

## Growing the Future

by Cheryl Scott, with Lorna D. McLeod

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The 2010 BIO International Convention isn't just about biotechnology-derived drugs and vaccines. The biotechnology industry as a whole seeks to address current global needs in other areas as well in light of diminishing resources and other environmental concerns. Biofuels development is entering its second wave. Agricultural researchers are finding ways to improve global access to both food and energy. And health-care policy is taking ethics and environmental sustainability into account while looking for new models that can help companies succeed in a changing global economic marketplace — models that could help them bring more and better vaccines and therapies to a more far-flung population than ever before.

### BIOFUELS/BIOENERGY

First-generation biofuels were initially hailed as a major avenue to lowering greenhouse gas emissions and diversifying energy supplies, but their potential may be limited by various factors. Today's advanced biofuels address the problems. To scale them up effectively, however, lessons learned must be applied to prevent mistakes that could hinder their commercial development. This will include making the most of their by-products, achieving real pilot and full-scale efficiencies, and securing feedstock supplies.

The US Renewable Fuel Standard (RFS) requires an annual biofuel production of 21 billion gallons by 2022, which represents  $\geq 250,000,000$  tons of biomass. New plant varieties will be needed to fulfill that mandate without costing too much agriculturally/environmentally or economically. New energy crops include grasses, trees, agricultural residues, and algae.



DIGITAL VISION (WWW.DIGITALVISIONONLINE.COM)

There is no one single solution for advanced biofuels to become a sustainable energy resource — just as biofuels alone will not solve the energy crisis. Many start-up companies are offering great concepts for innovation, but most address only one step in the energy process. A few, however, are taking a different approach by offering integrated operational and technology strategies to address biofuels R&D, processing, refining, distribution, and commercialization. Both types will be represented at the 2010 BIO International Convention.

Mark Finkelstein (vice president of biosciences for Luca Technologies) organized a session titled “Bioenergy from Buried Hydrocarbons,” which offers a new twist on an old energy source. Buried hydrocarbons (such as coal, shale, and oil) represent an immense resource that isn't as “tapped out” as you'd think. In the United States alone, >300,000 wells are classified as “marginal,” and many are plugged/abandoned each year. Companies taking advantage of microbial energy technologies (MET) with advanced genomic methods and microbial stimulation technologies

could open up a new avenue to greatly expand energy production in geographically diverse areas without increasing the energy industry's footprint or environmental impact in these areas.

Bioenergy from buried hydrocarbons? “Today people hear a lot about various feedstocks and biomass,” Finkelstein told BPI contributing editor Lorna McLeod. “What we're talking about is ancient biomass. Coal, oil, and shale came from plant and animal material buried millions of years ago. I'm a biologist by training, and before I joined Luca, I didn't realize that when you discover an oil reservoir and there's a billion barrels of oil in this reservoir, but in reality you typically extract about 25–35% of that oil economically. The rest is left in the ground. If you use all kinds of advanced secondary (and tertiary) recovery techniques, you might get that up to 40–60% recovery. The same applies to coal, much of which is deep underground. It's uneconomic to mine that coal under most circumstances. This session is about how we can take advantage of these resources below the surface that

might have been tapped only superficially before.”

The United States has more coal reserves than any other country in the world, said Finkelstein. “Much of it is either in environmentally sensitive areas or under cities, or it is uneconomic to recover. Much of this coal is hundreds to thousands of feet below the surface.” Similarly, much of the oil previously discovered in Pennsylvania, Oklahoma, Kansas, Texas, and California is still there today, but companies can’t extract it economically — unless the price goes to \$100–\$200 a barrel. Several companies and academic/research institutions are working on taking advantage of these resources.

Each of the speakers in this session have slightly different approaches to taking advantage of this huge underutilized resource. International interest is indicated by the opening session speaker, Terry Hazen (a senior member of Lawrence Berkeley National Laboratory) who works with the Energy Bioscience Institute, which is funded by British Petroleum — to the tune of \$500 million — to explore the utility of microbes for energy production. Hazen was one of the first investigators to use advanced genomic techniques to study microbial communities.

The next speaker is Steve Larter (University of Calgary professor), who’s founded a couple of energy companies. “Larter is one of the world’s foremost experts in oil biodegradation and the characterization of the microbial communities that exist in deep-water oil reservoirs. He and his extended team characterize microbes that degrade oil, and they’re also interested in converting oils to methane.”

Bhupendra Soni of Glori Oil will discuss his company’s efforts to boost oil recoveries from depleting oil wells. It adds to oil reservoirs microbes that produce biosurfactants to facilitate oil recovery. This “microbial enhanced oil recovery” is showing economically enticing results.

The session’s closing talk focuses on “Luca’s use of microorganisms already present in the ground. These microorganisms are ubiquitous, even

## INDUSTRIAL AND ENVIRONMENTAL SESSIONS AT THE CONVENTION

### Tuesday, 4 May 2010

8:00–9:00 am

Operational Excellence and Sustainability in a Competitive World

9:30–10:30 am

Industrial Biotechnology for Higher-Value-Added Products

2:00–3:30 pm

The Critical Path to Advanced Biofuel Commercialization

4:00–5:30 pm

From Fields to Wheels: Integrated Approaches to Solve Biofuels Biggest Questions

### Wednesday, 5 May 2010

8:00–9:30 am

Bioenergy From Buried Hydrocarbons

2:00–3:30 pm

Developing Economically and Environmentally Sustainable Biomass Supply Chains

4:00–5:30 pm

The Vision of Industrial Biotechnology: Processes Based on CO, CO<sub>2</sub> and H<sub>2</sub>

### Thursday, 6 May 2010

8:00–9:30 am

Crop Feedstocks for Biofuels: How Are We Doing?

in oil and coal reserves. In many instances, they’ve been historically responsible for producing methane (natural gas). Much of the natural gas we collect today is actually biogenic.” For traditional energy companies, gas is gas no matter how it’s made — biologically or thermogenically. Thermogenic gas typically takes millions of years to form. The oil and gas industry’s mind-set is to drill it, drain it, and when that gas runs out, they plug the well and move on. “Luca’s idea takes advantage of the existing infrastructure at gas-producing areas. One reason the gas stops flowing is that when you take the water out of those wells, the microbes are deprived of their ‘circulatory system’ containing the proper nutrients they need to make more gas. Luca determines what’s missing and makes a recipe of nutrients (we call them *amendments*), then add them back into the ground to restore the wells, which in turn

start producing natural gas again. And it works!” Luca spent its first three years studying microbial communities sampled from 25–30 reservoirs around the country. “In 2006, we transitioned our technology to the field, where we took over several hundred marginal wells, applied amendments, and got the wells fired up again. They started producing natural gas well above what they were producing before.”

Luca’s newly created natural gas is indistinguishable from what originally came out of the wells before. “The infrastructure is there,” Finkelstein went on, “the capital expenses have already been expended. These wells and fields are about to be plugged and abandoned. And the gas we’re producing is the most desirable fossil fuel out there. It sure beats burning coal or oil. The carbon footprint is smaller than coal’s by at least half. Utility companies as well as the government are aware of the advantages of natural gas. Ironically, a lot of folks in biotech are trying to make biogasoline and biodiesel, mimicking the existing fossil fuels. Luca’s technology leaves most of the carbon in the ground and does not further impair the environment: This approach could preclude the drilling of additional wells for the foreseeable future.”

Certain sources of natural gas are already considered to be renewable resources: e.g., landfills and anaerobic digester gas. That gas needs to be cleaned up before it can be turned into electricity or burned for heat. “If you’re getting energy from coal,” Finkelstein explained, “someone has to dig it up and transport it, and then burn it. You then try to capture all the waste gasses and then try to sequester them in the ground. But if you’re working with natural gas, you leave that coal in the ground and turn mostly its hydrogen component into methane.” A methane molecule is made of four hydrogens and one carbon. “So it is essentially a hydrogen ore. And we can go back and reseed, refertilize, rewater, and continue the process. A large portion of the gas in the ground was biologically made, so we’re not doing anything that Mother Nature hasn’t been doing for quite some time.” Luca ‘prequesters’ the

carbon instead. “And, you don’t have the associated costs of digging up the coal and transporting it because the pipelines already exist for distribution”

Considering the human danger of subsurface coal mining and the environmental damage of open-pit mining, the logic of this approach becomes clear. “In our first field study,” Finkelstein reported, “we made enough ‘Lucagas’ to heat 20,000 homes for a year. Luca’s technology also appears to work in oil, shale and lignite as well.”

Another question arises: Will this process truly deplete those coal and oil reserves one day, or is there a way to make them last? Finkelstein said, “We look at it as a sort of farming. Instead of drilling, draining, desorbing, plugging, and moving on, we’re essentially harvesting the hydrogen found in these buried hydrocarbons.” To some it may not be considered renewable, but Finkelstein says there are hundreds of years’ worth of hydrogen awaiting this process. “If we could capture 100% of it, there’s ~1,000 years’ worth of natural gas to be created. It’s unrealistic to think we can capture all of that, but how about 10% — or even 1%? That still represents a huge amount of energy.”

Many new technologies we hear about are a long way from commercialization. But Finkelstein said the products of his company’s first field trials “went right into the pipeline.” Whether it will affect energy prices any time soon remains to be seen. “We demonstrated commerciality about a year and a half ago,” when gas prices were considerably higher than they are today.

Luca views what it is doing as growing energy ‘crops’ underground. “We’ve been obtaining wells in concentrated areas where there are hundreds to thousands of them available. In particular, we have focused on the Powder River Basin in Wyoming, where right now there’s ~40,000 wells in an area about 100 miles long by 60 miles wide, with another 3,000–5,000 wells expected to be drilled in the next five years. A couple thousand wells become marginal every year in the PRB.”

At the time of the interview, Luca Technology owned and operated 630 wells in the PRB. “We have test programs going on in several other states,” Finkelstein said, “and I suspect we’ll have others soon. We’ve also been to several other continents, and by the end of this year we hope to announce a significant partnership with a large international company.”

So the energy companies are clearly taking this concept seriously. What about powering vehicles? Will this technology be about heating homes and electricity generation alone? Finkelstein told Lorna that the transportation industry would be driven mainly by economic considerations. “There are a fair number of compressed natural gas vehicles running in different situations,” he said. “It can be a viable and cost-effective energy source.” But there are challenges: Gasoline-powered engines must be converted to run on natural gas, and converted vehicles are limited in range with current technology. More natural gas on the market, however, could encourage development in that area.

“The economics become more enticing as gas prices edge upward,” Finkelstein admitted. “But we all need to make sacrifices and choices when looking at energy options. What we’re doing is much like farming: Water is the precious lifeblood of our microbes, so we choose to recirculate it. Microbes are like the seeds a farmer plants and the nutrients we add are much like fertilizer. We think we can continue growing and harvesting our ‘crop’ for a very long time.” As an aside, Luca won a Global Cleantech 100 award last year, which acknowledges its technology as clean, green, and sustainable.

#### **FOOD AND AGRICULTURE**

Modern agricultural practices deliver important solutions for increased food production (and environmental sustainability) to a growing world population. We have already witnessed some benefits, and the pipeline for future product is expanding. But consumers are increasingly less educated about how their food is

produced. As the population grows, resources remain essentially the same. Biotechnology innovators want to educate the public while helping to fuel, feed, and heal the world.

For example, most people don’t understand livestock agriculture or genetics. Although some may have ethical questions, the science can be explained and thus contribute to a greater understanding of animal biotechnology and the promises it holds. These issues will be addressed in a pair of animal-focused sessions at the 2010 BIO International Convention. But much of this year’s agricultural discussion involves plant biotechnology. Biotech crops help provide sustainable supplies of food, feed, fuel, and fiber for millions of people, although many are still unaware of that. Sadly, too many producers around the world are denied their benefits.

Biotech crops for sustainable supplies of food, feed, fuel, and fiber are subject to perceptions and laws that deny their environmental sustainability. As the WTO opens doors to foreign markets, sustainability standards and the Cartagena Protocol on Biosafety may close others. Biotech crops could play a crucial role in the coming “bioeconomy,” in which both carbon and water will face constraints. Drought-resistance, increased yield, and biosequestration of climate gasses are all potential benefits. But the companies involved must understand what the Roundtable on Sustainable Biofuels, ANSI SCS-001 Sustainable Agriculture, the National Environmental Policy Act, the Biosafety Protocol, and other legal barriers will mean to them.

The variety of agricultural biotech applications is expanding. With the advent of biofuels, biotech crops have a whole new “green-positive” outlook. Ongoing technological advances (e.g., control of gene transfer) are poised to revolutionize both crop improvement and biomass-based ethanol production. Just as in the pharmaceutical or “red” side of biotechnology, small idea-rich companies and big corporations with pipelines to fill need each other to advance these ambitious projects.

Partnering may be key to an ag-biotech renaissance.

Cutting-edge plant transformation and genome modification technologies are rapidly advancing and competing for market space. Gary Rudgers (global regulatory leader for new ventures at Dow AgroSciences) organized a session for the 2010 BIO International Convention called “Next Generation Technologies: Current State and Future Outlook” to provide a glimpse into the next generation of agricultural products.

“We’re now advancing the way we transform plants and modify their genomes,” Rudgers explained to BPI contributing editor Lorna McLeod. “In the past, we could introduce only a few traits at a time, five at most; now there’s a need to introduce stacked traits — 8, 10, or 12 — all at once. This will become more important as the world population grows and we have more people to feed. In addition, the climate’s changing, so we’re seeing drought conditions and rising temperatures in many farming areas. In the future, we’ll need to plant more food on less farm land and in different environmental conditions from what we experience today.”

To meet those challenges, he says, the agricultural biotechnology industry is working on drought-tolerance, nitrogen-use, and traits to make crops more nutritional. “As these new traits are developed,” he went on, “we need new ways to introduce them into plants because the current transformation technologies are insufficient. Right now, we’re pretty much maxed out at introducing three to five traits. Over the past decade, several companies have been developing new technologies such as plant minichromosomes and zinc fingers that will allow us to introduce stacked traits in plants. In the coming decade, we’ll see products in the marketplace as a direct result of those technologies — and positive economic and environmental impacts from them.”

Unlike the first wave of agricultural biotechnology — which seemed to be driven mainly by large multinational companies and public agricultural/research institutions, Rudgers says this time many smaller, more

## FOOD AND AGRICULTURE SESSIONS

*Sponsored by Bayer CropScience, Dow AgroSciences, DuPont, and Monsanto Company*

### **Tuesday, 4 May 2010**

8:00–9:00 am

Ethics and Biotechnology: Genetically Engineered Animals

9:30–10:30 am

Wheat, Don’t Pass Me By: Opportunities for Biotech Solutions for Wheat

2:00–3:30 pm

Next-Generation Technologies: Current State and Outlook

4:00–5:30 pm

New GM Crops: Implications of Asynchronous Approval for International Trade

### **Wednesday, 5 May 2010**

8:00–9:30 am

In Defense of Food

2:00–3:30 pm

Healthy People, Healthy Planet: Exploring (New, Unleveraged) Opportunities

4:00–5:30 pm

Legal Barriers & Sustainability Opportunities for Food, Feed, and Energy Feedstocks

### **Thursday, 6 May 2010**

8:00–9:30 pm

Healthy Traits—They’re Finally Here!

10:00–11:30 am

Little, Big: The State of the Art in Agbiotech Alliances

2:00–3:30 pm

Moving Alternative Crops Into the Mainstream

entrepreneurial companies are involved. “It’s a mix of both,” he explained. “We have several small companies. There’s Chromatin, which is developing plant mini-chromosomes. There’s Agrisoma in Canada working on engineered trait loci technology. And then there are the multinationals like Dow AgroSciences, Syngenta, and Monsanto, which are all using Chromatin technology to advance their pipelines. Most of these technologies have evolved from smaller companies, but it’s too expensive for them to move forward through the regulatory process on their own. So the multinationals help bring these technologies into the marketplace.”

We wondered about public perceptions, which have plagued agricultural biotechnology in the past. What are attitudes like now? Rudgers told Lorna, “It depends on the geography. In Europe, there’s still a lot of controversy around genetically modified products, even though farmers are having a difficult time producing and purchasing enough feed for their livestock. In most countries, such as the United States, there’s very little controversy these days. As we begin introducing traits that directly benefit society — like improving crop nutrition — I think we’re going to see further acceptance.”

Another issue that’s come up in the past couple years is the potential competition between food and potential biofuel crops for acreage. Which plants are the focus of these new technologies? Rudgers admitted that high on the list are the major US crops: corn and soybeans. “In the not-too-distant future,” he added, “we could be adding wheat to the list. We’re looking at rice mostly in Asia. As for biofuels, there is little competition at the moment. There has been some controversy over using corn as a biofuel crop, but that seems to be fading away. We’ll have to see how things play out, but it should be possible to use the new GMO crops for both fuel and feed.”

With all the technology involved, Lorna asked, “How is this going to affect the cost of food, particularly in underdeveloped countries?” The recent rice shortage comes to mind.

Rudgers answered, “These new technologies will help to introduce traits that allow for more food production on less land, which could help reduce to overall cost of food to the consumer. In addition, zinc-finger technology will reduce development time for developing new crops potentially by half. For example, instead of taking four years to develop a crop, it will now take two years. If we can produce crops more efficiently, the regulatory hurdles could be reduced, we could get crops approved faster, and that would be a substantial time and money saver. And if we cut a lot of time and money out of making

new products, that would benefit everybody.”

These new technologies could change the way agricultural biotech works overall. For example, Rudgers pointed to drought tolerance. “RNAi and zinc fingers can be used to regulate gene expression. For the first time, these technologies will allow us to produce crops and modulate the expression of specific native plant genes. Many plants already have drought tolerance genes, but it’s a matter of when and to what extent they are expressed. Using RNAi and zinc fingers, we can modulate these genes such that they are expressed to just the right level at just the right time, so plants can survive under drought conditions. Current technologies just can’t do that.”

RNAi is, of course, RNA interference, which is a recognizable concept to those on the pharmaceutical side of biotechnology. Its use in the above scenario is obvious. Zinc fingers are transcriptional factors, small proteins that fold into finger shapes because of a zinc ion in each one. A zinc finger recognizes a specific three-nucleotide DNA sequence, and scientists have learned how to design zinc-finger protein sequences to make them bind any given DNA sequence, so when linked together they can recognize longer, unique sequences. Add a functional domain — a nuclease, for example — and you can delete a gene. Then a cell’s repair machinery is either used to introduce a new sequence or simply allowed to knock out the gene.

“In 2008, Dow AgroSciences licensed zinc fingers for plant use,” said Rudgers, “from Sangamo Biosciences, which also has designed zinc fingers for use in mammalian systems.” The most common traits in development today include insect resistance and herbicide tolerance. Rudgers said the next generation will include stacked traits along with drought tolerance and nitrogen use traits. “Most products now are targeted for farmers. But in the near future, we will see products with increased nutrition targeted toward human health. Especially in Africa, there’s a big push to produce crops like cassava that have viral resistance and

with increased zinc and vitamin E so it’s more nutritious. That’s the main source of food for some people.”

Speaking of genetic traits and nutrition, Amanda Rinehart (marketing communications manager for Pioneer Hi-Bred) organized a session for the 2010 BIO International Convention called “Healthy Traits: They’re Finally Here.” For 15 years plant biotech providers have been discussing how biotechnology can help develop healthier foods — everything from vitamin-packed vegetables to soybean oil with a healthier fatty acid profile, and the first “consumer-oriented” products are coming to market soon. Early agricultural biotech traits were focused on “input traits” and agronomic benefits for growers, such as herbicide tolerance and pest resistance. This next generation of “output traits” involves development timelines of 8–10 years.

“This panel will educate the public on biotech traits with direct consumer benefits, as well as illustrate the business model and regulatory path for adoption,” Rinehart explained.

“Public and private researchers will preview the newest commercial traits and those still in the pipeline. Speakers will discuss the global regulatory environment for these high-value traits. And a dietician and food industry executive will share views on consumer demand and acceptance.”

Of course, genetically engineered foods have been at the center of much controversy. “Several organizations in addition to the agriculture industry have addressed this over the years,” Rinehart said. “These will be, GMO products and we hope ongoing dialogue regarding the safety of biotech products and the stringent regulatory process will help to educate the public on the benefits of agricultural biotechnology.”

Rinehart calls this the next step in ag-biotech. “The industry is excited about the launch of input biotechnology traits with benefits to everyone from farmers to consumers.”

**Wheat** is one crop that hasn’t yet received much biotech attention. Slow yield growth and competition with other crops for acreage have slowed its

advance in the second “green revolution.” Much of the industry has begun to call for renewed and escalating investment both in advanced breeding technologies and biotechnology to improve the crop’s sustainability. Alan Scarborough (industry relations manager at Bayer CropScience) organized a session for the 2010 BIO International Convention called “Wheat, Don’t Pass Me By: Opportunities for Biotech Solutions for Wheat” to address the opportunities and challenges ahead.

“There are some fairly immediate needs,” Scarborough told BPI contributing editor Lorna McLeod, “and a lot have to do either with weather tolerance and or disease resistance. Traditional breeding programs have been very successful, but they necessarily take a long time. New technologies include genetic engineering, but the first advances will use genetic markers to increase efficiency in the selection process. This is about sustainability. Crops developed with advanced technology should produce more yield on a given acre — and areas that aren’t as conducive to growing wheat might be able to in the future.”

Scarborough admits that “It’s hard to say what will come. Early objectives are likely to include drought tolerance, disease resistance, and more efficient use of nutrients. There also may be the potential for improving nutritional qualities.”

This session, Scarborough says, is “not a panel of proponents strictly, although a lot of people throughout the value chain and academia see technology as key to the future, and certainly the speakers will point out the positives as well as the barriers to bringing technology forward.” He plans for five speakers moderated by William Wilson, an economist from North Dakota State University. “He provides a very good presentation on the history of wheat, the economics, the global and trade aspects, and that’s a good way to start the session. We have Mark Darrington, a farmer a farmer from Idaho who will provide a grower’s perspective. Then we have Hayden Wands, who’s with Sara Lee

and is currently chairman of the commodity and agricultural policy group for the American Bakers' Association. And John Miller is president and CEO of a milling company in Bloomington, MN, to provide a miller's perspective. Dr. German Spangenberg from Australia, who's very renowned in transgenics and cellular biology, will also participate. He's also very familiar with cereals from a global perspective." A joint statement of support for this technology was signed last year by stakeholders in the United States, Canada, and Australia.

Some years ago, early steps were made with an herbicide-tolerant wheat, but commercialization was halted by market acceptance issues. A significant portion of the wheat value chain is considering what new technology can bring and over the next five to 10 years will thoughtfully discuss the potential. Scarborough explained that other crops are already clearly benefiting from biotechnology. "So wheat yields have not increased at nearly the same rate; in fact, US acreage has declined. Technology will help in those areas. Certainly there's competition for acreage from other crops, and that's had some impact. It will be a five- to 10-year process before any biotech traits are commercialized."

### **ETHICS, POLICY, AND GLOBAL ISSUES**

Among other things, 2009 will go down as a legendary year in the perennial US battle over health reform. Both health care and patent reform, along with overall changes in health care reimbursement, may dramatically affect drug, biologic, and medical device companies. Nikolas Burlew of Regulus Pharmaceutical Consulting organized a session for the 2010 BIO International Convention called "How Health Care and Patent Reform May Affect Pipeline Development for Drugs, Biologics, and Devices" to examine how development strategies should consider the risk of potential price controls/caps, perhaps price negotiation as in Europe.

"As we've initiated the discussion among people in both the pharma and device arenas, as well as university

tech transfer," Burlew told BPI contributing editor Lorna McLeod, "we've found a broad spectrum of responses to the specter of health-care reimbursement changes — everything from 'We haven't thought about it' to 'It's playing into our risk models and guiding what candidates come through our pipeline.'"

*Risk* is a word often heard in drug development these days. It's become a big part of decision-making at many companies. "I hope our discussion centers around, not just what the specific risks are, but how to apply a risk-based model to looking at these potential outcomes," he explained. "This is what I'm used to in a GMP environment: assessing severity, the likelihood of occurrence, and how to apply those tools to pipeline development strategies and evaluations."

It's not easy to do that, of course, when the health-care reform process has proceeded in fits and starts for a year. "That poses an enormous challenge," Burlew admitted. "But with any level of uncertainty, you have to make best guesses. When we judge risk, it's rare that we can say something will happen with 35% certainty, and we often don't have volumes of data to look at. On the process side, you consult subject matter experts. We will be fortunate enough in our session to have these experts: Patty Telgener, a reimbursement consultant, and Thomas Novelli, who's in federal affairs at the Medical Device Manufacturers Association (MDMA). They know what's going on, what's actually in the legislation, and they can help people understand the risks. What's the likelihood that controls will come with this round of legislation, or what's likely to follow in 12–18 months? There's no reason this will be the end of it."

Traditional models consider low, medium, and high likelihood and severity of outcomes. "Putting better resolution on it is challenging," Burlew explained. "If people stay plugged into what's going on and tap the expertise of reimbursement consultants, MDMA and PhRMA, who are looking very closely at these issues, then they should

## **POLICY CONVENTION SESSIONS**

### **Tuesday, 4 May 2010**

8:00–9:00 am

How Health Care and Patent Reform May Affect Pipeline Development for Drugs, Biologics and Devices

9:30–10:30 am

One Year Later: Comparative Effectiveness Research and the Government Role

2:00–3:30 pm

Bioethics: Synonymous With Good Business

4:00–5:30 pm

Commercializing Stem Cell-Based Therapies: Meeting FDA and Other Requirements

### **Wednesday, 5 May 2010**

8:00–9:30 am

"Is The Price Is Right?" and Other Mysteries of Government Pricing Revealed

2:00–3:30 pm

Globalize the Evidence, Localize the Decisions: Assessing the Value of Innovation and Improving Access to Novel Drugs

4:00–5:30 pm

The 111th Congress: What Happened in the First Session and What's to Come

### **Thursday, 6 May 2010**

8:00–9:30 am

Academia and Industry Interactions: The Role of Patents in Attracting Industry Interest in This Economy

be able to come up with a cogent risk assessment.

As of this writing, the legislation has yet to pass, and the election of Massachusetts senator Scott Brown threw a monkey wrench into the proceedings. By the time of the BIO convention, many hope current questions will have been settled one way or the other. Burlew said, "We will have an opportunity to infuse our presentations with the aftermath, hopefully by that point, of what really has come about. What lessons are learned by companies that either fail to or successfully implement risk-based approaches for their pipeline development in light of whatever legislation that's passed?"

Burlew has worked in the biotech industry for 17 years. He says pipeline development is of great concern in

## GLOBAL BIOTECHNOLOGY ISSUES SESSIONS AT THE CONVENTION

Sponsored by sanofi-aventis

### Tuesday, 4 May 2010

4:00–5:30 pm

The New Face of Orphan Drug Policy:  
Addressing Rare Diseases in the  
Developing World

8:00–9:30 am

Phony Drugs, Real Solutions: Practical  
Anti-Counterfeiting Considerations

### Wednesday, 5 May 2010

10:00–11:30 am

Pandemic Preparedness: Therapeutics  
Policy and Deployment

4:00–5:30 pm

The Aftermath: The Future of the Life  
Sciences Industries Beyond the Global  
Recession

### Thursday, 6 May 2010

10:00–11:30 am

Biotechnology and Global Health: The  
View From Europe

2:00–3:30 pm

Going Global Overnight? Do's and  
Don'ts of Expansion in Emerging  
Markets

2:00–3:30 pm

Beyond the Horizon: Tearing Down  
Borders to Forge Alliances Between  
Biotech Clusters

these trying economic times.

“Everyone's trying to cut costs. A ‘risk-based approach’ is now on the lips of everyone in the pharmaceutical industry, as it should be — and has been in other industries for years.”

They too may be looking for optimization and best practices in this economic environment, but most other industries aren't facing the threat of legislation that could effectively cap their profits.

“The chair of our session is Paul Wilkinson,” Burlew said, “a consultant who's spent many years in drug development. We also have Jim Cloar (an executive with Medtronic in the device arena) and David Poticha (a senior licensing manager with Colorado University Denver's tech transfer office). Healthcare reimbursement is not the only area of possible reform to affect the pharmaceutical and medical device industries. The USPTO has been struggling with severe shortages in

personnel while pending patent reform legislation adds uncertainty into the decision making of innovator and generics companies alike. David will speak to these issues and their impact on pipeline development.”

#### Environmental Issues:

Pharmaceutical companies use “lean manufacturing” and six sigma methodologies to increase product quality and decrease process waste. Meanwhile, many industries are seeing tangible and significant cost benefits of environmentally sustainable operations, including green chemistry, water and energy optimization, and decrease of solid waste. The same culture of improvement is useful for both endeavors. Adherence to the highest environmental standards (ISO 14001) are becoming more attractive to companies looking to raise their public image and improve costs, eliminate needless waste, lower carbon footprints — not to mention simply respecting the environment. That alone can engender good will from the public, empower employees with pride in their companies, and ensure compliance with environmental regulations. All these concepts are complementary and can help companies achieve competitive advantages.

Paul Marshall (senior vice president of operations for Amylin Pharmaceuticals) organized a session for the 2010 BIO International Convention called “Operational Excellence and Sustainability in a Competitive World” to discuss how environmental sustainability complements good business. The former, he told BPI contributing editor Lorna McLeod is defined by the United Nations as meeting the needs of the present without compromising the ability of future generations to meet their needs. Many companies use the term in a wider sense to mean environmental, social, and economic endurance. “I like the simplest one,” Marshall said, “which is ‘the capacity to endure.’ Sustainability is not a stand-alone concept; it's part of an overall management culture. As Amylin adopted tools and techniques of operational excellence and environmental excellence, we noticed unexpected but welcome collateral

benefits to our organization. If you generate a collective of smart people who constantly think of ways to improve — and give them the tools of improvement — then the parts of the business it applies to are nearly unlimited.”

Many companies face cultural barriers when it comes to environmental considerations, especially in tough economic times. Marshall counters, “Often, difficult times introduce opportunity. The industry is currently in crisis. As we biologists know, during significant environmental change, those who adapt the best will reap competitive advantages. Much is being written right now about changing operating models in our industry, and cultural shifts typically revolve around people. Knowing what to do is important, but getting people to want to do it is another matter. One technique is to make sure they understand the need for change — and that a sustainable business model will lead to greater things for the company, the products we make, the patients we serve, and thus our own job satisfaction.”

Marshall says the time is now for sustainable business in the pharmaceutical industry. “Due to the global financial crisis, two trends have emerged: mergers and the move away from vertical integration. Both are driven by a need for business sustainability. Larger companies are looking to bridge pipeline gaps through acquisition of products and companies. I question the long-term sustainability of this unless significant in-roads are made in pipeline development, but it does buy them some time. The second trend is the move from FIPcos (fully integrated pharmaceutical companies) to FIPnets (fully integrated pharmaceutical networks).”

Much is being written about that, Marshall says, but the premise is simple: “Direct the right resources to the right items of expertise in a highly networked and collaborative way. At Amylin, we constantly identify the capabilities we need to build or retain internally versus simply having the competencies in a knowledge area (but relying on someone else's capability).

Doing this well conserves cash, optimizes success, and fosters an environment of collaboration. This simple principle governs our decision-making. Companies that have not done it historically but wish to do so may have very high cultural hurdles to clear internally.”

The Dow Jones Sustainability Index (DJSI) lists companies across all industries that have learned to operate in this new way. Most have a history of succeeding in business environments with low profit margins and lots of competition, Marshall says. Creativity, focusing on sustainability, and constant awareness of the bottom line represents good business for them. They lead in energy conservation, in reduction of emissions and solid waste, and in fulfilling public environmental commitments. For this session, he specifically looked for representatives of biotech companies that have distinguished themselves by deploying a program of total improvement. “Objectively, I selected those known for their operational excellence programs and achieving ISO 14001 certification. Two speakers for my session are from Baxter Bioscience (Raphael Picardo, vice president of manufacturing) and Bayer Healthcare (Edgar Sur, director of supply chain operational excellence).”

In this difficult business environment, Marshall told Lorna, these approaches are paying off. “Good problem solving teams use the tools of improvement not only to improve the quality of their operations, but also to increase safety in their working environment, conserve energy, reduce emissions, increase the use of recyclables, and decrease solid waste. In short, it’s good business.”

#### **Ethical and International Issues:**

The applications of biotechnology often raise controversial ethical issues. Some companies have developed strategies to address these issues responsibly. Those adopting policies of transparency and responsibility should thrive as their science moves forward.

Under the current system, some people say pharmaceutical companies support only those products that can yield the biggest return, even if they’re

not likely to help patients worldwide. Critics claim that pharmaceutical companies are far more interested in producing Viagra, for example, than filling unmet medical needs. Others point to the high costs of research and development (R&D) and the critical importance of blockbuster drugs to the future of less-profitable drugs and technologies. Without the former, goes the argument, the latter isn’t possible. Jennifer E. Miller (executive director of Bioethics International) organized a session for the 2010 BIO International Convention called “Ethics and Biopharmaceutical R&D: Who Should Be Responsible for Tomorrow’s Drugs?”

Industry panelists will identify ethical challenges involved in pharmaceutical R&D “including balancing the interests of public health, innovation, and corporate sustainability.” Panelists will ask the difficult and critical questions of “Are these the best R&D decisions companies can make for domestic and global public health? Are these innovations priced optimally? It’s great to have new innovations and drugs, but if few can afford/access those drugs, well that’s another critical consideration.” Panelists will explore if and how the necessity for return-on-investments (ROI) and fulfilling unmet medical needs are aligned. Miller, a bioethicist, along with Stephen Latham, Deputy Director of Yale’s Interdisciplinary Center for Bioethics and Yale will discuss ethical frameworks and best practices for managing competing and varied interests in global R&D.

Miller will have Richard C. Hubbard, of Pfizer, Mark Feinberg, of Merck, Robert Baughman, of MannKind Corporation and Stephen Latham discuss these issues on the panel, which is a follow-up to a United Nations affiliated one she hosted during summer 2008. “We discussed the Orphan Drug Act and who should be responsible for paying for drugs on the UN affiliate panel. I’m encouraged that BIO has decided to tackle this issue. If we do not prioritize certain treatments and optimize access, we end up with sicker people and more

deaths around the world. It’s courageous and admirable of the industry to really take a look at this. They’re willing to explore how to make the best products that are affordable and accessible. It’s a complex issue because vaccines and drugs can require a lot of upfront investment.”

Miller says both the industry and the public need to be aware of how those costs are built in to the products that make it to market. “As much as a company might want to provide a drug for a lower cost, that could stifle overall innovation. We work extensively with educating both the industry and the public, which is critical for the industry. It’s also a trust issue, particularly in the United States, where interestingly an industry of helping and healing and curing people is seen as untrustworthy and profit driven. In one poll, just 11% of the US population called pharmaceutical companies generally honest and trustworthy — ranking them barely above the tobacco and oil industries! R&D prioritizations not only affect public health and individual lives, but also the company bottom line and public trust — which are essential to industry and company sustainability.”

Talking to a BIO audience may be seen as preaching to the choir, but Miller says the need for education goes both ways. “Trust must be earned and its synonymous with ethics. People trust ethical companies. However, it’s hard for companies and the industry itself to say, ‘Trust us, we are trustworthy.’ You need a third party to assess trustworthiness, aka a companies’ ethics, and to communicate the efforts to the public. Bioethics International formed the World Council for Ethical Standards. Participants include Merck and Pfizer representatives — nonvoting because they’re industry, former FDA commissioners and AARP executives, healthcare providers from diverse specialties, ethicists, patient advocacy and disease groups such as Susan G. Komen for the Cure, all collaborating with myself and G. Steven Burrill, our chairman, to tackle the most critical of ethical issues affecting innovation,

## INTERNATIONAL CASE STUDIES SESSIONS AT THE CONVENTION

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### Monday, 3 May 2010

2:00–2:45 pm

Taiwan's Biotech Industry Development  
Outlook to 2014: Research Focus, Policy  
Formulation, Funds and Growth  
Opportunities

3:00–3:45 pm

(Russia) From Bioeducation to  
Bionanotechnology

4:00–4:45 pm

(UK) Lost in Translation: Translational  
R&D as the Road Map to Market

### Tuesday, 4 May 2010

8:00–8:45 am

Beyond Classical Diagnostics:  
Breakthroughs in Molecular Diagnostics  
and Biomarkers from Germany

9:00–9:45 am

From Regional to Global: Open  
Innovation Giving Boost to Japanese Bio  
SMEs

1:15–2:00 pm

Competitive Cooperation: How  
Partnerships Drive Life Sciences in The  
Netherlands

2:15–3:00 pm

Emerging Trends and Issues for  
Commercial Biotechnology Expansion in  
Mexico

3:15–4:00 pm

Innovative Structures to Enable Fruition  
of Life Sciences Companies in Israel

### Wednesday, 5 May 2010

8:00–8:45 am

A Thai-US Joint Venture: Antibody Array  
— Future Screening for Food Safety

9:00–9:45 am

Role of Indian Biotech Industry in  
Promoting Global health

10:00–10:45 am

Plaques, Tangles and Beyond:  
Therapeutic and Diagnostics Avenues  
for Neurodegenerative Diseases in Spain

11:00–11:45 am

Innovative Platforms for Binding Protein  
Therapeutics

2:00–2:45 pm

Monoclonal Therapeutic Proteins,  
including Antibodies: New Challenges

3:00–3:45 pm

The Global Innovation Network

4:00–4:45 pm

BR Biotech Brasil: A Brazilian Biotech  
Overview

public health, access, lives, quality, and the like and to draft ethical standards. We've developed the concept of an 'ethics seal,' which will represent the ethical standards. The seal will be a way to both encourage a demonstrative commitment to ethical behaviors and to communicate this commitment to the public. This might be the largest public and industry education and ethics quality improvement initiative to date in the United States." And, she says, it's just beginning.

Miller concluded that companies sometimes decide against certain development projects because they represent formidable (and expensive) scientific challenges. "Solving those problems requires major investment," she concluded. But the science problems, prioritization challenges, and distribution issues are solvable. The industry would do well to maintain transparency and dialog with the public while it puts its best efforts forward.

One way some of those problems can be solved is through the assistance of biotechnology economic development initiatives. Nancy Levy (managing partner of Biohealth Management) organized a session for the 2010 BIO International Convention called "Thinking Beyond the Horizon: Tearing Down Geographic Borders to Forge New Alliances Between Biotech Clusters" to discuss differences and innovative ways to increase their success. Biotech clusters in the United States are often thought of as more successful than their European counterparts. Supporting that success are the many scientists who both own their innovations and understand the value of commercialization. US entrepreneurs also have access to risk-taking investors, and the US public is more positive about biotechnology. Europe's own advantages are not so well documented.

Levy told BPI contributing editor Lorna McLeod, "We're really looking to help these organized clusters in Europe take advantage of their association together, then create value by connecting them with other clusters globally. There's a lot of interest in going global, in understanding how

other areas of the world work. What gets in the way is often cultural: If we're used to how we do things, sometimes it's hard to embrace new ways of thinking. Risk-taking is a good example. In Europe, that kind of entrepreneurialism is less common because failure is not highly accepted; whereas in the United States, failed entrepreneurs are supported, and they usually go on and try again." In many ways, the country itself was built on the willingness to take risk.

Levy says a big part of this kind of globalism is helping others feel more comfortable in those situations, and then build up. "Right now, the Europeans have a couple areas where they need support," she went on. "One is financing, and the second has to do with management — two areas people in the United States can help with. Financing goes back to the risk-taking I just mentioned. US entrepreneurs who've made a lot of money often go back and invest it into other companies, so there's an ongoing source of finance. That's not the case in Europe. And there isn't a lot of management there either. But the United States can look to Europe for a lot of technology. Their science and innovation is world-class, so we can look at them for strong partnerships with very strong scientists in Europe. I see it as a winning scenario for both sides."

One thing that's held back entrepreneurialism in Europe is that many scientists there don't own the results of their work. "So they haven't had a real incentive to go and commercialize it," said Levy. "In some countries they do, in some they don't. But the academics themselves are very strong." Technology transfer has been slower. Levy says many Europeans are now starting to build bridges between industry and academia, with Germany and Switzerland leading the way. The United Kingdom is following close on their heels, and the Latin countries — France, Spain, and Italy — are beginning to catch up. Levy's consultancy has supported companies from bioclusters in Italy and Canada working with others in Boston and elsewhere in the United States.

Traditionally, they have been more

interested in science for its own sake, but that is changing. “How do we capture that?” Levy asked. Her panel’s speakers will address that question. They include Lita Nelsen (head of technology transfer at MIT) who represents the powerhouse Boston biotech cluster. “This panel offers Europeans and Americans an opportunity to see what has worked and what hasn’t worked, how to explore new avenues of collaboration. We want to come up with some ideas that we can measure through the year to come, and possibly have a follow-up meeting in the fall.” Then at next year’s BIO International Convention, they could see what worked and what didn’t. “It could be incredibly valuable,” Levy said. “Nothing works perfectly. We should be able to come up with ideas that work well — and some that don’t. We just have to figure out how to get people working together.”

It’s another sign of the traditional “silo” mentality breaking down. “Siloed pharmaceutical companies are giving up that model,” said Levy. “Scientists weren’t always educated to collaborate either, but now they really need to do that. That way we come up with better drugs, better devices, and better diagnostics faster — by working together as a team.” Economic factors are pushing the whole industry in this direction. As Levy put it, “Why should we be reinventing things if they’ve already been developed? These economic factors are important to the pharmaceutical companies, themselves. And if we have a good handle on where things are, then we expedite it. They don’t care whether something is created in the United States or Europe — or both.”

This could lead to some new and different business models. “One could hope, over the next 10 years,” Levy said. “These organizations need to see that economic development isn’t necessarily just about getting things financed in their own region. A lot of companies come to the United States to develop their technologies because there’s more financing available and capabilities. But that doesn’t mean they can’t go back home once they get to a certain place. Let’s get them moving so

that they can attain certain milestones.”

And big (bio)pharma also has a part to play. “We can look at them as the organizations that do the clinical development, sales and marketing,” said Levy, “if they get their innovation from smaller biotechnology companies. That allows them access to more well-developed technologies. So I hope they will continue to support biotech, which they’ve always done. In Europe, a lot of medium-sized privately held biopharmaceutical companies also need to evolve. And I’m hoping that they’ll also recognize the advantage of working with these clusters over there, over here, and elsewhere. That’s a whole other BIO panel I’d like to do next year. I think it’s another area where growth needs to occur.” 🌐

**Cheryl Scott** is senior technical editor, and **Lorna D. McLeod** is a contributing editor to BioProcess International.