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NOVEMBER 8/15, 2010 • \$12.00 U.S., \$15 ELSEWHERE • PMA 40063731

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# Industrial Biotechnology

## Turning Process Engineering into Profits

The promise of producing chemicals from renewable feedstocks is becoming a reality thanks to advances in metabolic engineering and process development. Several bio-based plastics are already being produced at commercial scale, and many biochemical firms are in the late stages of process development. The introduction of lower-cost, biobased versions of existing chemicals and promising new platform chemicals could help the ag-rich U.S. stay competitive in the global marketplace.

**E**xecutives expect chemicals produced via bioprocesses to eventually replace at least 15% of the current chemical production base, although levels of penetration and timelines vary greatly. The fact that many bioprocesses are already cheaper than equivalent petroleum-based production leaves only the challenge of bringing large-scale units online and waiting out the lifetime of embedded petrochemical production capacity as obstacles, executives say. The implementation of cost-competitive bioprocesses also promises to bolster the U.S. chemical industry, which has been increasingly losing investment to the cost-advantaged Mideast region.

McKinsey & Company (New York City) predicts the global biobased chemicals and pharmaceuticals market will reach \$220 billion-\$430 billion by 2020, up from \$100 billion in 2008 and eclipsing the projected \$180 billion in biofuels revenues by 2020.

Unfortunately, commercialization of industrial biotech processes has been

"slightly" behind projections, says Volkert Claassen, v.p./white biotechnology at DSM. The problem is not so much due to process development, but has more to do with the recent economic downturn, he says. "There's a lot of technology ready to be implemented, but we have seen some hesitation to make investment decisions."

Finding financing for biochemical development faces several hurdles, says Nicolas Denis, a partner in McKinsey & Company's sustainability and resource productivity practice. The chemical industry is focused on cost, and biochemicals do not benefit from the same level of government support as biofuels, he says. Investors tend to adopt a "wait-and-see" approach, and "every step in the development of these processes tend to take a couple of quarters," Denis says.

Still, the industry is poised to make significant headway, and some executives predict as much as 20% of the chemical industry will be biobased by 2020.

For industrial biotechnology to be

successful, companies must meet a combination of market demands and technology advances, especially the ability to effectively scale-up the process, says Stephen Gatto, founder, chairman and CEO of biochemical firm Myriant Technologies. "As we see successes in metabolic engineering and directed evolution, organisms are being adapted in ways that 10 years ago we couldn't think of," he says. "What will make and break these businesses is not just being able to create a bug that does something great, but how you introduce that into a system so that the product meets quality specifications and price points, and can be delivered at a scale that is commensurate with the current market dynamics."

Myriant has developed a system that genetically modifies E-coli bacterium, yeast, thermophiles and other microbial hosts through the chromosome and not just the cell wall, making the resulting organism much more stable at large-scale production. The company expects to begin

construction later this year on a commercial-scale biobased succinic acid plant at Lake Providence, LA. The plant will initially produce 30 million lbs/year, using locally sourced sorghum, and will be scaled up to 170 million lbs/year in the following couple of years, Gatto says.

Myriant's production technology will spur market applications for succinic acid, Gatto says. The company's first target markets are chemicals made from butanediol, such as spandex fibers, and as a substitute for adipic acid in polyurethanes production, both high-volume markets. Nearly all of the site's initial 30 million lbs/year has already been contracted out, he says. The company also will eventually be able to commercialize succinic acid-based polymers. "Overall, we see succinic acid as having a potential market total of about 8 billion lbs/year in all applications."

Succinic acid can be used in place of high-volume chemicals such as 1,4-butanediol (BDO), but the high cost of producing succinic acid from petroleum-based feedstocks has kept the market small. That potential has attracted investment plans from large chemical companies, including BASF, DSM, and DuPont. BASF and Purac, the lactic acid subsidiary of food ingredients firm CSM (Amsterdam), last year formed a partnership to produce succinic acid from renewable raw materials.

DSM and DuPont entered into separate biosuccinic acid agreements this past summer. DuPont Applied Sciences licensed certain technologies related to the processing of biosuccinic acid derivatives to Bioamber (Pomacle, France), a JV with DNP Green Technology (Princeton, NJ), and Agro-Industrie Recherches et Développements (Pomacle). The deal gives DuPont the right of first refusal to source product from any future commercial plants using the technology. DuPont also operates a 100 million lbs/year biobased 1,3-propanediol (PDO) plant at Loudon, TN through its joint venture with Tate & Lyle. The PDO is used in apparel, residential flooring, sporting goods, personal care and household products, and automotive. Bioamber operates a 2,000 m.t./year biosuccinic acid plant at Pomacle, using wheat-derived glucose as feedstock.

DSM announced an equally owned JV in June with Roquette Frères (Lestrem, France) to produce succinic acid using starch feedstock. The agreement follows a three-year collaboration between the two companies for the development of fermenta-

tion technology to make biosuccinic acid. The companies operate a demonstration plant at Lestrem, where Roquette operates Europe's largest biorefinery. The 300 m.t./year unit started earlier this year, and the decision to boost the site's output by at least a factor of ten is "in the very near future," Claassen says.



SCHILLING: Biobased routes to chemicals with existing markets.

DSM is seeing a lot of interest in biosuccinic acid, particularly on the material side, but also as a butanediol replacement, Claassen says. DSM is targeting applications such as polybutylene succinate, a plastic that could be used as a substitute for petroleum-based commodity plastics, replacement of adipic acid in polyurethanes production, and various other applications. DSM's yeast-based production system produces high-quality biosuccinic acid necessary for such applications, and delivers superior environmental performance by sequestering carbon dioxide within the molecule.

Other biobased chemicals produced by DSM include a long-chain polyamide and other biobased nylons. DSM's industrial biotechnology business is also developing yeasts and enzymes to bring down the cost of cellulosic ethanol, advances that also could yield enormous cost advantages in developing biochemicals from cellulosic materials. "The ultimate goal is to use yeast and enzymes not only for second-generation biofuels but also for more valuable compounds beyond bioethanol," Claassen says. DSM and Abengoa Bioenergy (Madrid), which already manufactures biofuels and has expertise in areas including pre-treatment of biomass, are developing enzymes and yeast that by 2012 will have significantly improved the cost position of cellulose.

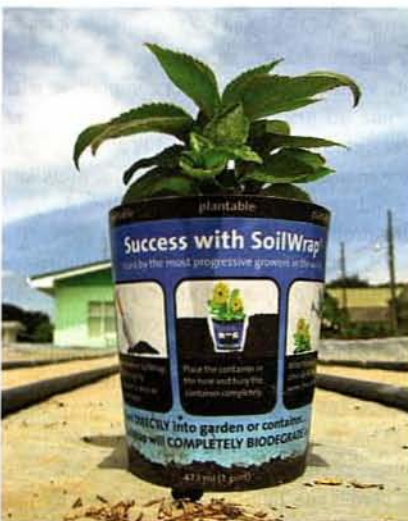
While producers of biosuccinic acid expect the introduction of a low-cost production method to greatly expand the global succinic acid market, other firms, like Genomatica, are looking to develop biobased routes to chemicals that already have an established, high-volume market. Genomatica announced last June that it has achieved pilot-scale production of biobased BDO. CEO and founder Christophe Schilling says he expects to have a demon-

stration-scale unit operational next year and commercial-scale production by the end of 2013. The global market for BDO is about \$3 billion, with a global capacity of about 3.2 million lbs.

Founded in 2000, Genomatica has been solely committed to developing bio-based chemicals for about four years, Schilling says. Unlike biofuels, the company knew it could produce biobased chemicals including BDO that do not require government incentives to be profitable. "We felt that [producing chemicals] brings a great blend of both large market volume and attractive margin opportunity that differentiates it from biofuels. We don't have to rely on government subsidies in order to create a market for our technology to one day be competitive without them," he says. At current sugar prices, Genomatica's BDO is competitive with petroleum-based BDO at oil prices of \$40/bbl and above, and consensus forecasts for sugar and oil prices indicate a continued, long-term advantage.

Genomatica also has intellectual property covering the production of 25 other basic and intermediate chemicals, including major nylon intermediates, from renewable sources. Similar to the decision to focus on BDO, the selection of the next product to commercialize will require that chemical have an established and growing market. "We make sure we can do it at a lower cost, and then leverage the fact that it's a renewable to gain market entry," Schilling says.

Overall, Schilling is bullish on the market potential for industrial biotech. "There's obviously growing consumer demand for renewable chemicals. These biomannu-



SOIL WRAP: Metabolix is targeting agricultural applications where biodegradability adds value.



**SCALING UP:** Genomatica is producing bio-BDO in 3,000-liter fermentation tanks.

turing processes deliver competitive, if not advantaged, cost structure for major intermediate and basic chemicals," he says.

Damien Perriman, v.p./business development at Verdezyne (Carlsbad, CA), says cost-competitive biochemicals with the same performance could overtake petrochemicals in some cases, up to 60%-70% of certain markets depending on the chemical. Verdezyne has developed a metabolic pathway in yeast that produces adipic acid in a single-step fermentation process from plant-based oils, paraffins, and sugars. The company is planning to begin a pilot plant using plant-based oils next year, with sugar fermentation work to begin by the end of the 2011, Perriman says.

The feedstock flexibility and low cost of Verdezyne's process, as well as the existence of an established market for adipic acid, are key elements to successfully commercializing a biobased product, Perriman says. Using crude coconut oil and palm kernel oil, Verdezyne's process is competitive with crude oil prices of \$60-\$70/bbl or higher, Perriman says. Adipic acid is a key precursor to polyamide, polyurethanes, diols and certain amines, and about 5 billion lbs/year are produced globally, Perriman says. "It's used today, people are very comfortable with it, its properties are very well understood, and there isn't the commercial risk that comes with launching a new chemical," he says. With products like biosuccinic acid, where the existing market is "miniscule," extensive testing must be done before customers can adopt it.

Verdezyne has been approached by just about all petroleum-based adipic acid producers, Perriman says. "Some see it as an exciting future prospect, others see it as

a threat to what they're doing," he says. Asian agricultural oil processors have been particularly interested, inquiring about co-locating Verdezyne fermentation units at their facilities, even at small-scale and with rapid deployment, Perriman says. "While chemical giants like Dow Chemical, BASF, and DuPont have traditionally been the custodians of innovation, we're seeing a real desire from our Asian colleagues to be at the forefront of this technology."

Overall, the chemical industry's attitude toward renewables has turned the corner, says Jim Stoppert, CEO of Rivertop Renewables (Missoula, MT). "In 2001, 2002 when I approached chemical companies with renewable-based technologies their response was, 'I don't think it's ever going to happen.'" Now that the technology has been proven, chemical companies are welcoming an alternative source of feedstock. "Soon the only barrier to investment will be embedded petroleum-based assets, which will continue to run as long as there's incremental profit to be made," he says. Stoppert also co-founded the bioplastics joint venture between Cargill and Dow now known as NatureWorks; incubated several renewable chemical firms including Elevance and BiOH; and was the first CEO of Segetis.

Stoppert expects 15% of the global chemical industry to be biobased by 2020. But in the meantime producers must develop the technology to bring down the processing costs. "We already have low-cost feedstocks, which will get even cheaper as we move into cellulose," the "holy grail" of industrial biotechnology, Stoppert says. However, a biochemical industry can develop without cellulose by finding market applications developing novel products from other sources of sugar, he adds.

Rivertop has developed a catalytic oxidation to make glucaric acid from glucose. While the current market for glucaric acid is very minor, "it has huge potential," Stoppert says. Rivertop is initially marketing glucaric as a drop-in replacement for phosphates in detergents, a \$10 billion market. The U.S. banned phosphates in automatic dishwasher detergents last year, and earlier this month

the European Commission proposed restricting phosphates and phosphorus-containing compounds in all domestic laundry detergents across the European Union. Phosphates are blamed for stimulating algae growth, which in turn reduces oxygen supply for other aquatic life.

Glucaric acid also has corrosion inhibition properties, and Rivertop expects to build a market presence in applications such as cooling towers and boilers. Glucaric acid can also be polymerized, although commercializing a polymer is probably 5-7 years away, Stoppert says. Rivertop aims to have a commercial-plant on the order of 60 million lbs/year operational by 2013. "Penetration of renewables is limited by the extent technology can deliver cost-competitive performance," says Elevance CEO K'Lynne Johnson. "We are at cost parity or are advantaged in the streams we produce. In specialty chemicals, the threshold determiner is whether the renewable delivers functionality, and for that functionality, if the value cost-compelling." Elevance's biorefinery technology converts the triglycerides and fatty acids found in natural oils into multiple streams, including internal and alpha olefins, oleochemical fragments, standard oleochemicals, and chemical intermediates such as C18 dicarboxylic acids and esters at purity levels sufficient for applications in specialty nylons, powder coatings, and polymers.

Elevance currently has 13,000-14,000 m.t./year manufacturing capacity, which will increase more than 10-fold by 2012 through a joint venture deal with agribusiness giant Wilmar International (Singapore). The JV is building a biorefinery at Wilmar's Surayaba, Indonesia complex using renewable oil feedstocks such as palm, mustard, soybean, jatropha, and waste oil. It will be the company's first commercial-scale facility. The deal was signed in July, just over two years after Elevance was spun out of Cargill, Johnson says. The company is also in the "process of finalizing" the acquisition and conversion of an undisclosed biodiesel asset.

## BIOPLASTICS

While biobased chemicals such as glucaric acid and succinic acid are being produced only at small scale, many bioplastics producers such as Braskem, NatureWorks, and Metabolix are already in the market with commercial-scale quantities.

Metabolix (Cambridge, MA), founded in 1992 on PHA platform chemistry licensed



**JOHNSON:** Renewables must deliver functionality, be cost-competitive.

from MIT, is one of the few companies with a commercial-scale industrial biotechnology process. The company has formed a 50:50 joint venture with ADM to commercialize PHA resins based on a 110 million lb/year manufacturing facility at Clinton, IA. The resin, trade-named Mirel, can be used in film, thermoforming, injection-molding, and sheet products, and the company is doing development work in foam, paper coatings, and nonwovens. Mirel can replace polypropylene (PP), polystyrene (PS), and various forms of polyethylene (PE), but Metabolix is targeting end markets where Mirel's biodegradability is a key performance attribute, such as agricultural applications such as mulch films, compost bags, marine and aquatic applications, says CEO Rick Eno.

The Clinton plant took three years and more than \$300 million to build, with start-up beginning earlier this year. The plant is expandable to 400 million lbs/year, and Metabolix says it is currently evaluating options to increase its capacity. ADM owns the facility and provides feedstock sugar from an adjacent wet mill. Initial profits go to ADM, which fronted the capital to build the plant. The partners ultimately will split the profits equally. Metabolix is also applying PHA chemistry to the C4 chemical value chain to find new routes to gamma-butyrolactone (GBL) and pyrrolidones, chemicals downstream from BDO with a combined market value of about \$800 million annually.

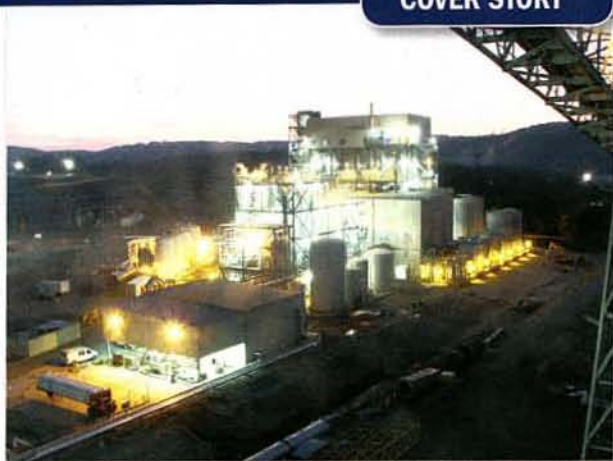
"Metabolix is unique in pursuing product lines in both drop-in chemical replacements, such as our C4 chemicals activities, and a unique plastic, and the commercial strategy for each varies greatly," Eno says. With Mirel, the company does not intend to be at price parity with PP, PE, or PS because its biodegradability provides a physical property that defines its downstream applications. "It's a market-driven strategy," Eno says. "However, in commercializing a biobased chemical that is already produced at large scale by the petroleum-based chemical industry, such as GBL and pyrrolidones, the company is employing a cost-based strategy. For drop-in molecules it's all based on cost. Some people point to a biobased premium, but we're not counting on it in our commercialization strategy. We want to be competitive without it," he says. Metabolix is estimating its C4 chemicals process is cost-competitive with petroleum-based processes at \$60-\$70/bbl oil.

A unique molecule takes longer to

develop—the company had been developing its PHA production technology since the 1990's—but finding the right segment can yield very good returns, Eno says. Biobased versions of existing chemicals are not without their own challenges, with producers having to deal with removing impurities not found in petroleum-based processes, Eno says. "But that's typically a smaller hurdle to overcome than the commercialization of an entire new family of materials."

Metabolix is also engineering metabolic pathways in plants to express chemicals of interest, primarily poly-3-hydroxybutyrate (PHB), part of the PHA family and a base chemical from which propylene, acrylic acid, and maleic anhydride can be derived. PHAs are found in plants as a carbon reserve but at levels that are nearly undetectable. The company is working to increase these yields in camelina, sugarcane, and switchgrass.

NatureWorks is also among the first wave of firms to reach commercial scale. The company produces PLA-based resin, trade-named Ingeo, from sugar in about 20 different grades. The company has 140,000 tons/year of capacity, all at its Blair, NE location, and is assessing locations for a second plant, potentially in Asia, says Steve Davies, director of marketing and public affairs. Demand for biobased resin is



**NOVEL GROWTH:** DuPont is expanding biobased PDO capacity by 35% at the Loudon, TN site operated by its JV with Tate & Lyle.

growing 20%-30%/year, and the company predicts it will sell out in 2013 or 2014.

Overall, NatureWorks says the potential market for biobased plastics to be roughly 26 million tons out of the broader plastics market. "If you add up all of the bioplastic producers operating today, we're at less than 500,000 tons," Davies says.

The company started up the Blair site in 2002, the world's first and still the world's largest bioplastics plant. "One of the reasons NatureWorks has been successful is because [we] built big to get a commanding economy of scale," Davies says. The company targets diverse markets, including both fibers resins and plastics, by tailoring Ingeo resin grades to make it as easy as possible for the various resin processors to make the switch, he says.

NatureWorks also developed relationships further down the supply chain from resin processors to create some pull from consumer product companies. The company has deals with Walmart, Frito-Lay, and Coca-Cola to include Ingeo in product

## BIOTECH BOOM WILL HELP ABATE STEEP U.S. JOB LOSSES

Industrial biotechnology is expected to be a new driver of jobs in the U.S. chemical industry, which has suffered significant declines in employment as the global production base moves to the feedstock-advantaged Mideast.

According to the Biotechnology Industry Association (BIO; Washington, DC), chemical jobs in the U.S. have declined 20% since 1990, to 800,000 in 2009. Plastics shed 12%, or 116,000 jobs, in the last seven years alone. The development of a biobased chemicals industry could create tens of thousands of jobs in the U.S. in the next five years alone, BIO says.

"Industrial biotechnology has the potential to reinvigorate the U.S. chemical industry," says Metabolix CEO Rick Eno. "The U.S. is already

the innovation leader in industrial biotech, and the chemical industry infrastructure and workforce here is well-suited to commercialization of these products. As a country, we would be amiss to let this opportunity pass us by." Through a joint venture with ADM, Metabolix produce sbioplastics at Clinton, IA with feedstock from an adjacent wet corn mill.

The U.S., with the world's largest amount of arable land, can also leverage its considerable agriculture advantage. However, to foster growth in biochemicals, federal policy should provide strong support for R&D, including grants for biorefineries and tax incentives for pioneering commercial production, BIO says.

—REBECCA COONS



**BIOBASED APP:** NatureWorks's PLA-based resins are being used in iPhone and iPod covers.

packaging. Food packaging and food serviceware are Ingeo's largest end markets, but NatureWorks also recently developed resin grades suitable for nonwoven fiber applications and durables. At the resin level, Ingeo's cost compared with petroleum-based resins typically ranges from parity to plus-20%, and, in many cases, brands are willing to absorb the slight cost difference and leverage its use of Ingeo in its products to get more shelf space, Davies says.

NatureWorks also recently signed a deal with Avantium (Amsterdam) to develop the commercial potential of Avantium's furan-

based polymers. NatureWorks will be conducting in-house testing for a range of applications including personal electronics, automotive, fibers, and other engineering plastics applications.

Meanwhile, large petrochemical companies are adding bioplastics to their portfolios, often by partnering with biotech startups. In April, Futero, a 50-50 joint venture between Galactic (Brussels) and Total Petrochemicals, inaugurated a 1,500 m.t./year PLA pilot plant at Escanaffles, Belgium using renewable vegetable sources. Futero is the first company to operate this type of unit in Europe. "Futero will allow us to diversify to an even greater degree with regard to the raw materials used in the production of our plastics," says François Cornélis, vice chairman of the executive committee and president/chemicals at Total.

Arkema and Purac signed an agreement in September to jointly develop lactide-based block copolymers that will enhance the properties of PLA. The copolymers, produced using Arkema's organic catalysis

ring-opening polymerization technology and Purac's L- and D-lactide monomers, will improve the thermal resistance and impact strength of PLA, the firms say.

Biobased versions of commodity plastics are also being produced on a commercial-scale, although they are not biodegradable like PLA and PHA. Using sugarcane as feedstock, Braskem last September started production at its \$278-million ethanol-to-ethylene plant at Triunfo, Brazil. The 200,000 m.t./year ethylene produced at the site will be converted into PE at existing plants in the Triunfo complex. Braskem also announced plans last month to invest \$100 million to build a commercial-scale propylene plant in Brazil also using sugarcane-derived ethanol as a feedstock. The propylene will be used to produce PP. Company officials say they expect to complete basic engineering in 2011, and for the unit to be operational in the second half of 2013. The plant will have a minimum capacity of 30,000 m.t./year. Site location was not disclosed.

—REBECCA COONS

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