cost. New products made through biobased approaches will offer new opportunities.

DSM’s first target using a biobased approach is the production of succinic acid. The biological route has several advantages:

- environmental benefits
  - — feedstocks are bio-renewable
  - — no petroleum is used

    — the process absorbs CO_2
    — cost proposition allows high-volume production of "green" chemicals and materials
- new biobased and biodegradable applications are feasible
    — production of "green" plastics, like polybutylene succinate for agricultural film
    — biobased fibers for clothing
    — biobased resins, such as bio-succinic acid polymer.

In partnership with ROQUETTE, a biosuccinate demonstration plant in Lestrem, France, is expected to be operational by late 2009.

DSM is also involved in an extensive enzyme-development program that will focus on finding applications in cellulose-based biorefineries for the production of bioproducts, including biofuels. Many challenges remain to be addressed in the production of second-generation biofuels; new enzymes and microorganisms will be necessary. Their vision is that chemistry and biotechnology will merge and, with the right tools for the right processes, biorefineries will produce not only biofuels but also chemicals and materials.

Paul Dalby said that he would discuss challenges involved in putting together a new program for producing synthetic intermediates using biobased methods.

Many products traditionally made from petroleum are being considered for synthesis from biofeedstocks. With the petrochemical approach, a few categories of chemicals of similar energy level have to be separated and then diversified into many compounds of varied energy level. In contrast, biomass already contains many molecules of varied energy level.

One of the key drivers is to add value to biorefineries, for example co-products from biofuel synthesis may be used as feedstocks for production of chemicals and pharmaceuticals. Speed to market is another driver; for a high-value product for the pharmaceutical industry, getting it to market may be the critical step rather than optimizing the production process. Sustainability has become of particular interest in recent years. And pharmaceutical markets are largely product-driven; particular compounds are requested, rather than bulk chemicals being converted to supply the need.

The challenges include:

- breakdown and utilization of complex biomass (lignin, cellulose, *etc.*)
- taking advantage of existing biotechnology infrastructure, including biofuels, for high-value use of sugars
- creation of new biocatalysts (microbes and enzymes) will be needed for conversion of sugars to high-value compounds and bulk chemicals
- taking advantage of tools that have become available over the past decade, particularly metabolic engineering, enzyme engineering and synthetic biology.

Also important in developing a new process is the decisional space that has to be dealt with, which can be less than straightforward:

- Should the route taken be chemical, biocatalytical or via synthetic biology, or a combination of these?
- At some point a decision may be necessary on engineering the biology versus engineering the process, or should an integrated approach be taken?
- A decision may be needed on speed-to-market versus improving process efficiency.
- Impacts on the downstream process must be appraised.
- Manufacturing costs are critical, and built-in flexibility will be advantageous to accommodate new needs as markets change.

Their focus is the construction of *de novo* pathways using multiple enzymes to achieve aminodiol functionality, which provides opportunity for synthesis of a range of high-value pharmaceutical compounds including antibiotics. The BICE program at University College London (bioconverstion integrated with chemistry and engineering) highlights the teamwork and necessary integrated approach, and involves a chemist to examine the chemistry and biocatalysis options, metabolic engineering, enzyme engineering, directed evolution, microscale processing to appraise large-scale potential, and large-scale process modeling. A critical component was the industrial steering group, as well as financial support; representatives of thirteen companies were able to provide advice to solve problems as they emerged. In developing a microscale automated process, a critical trade-off to be considered is between the degree of process improvement and the time required to implement that improvement. A new biological entity may be created to achieve significant process improvement, but only after significant investment in time. Alternatively, process change usually takes less time, but results in less improvement.

A common approach in synthetic biology is to express a pathway heterologously in fast-growing *E. coli*, which works well provided that the compound of interest can be readily identified. In reality, pathways may have to be created from scratch, which is the approach adopted by Dalby and colleagues: enzymes are assembled into a pathway forming a product not found in nature. Their first objective was the synthesis of aminobutanetriol using a *de novo* transketolase/transaminase pathway, which provided a 20% conversion at the first attempt. To diversify and make more derivatives of the aminodiol functionality, they evolved the transketolase for substrate specificity, enantioselectivity and increased activity, and, using metagenomics, they isolated new transaminases again for broader substrate range and increased activity. Each step of the new, evolved pathway worked well in isolation, but overall conversion was poor. The key question was whether to attempt to enhance the enzymes further or use a process solution. They changed the process and moved away from the pathway approach, *i.e.* the two reactions were separated and run sequentially. The acetate extract of dihydroxypentanone (DHP) from the first step is placed into the second step and the product, amino pentanediol (APD) is purified by ionic exchange.

The key message from this project is that interdisciplinarity is essential, with integration of chemists, biologists, modelers, process engineers and decision-makers. Also, speed to market sometimes is more important than optimizing process efficiency, at least early when it's advantageous to get the pharmaceutical intermediate into the market. As sustainability becomes more of an issue, process efficiency may become paramount.

Globally, the textile industry constituted an $18 billion market for processing chemicals (desizing, bleaching/scouring, finishing and dying) in 2007, reported **Glenn Nedwin**. Since then, the economic downturn has contracted the market by about 30%. Enzymes make up only about 1%, but there is untapped potential to replace chemicals, particularly with a new emphasis within the industry as a whole on sustainability. Enzymes offer low-temperature and systems-integration processing. Also, there is pressure in many parts of the world to conserve water, including south Asia, and European regulatory agencies are rendering obsolete many chemical applications.

Textile processing potentially comprises a number of enzymes:

- catalases, pectate lyases and aryl esterase for scouring and removal of hydrogen peroxide used in bleaching
- amylases for starch removal in desizing
- cellulases, proteases and laccases for various finishing applications
- laccases used also in dying.

Genencor's strategy is to replace chemical processes with sustainable biotechnological alternatives. Their PrimaGreen™ enzyme-system platform provides sustainable methods for processing textiles and garments with:

- lower processing temperatures to decrease energy consumption and CO_2 emissions
- less rinsing to conserve water
- neutral pH providing gentle and safe processing conditions
- lower dosages for less waste
- new processes that replace harsh chemicals.

Wet processing is the most environmentally hazardous stage of production within the textile supply chain. During cotton processing, huge amounts of water and much energy are consumed, effluents are contaminated, and workers are exposed to a number of potential health hazards. Genencor has developed the first enzyme system for the bleaching segment. In collaboration with Huntsman Textile Effects, providing Gentle Power™ bleach, Genencor's breakthrough enzyme technology—PrimaGreen EcoWhite™—permits textile bleaching at 65°C (down from 95°C) and at neutral pH (down from pH 13). Water and energy savings of 40% are achieved, with a 50% reduction in loss of fabric. The latter aspect is particularly important in that the standard process destroys 80% of cotton; significant benefits thus accrue not only to the processor but also to the environment. New textile products were launched a few months ago; they are softer to the touch and whiter, have superior dyability and sewability, and resist creasing.

Preliminary results of life-cycle assessments of the new and standard bleaching methods have revealed significant benefits in terms of CO_2 emissions, energy consumption, and impacts on human health and ecosystem quality.

PrimaGreen EcoFade LT100 is a ready-to-use enzyme product for denim bleaching and shading. A new laccase and a new type of mediator are incorporated into one product, allowing creation of new looks while reducing environmental impact. This new technology enables bleaching at neutral pH and low temperature, providing savings in rinsing water and neutralization chemicals, and reducing energy use.

Such sustainable solutions are attractive not only to processors, but also to merchandizers. Walmart and Target demand life-cycle data. Abercrombie and Fitch, and Ralph Lauren care about sustainable textile processing.

Topics in Synthetic Biology

Moderator: Philip Schwab (BIOTECanada)

Kristala Jones Prather (Massachusetts Institute of Technology),

Arthur Caplan (The University of Pennsylvania)

Kristala Jones Prather asked, "What is synthetic biology?" and suggested that it means different things to different people. One aspect of consensus is that the field is growing rapidly, and a measure of this is that the key term "synthetic biology" turns up just two references in literature indexes for the years 2000–2003, whereas more than 120 articles were published in 2008 and ninety-nine were published in the first half of 2009. Another aspect of consensus is that interest in synthetic biology is global. The International Genetically Engineered Machines (iGEM) competition, piloted at MIT 5 years ago, attracted entries from over a hundred groups affiliated with universities in more than twenty countries in 2009.

In 2000, *Chemical and Engineering News* defined synthetic biology as "using the synthetic capability of organic and biological chemistry to design *non-natural*, synthetic molecules that, nevertheless, function in biological systems." Prather suggested that synthetic biology has two parts:

- The design and construction of new biological "parts," "devices," and "systems."
  - — Parts, devices and systems are increasing levels of biological complexity, aligned with engineering. A part may be a DNA sequence that encodes a protein. A device may be that protein linked with a regulatory element that turns on gene expression in response to a cue. And a system may be a cell engineered to activate the protein in response to the cue to synthesize a biochemical of interest.
- The redesign of existing *natural* biological systems for useful purposes.

As synthetic biology has developed, there has been increasing focus on the natural part, with particular emphasis on design applications, building new biological systems with predictable behavior. A practical definition of synthetic biology from the Synthetic Biology Engineering Research Center[1] (SynBERC) is "Making biology easier to manipulate by applying engineering principles." "Engineering principles" implies designing a system that operates in a predictive manner; this usually means that an equation is available, therefore mathematical modeling is an essential element of synthetic biology. It also implies having a way of characterizing the system, with a feedback loop, if it fails to operate optimally, to redesign it to ultimately achieve the end-goal.

A key enabling technology is DNA synthesis. Prior to the 2000 definition, chemical synthesis was employed to make biological *mimics*. For the SynBERC definition, the tools of chemistry are used to make something *chemically* identical to a natural biological system as well as *functionally* identical.

Examples of how synthetic biology is used follow:

- In 2006, inexpensive production of the antimalarial drug precursor artemisinic acid was reported in engineered yeast[2]. This technology has been commercialized by Amyris.
- In 2009, control of gene expression in subcutaneous implants by topical application of a lotion was reported[3].
- In 2008, the design of new pathways in *E. coli* producing novel branched-chain molecules as gasoline substitutes with higher energy density

[1] SynBERC is a program of the California Institute for Quantitative Biosciences (QB3). A partnership between the state of California, private industry, venture capital, and the University of California campuses at Berkeley, San Francisco, and Santa Cruz, QB3 is developing solutions to urgent biomedical problems through multidisciplinary research, innovative educational programs, and industrial and venture-capital partnerships.

[2] *Nature* 440: 940–943 (2006).

[3] *PNAS* 106: 10638–10643 (2009).

and lower hygroscopicity than straight-chain alcohols was reported[4].

These exemplify progress in synthetic biology with commercial potential.

Another aspect of this new field is biological computing or programmability, to manipulate cells to function analogously to electronic components, and extend our understanding of how natural systems work. The seminal paper, published in 2000, described a "repressilator," *i.e.* a series of proteins that function as oscillatory networks[5]. Follow-up work in 2005 described a similar oscillatory function with intracellular metabolites as drivers[6], and more recent articles described tunable synthetic gene oscillators, not just in microbes[7] but also in mammalian systems[8].

An important application of synthetic biology is the creation of new life forms. Work at the J. Craig Venter Institute has resulted in the chemical synthesis of the 582,970-base-pair genome of *Mycoplasma genitalium*[9], which presents the potential to produce new micro-organisms for specific functions. Although this application is often thought of as the essence of synthetic biology, it is important to understand that this field of endeavor is diverse. Miscellaneous problems are being tackled via various approaches, with the long-term objective of making biology easier to engineer, with many application in industrial biotechnology.

Arthur Caplan first heard about synthetic biology in 1996 when, in a presentation at the National Academy of Sciences, Craig Venter announced his intention to make a novel life form and then turned to Caplan and asked if there would be ethical implications. It is noteworthy that the first paper on the ethics of synthetic biology preceded the first paper on synthetic biology. The former appeared in *Science* in 1999, dealing with issues that largely remain relevant[10].

Concerns over safety, environmental impact and ownership and control of technology are not more germane to synthetic biology and genomics than they are to other areas of the biological sciences. Transparent regulations will ensure that synthetic biology is safe and that its environmental impact will be minimal, and will provide necessary guidance for patenting, ownership and control issues; we should not view regulators as enemies. Also, two larger questions need to be addressed. First, people often raise the issue of "playing God." A second issue, raised by those more knowledgeable, relates to accountability and publication of data that could fall into the wrong hands. Samuel *et al*. stated recently[11]:

> *The synthetic life sciences seem to have emerged from nowhere, and their potential uses and misuses have taken the scientific and regulatory community by surprise…it is a reminder of how scientific development might leave moral, social, legal discourse in its wake…*

Caplan opined that this is not necessarily true, as indicated, for example, by his presence at this conference. Although he agreed that abuses are possible that society doesn't understand, or hasn't be alerted to, it should be borne in mind that many technologies can be misapplied and put to pernicious use. A zero-risk environment is unattainable.

Returning to "playing God," it's noteworthy that major religions accept the manipulation of nature. There has been no objection by any major religion to genetically modified organisms or to the elimination of smallpox, for example. Representatives of religions may query the purpose of genetic engineering and whether risks are borne and benefits accrue fairly, which are reasonable questions. A different version of the "playing God" argument comes from those who disapprove of "meddling" in nature, some of whom are opposed even to vaccines; the emphasis is on the "playing" part with the complaint that scientists abrogate their responsibilities to provide stewardship for nature and for the world and its resources, but rather impose risks for purposes of profit or mere curiosity. Again, this is where transparency, accountability and enforcement of rules become important.

Caplan suggested that it is ironic that although scientists defend the right to withhold publication until patent protection has been obtained, some object to withholding publication of, for example, the small-pox genome. To ensure public trust, it is vital that the industry be seen to expend every effort to protect national security.

[4] *Nature* 451: 86–89 (2008).

[5] *Nature* 403: 335–338 (2000).

[6] *Nature* 435: 118–122 (2005).

[7] *Nature* 456: 516–519 (2008).

[8] *Nature* 457: 309–312 (2009).

[9] *Science* 319: 1215–1220 (2008).

[10] *Science* 289: 2087–2090 (1999).

[11] *EMBO Reports* 10: 7–11 (2009).

International Perspectives on Industrial Biotechnology Business Solutions

Moderator: Philippe Lavielle (EuropaBio)

Jean-Marie Chauvet (Industries & Agro-Resources Association),

Manfred Kircher (Cluster Industrielle Biotechnologie 2021), Hans-Peter Meyer (Lonza)

Jean-Marie Chauvet opened the session with the observation that, in France, the bioeconomy and sustainable development are increasingly intimately linked in the "post-oil" age and within the context of addressing climate change. Industrial or "white" biotechnology has been identified by the French government as key for future production of energy and chemicals; the target of 15% has been proposed for the fraction of chemicals originating from biofeedstocks by 2017.

Formation of industrial clusters is an initiative of the French government to encourage research and enhance competitiveness within defined geographical areas, comprising public and private R&D entities and educational institutions that are committed to forging partnerships and creating synergies for innovation. Seventy-one clusters have been formed of which seventeen are defined as "world class" and of which one is focused on biomass, the Industries & Agro-Resources Association (IAR). The IAR cluster is situated in the Picardie and Champagne-Ardenne region in northern France, a major agricultural area. Focused on non-food uses of biomass—biofuels, polymers, chemicals and ingredients—it comprises over a hundred member institutions, including private companies, universities, graduate schools, INRA[1] centers and three demonstration plants.

In its 25 years of existence, IAR has had close involvement of farmers and farming cooperatives. Biomass is viewed as a feedstock for agricultural ("green") biotechnology as well as for "white" biotech, mainly as a source of sugars. Local growers understand the need to be active stakeholders in the bio-based economy, since agriculture will increasingly be a source of both food and non-food products.

Industrial biotechnology is already a commercial reality, with products including cosmetics, detergents, chemicals, enzymes and biofuels. Four of five recently constructed biofuels plants are IAR members.

In response to a request from the French government, IAR recently formulated a 5-year plan. The R&D priorities include second-generation biofuels and chemical intermediates. The processes involved in producing second-generation biofuels are seen also as a means of producing sugars inexpensively for various uses, particularly in the chemical field.

A major effort within the IAR cluster is the Futurol bioethanol project, launched in 2008 by eleven partners from research, industry and finance. Completion of a pilot plant is expected in 2010, producing 180,000 liters annually. The prototype biorefinery is expected to be in production (3.5 million liters annually) in 2013 and the industrial unit is projected to be operational in 2016 (180 million liters annually). The objectives of the project are to bring to market a process, technologies and products (enzymes and yeasts) that can be used as follows:

- to produce bioethanol from diversified raw materials (agricultural by-products, forest biomass, dedicated crops, urban wastes, *etc.*)
- to develop the most suitable cellulose-extraction techniques, select the enzymes and yeasts required and develop the hydrolysis and fermentation processes best suited to each raw-material configuration
- to obtain the best possible energy and greenhouse-gas balances throughout the entire production process
- to ensure that these biofuels meet the requirements of long-term sustainable development, throughout the field-to-wheel process.

The ACDV[2] (Association Chimie du Végétal) brings together major economic players in the agri-

[1] National Institute for Agricultural Research.

[2] Biobased Chemistry Association.

cultural resources and chemicals sectors, and other sectors downstream, in an effort to promote the industrial development of biobased chemical production in France and Europe. Their objectives are to:

- represent and promote the biobased chemicals sector
- identify major challenges facing the industry
- implement a survey on economic and technical intelligence
- embark on strategic planning.

Manfred Kircher reported that the industrial cluster CLIB[2021] (Cluster Industrielle Biotechnologie, located in Düsseldorf) is a biotechnological effort focussed on polymers, fine chemicals, pharmaceuticals, detergents and body-care products. It has more than sixty members including household names in the chemical industry, thirty-four small and medium enterprises (SMEs), nine academic institutions and investors, thus combining scientific with commercial competence. It has directed about €60 million into R&D projects and time-to-market is shortened by linking scientific excellence with market demands. Their main strategic ambition is the creation of a lively SME landscape providing early technology and product opportunities to established industries. Although founded in Germany, the CLIB-[2021]cluster pursues an international perspective.

Unlike, "red" or pharmaceutical biotechnology, "white" or industrial biotechnology does not contribute significantly to Switzerland's gross domestic product, according to **Hans-Peter Meyer**. On a *per capita* basis, Switzerland is #1 globally for red biotech, whereas at present there is no biofuel or other bio-commodity activity. However, when he talks to his colleagues involved in white biotech, the following issues come up:

- Business potential is huge, larger than for red biotech.
- There is potential for sustainable operations.
- Investments are lower than for red biotech.
- Spending on R&D for white biotech is a sixty-fifth of that spent on red biotech.
- The potential held by white biotech encompasses diverse products and markets.
- Much unfocused lobbying occurs, with attempts by individuals to attract attention and funds into specific disciplines.
- Assessment standards are missing by which relative evaluations would be possible.
- In Switzerland, an integrated roadmap is needed.

It is clear that Switzerland, like many other countries, is a non-competitor in the field of agro-commodities. It does not make sense to move into biofuels or biobased bulk chemicals. On the other hand, Swiss agriculture is geared towards specialties such as chocolate and cheese, and biobased approaches may make sense for some niche markets.

Waste generated by per kg of product in the bulk-chemical industry is highly favorable (0.1 kg), but less so for fine chemicals (5–50 kg) and pharmaceuticals (25–100 kg)[3]. The trend to ever-more complex molecules exacerbates this situation. For example, the production of 20 kg of a 9mer peptide requires 0.4 tons of amino acids, 6.5 tons of piperidine, *etc*.[4] The global market for fine and specialty chemicals will soon reach US$1 trillion, which we sometimes forget because of the emphasis on biofuels. White biotechnology has the potential to provide economically and ecologically superior processes with immediate impact.

3 Trends in Biotechnology 26: 321–327 (2008).

4 Handbook of Green Chemistry, Volume 3, 171–212. Wiley (2009).

Future of the Biofuels Value Chain

Moderator: Jim Lane (*Biofuels Digest*)

Katherine Dunphy-Guzman (Sandia National Laboratories), Ross MacLachlan (Lignol), Bill Baum (Verenium), Johnathan Wolfson (Solazyme)

Katherine Dunphy-Guzman stated her intention to discuss the *90-Billion Gallon Biofuel Deployment Study*, a joint project involving General Motors and Sandia National Laboratories. A number of organizations have provided direct input and reference materials. This was not intended as an endorsement of biofuels in general; the focus was on ethanol. However, they would like to expand the study to include other fuels. They took a supply-chain approach, comprising feedstock production, storage and transport of feedstock, conversion, and distribution of product. They constrained corn-starch as a feedstock to 15 billion gallons, with the assumption that 75 billion gallons would be produced from lignocellulosic sources.

Questions addressed were as follows:

- What must happen to grow ethanol production to 90 billion gallons by 2030?
- What is required for cellulosic ethanol to be cost-competitive with gasoline?
- What greenhouse-gas, energy, and water footprints will be associated with this level of production of ethanol?
- What risks may affect the production and competitive goals of cellulosic ethanol, and how may they be mitigated?

A "seed-to-station" system-dynamics model was built to explore all of the components of the supply chain. At each point, volume, cost, greenhouse-gas emission and energy use were tracked. A 2006–2030 timeframe and state-level granularity were included in the model. One reason for examining system dynamics was to include changes, such as technology evolution.

To address production levels, they defined a reference case whereby technologies and feedstock availability would be such as to allow production of 90 billion gallons of ethanol annually by 2030 without reducing current active food-cropland usage. This would require a mix of feedstocks, projected as 44 million acres of pasture and idle cropland used to produce energy crops, 40 million acres of non-grazed forest land, no land-use changes for production of agricultural and forest residues, and corn-ethanol acreage equal to that for 2006.

Regarding feasibility of large-scale production, a constraint that is often mentioned is transportation and distribution infrastructure. Their analysis indicated that the infrastructural issues will be challenging, but not a fundamental obstacle. Construction of new rail tank cars needed for transportation of ethanol, approximately 8,000 per year, is well within production capacity. Furthermore, growth in trucking to support road-transportation of ethanol is projected at less than 5% beyond the current total semi-truck fleet. On the other hand, investment will be necessary to overcome projected rail-line capacity constraints, but this constraint will pertain with or without biofuels. The 2030 ethanol tank-car tonnage is projected to be only a few percent of total rail freight.

To address cost competitiveness, a number of sensitivity analyses were run with various assumptions to identify key factors, the most important of which was oil price. For example, cellulosic ethanol can compete with oil priced at $90 per barrel, assuming:

- an average conversion yield of 95 gallons per dry ton of biomass
- conversion-plant capital expenditure of $3.50 per installed gallon capacity
- a delivered feedstock price of no more than $52 per dry ton.

A key aspect of environmental impact is water use. Their estimates suggest that 50 billion gallons of ethanol could be produced in states requiring little or no irrigation, and additional ethanol production will be possible in low-irrigation areas of states in which water use is high on a per-state basis.

Another important aspect of environmental impact is greenhouse-gas emission. Excluding land-use change considerations, for their reference case they calculated that the total savings between 2006 and 2030 would be 3.5 billion tonnes of CO_2, a savings of 25% of the emissions for the current fleet of gasoline vehicles.

They saw no fundamental supply-chain constraints to large-scale production of biofuels, assuming that the technology matures as projected. However, the following actions could enhance the success of the cellulosic biofuels industry:

- increased R&D and commercialization-associated funding, despite current relatively low oil prices
- supportive policies, including well planned market incentives and carbon pricing to minimize investment risks in light of oil-price volatility and periodic economic dislocations
- investment in infrastructure to ensure that the rail and road networks in the United States can support expanded economic activity including significantly increased production of biofuels.

Ross MacLachlan asked, "What are the implications of biochemicals in the biofuels value chain, and how do they impact the findings and conclusions of the Sandia report?" He made the observation that the report is based largely on assumptions drawn from a conventional cellulosic model to produce, as cost-effectively as possible, as much ethanol as possible from a unit of biomass and to burn the residuals, largely lignin, for power. As costs come down, this model will work well. However, it contrasts with a biorefinery model, which produces chemicals in addition to ethanol; although costs are again important, more important is maximizing the "top-end revenues" from the biomass. Also government policy objectives for oil displacement and greenhouse-gas (GHG) savings can be substantially enhanced with inclusion of biochemicals. Simply put, there is much more of value in wood than ethanol. Lignol is focused particularly on lignin because it is the major source of aromatic structures in nature and is a huge potential resource for the chemical industry.

Embedded in the Sandia report is the objective of achieving a savings of 250 million tons of CO_2 emissions, resulting from production of 75 billion gallons of cellulosic ethanol and 15 billion gallons of corn ethanol, equivalent to an oil-displacement of 950 million barrels. The criteria of economic feasibility are as follows:

- oil price in the range of $70 to $120,
- biomass at $40 per dry ton,
- plant capital expenditure of $3.50 per gallon of installed capacity,
- yield conversion of 95 gallons of ethanol per dry ton.

By burning the lignin, the total value from this feedstock works out at $258 per dry ton.

In a biorefinery model in which the ethanol is synthesized from the C6 sugars in cellulose and in which clean streams of hemicellulose and lignin are produced in the Lignol process as chemical sources that displace petroleum, the total value from the feedstock becomes $440 per dry ton, with a savings of 400–600 million tons of CO_2 and an oil-displacement of 1.5 billion barrels. These data imply that oil-displacement and GHG targets can be achieved more rapidly and with about half the target cellulosic-ethanol production; in short, we may not have to wait until 2030. With these enhanced economics, there will be less reliance on high oil prices and low feedstock costs. There will be less reliance also on large-scale plants and on long-term government subsidies.

Establishment of the biofuels value chain is fundamentally important. **Bill Baum** reminded the audience that the current value chain enables farmers to change crops depending on current markets, whereas this cannot be done with cellulosic-ethanol feedstocks, because long-term agreements with farmers are required.

Verenium runs a 50,000 gallons per year ethanol pilot plant primarily using bagasse and energy cane as feedstocks; it serves as a research unit with which batch-to-batch variations are possible to obtain technology improvements. A demonstration plant, completed in 2008, has a capacity of 1.4 million gallons per year and is in the optimization phase; it's a fully integrated cellulosic facility built to test a wide range of feedstocks and enzymes. Ground will be broken in

2010 for Verenium's first commercial-scale plant in Highlands County, Florida. Operations are scheduled to begin in 2012. A long-term partnership with Lykes Brothers will provide harvested and transported energy cane from 17,000 to 20,000 hectares in Florida for annual production of 36 million gallons of ethanol per year. Billing cost will be $250–$300 million and government support will be critical.

A joint venture with British Petroleum will accelerate commercial-scale development and value-chain capture. The innovation and biotechnology know-how will be contributed by Verenium and global process engineering, operations, fuel blending and transport expertise will be provided by BP. A second joint venture has been forged, Vercipia, which will be responsible for design, engineering, and commercial development. Vercipia will build plants in the southeast of the United States, where the biomass crops will be grown.

Solazyme takes advantage of algae's efficient lipid-production pathways, stated **Johnathan Wolfson**. Algae can consume carbohydrates in a variety of biomass feedstocks in standard industrial fermentation facilities in the dark, and synthesize oil that is refined into a variety of fuels. Solazyme is probably the only industrial-scale microbial biotechnology company manufacturing oil-based fuel. Although they are not yet a commercial entity, they have produced fuels that meet US and some European fuel specifications, *e.g.* a biodiesel that meets ASTM D6751 and EN 14214 specs and a renewable, standard hydrocarbon diesel fuel that meets ASTM D975.

One of the objectives is to help secure a stable, secure domestic supply of fuels, but also to dramatically reduce carbon and other emissions. Extensive field-to-wheel assessments have shown reductions of 85% to 93% in the full carbon life cycle and decreases in particulates and hydrocarbons of 30%. Although biofuels constitute a major focus of the company, their first products, due for commercialization in 2009, will be aimed at the cosmetic and nutraceutical markets.

Wolfson described the biofuels value chain as a fusion of two: the fuels and agriculture value chains. It's noteworthy that the value chain for first-generation biofuels may be significantly different from that for second-generation biofuels, and different again for biofuels advanced beyond second-generation products.

Advanced biofuels will be midstream in the value chain, which is relevant because one has to figure out what value is being provided, partially because of renewable fuels mandates and costs being levied on carbon. Above that is the arbitrary value of biomass versus petroleum, which requires a new value share beyond the traditional view for ethanol and diesel. The new value share must be weighed against the risks that accompany deployment of new technologies.

Of course, the value chain will always adapt, due to the creativity of the people involved, in forming partnerships, for example, so that all parties gain advantage. Wolfson views the infrastructure as much less adaptable than the value chain. Compatibility at all steps of the infrastructure will be important, although further development of infrastructure will be needed to handle advanced biofuels. He believes that existing multinational oil companies will play a large part in the deployment of this technology, partly due to infrastructural requirements, but also because of specific needs with respect to renewable fuel standards, carbon pricing, *etc*. Partnership models will vary dramatically and big oil is likely to upstream-integrate into agriculture.