More Than a Feeling

West Coast Flavor Forum addresses food science's critics and the right-to-know movement, and highlights the promise of genetic modification, biotech and other technologies.

Jeb Gleason-Allured, Editor in Chief

The Pew Charitable Trusts has recently increased its scrutiny of food additives, including the GRAS process. Though naturalness has no direct correlation to safety, John Hallagan, senior advisor to Verto Solutions, noted that "natural" is a consumer awareness and preference issue. Meanwhile, the U.S. Congress continues to look into caffeine levels in energy drinks and a new generation of taste enhancers and sensates present a new frontier in flavor, food and beverage safety protocols. In short, the food, beverage and flavor industries have their hands full defending food science in an evolving consumer, regulatory, NGO and legislative landscape.

Jason Kelly of Ginkgo Bioworks provided a simple description of the mechanics of genetic engineering.

This was the focus of the 13th Annual West Coast Flavor Industry Forum in Anaheim, California, which took as its theme the ongoing dissonance between food science and public perception regarding genetically modified organisms (GMO) in the food chain. The topic was particularly timely as the event took place one day before grocer Whole Foods Market announced it would label all GMO-containing products by 2018—a move the company called "consumer's right to know."

"The prevalence of GMOs in the U.S. paired with nonexistent mandatory labeling makes it very difficult for grocery stores to source non-GMO choices and for consumers to choose non-GMO products," Whole Foods Market said in a statement, which continued, "[M]any U.S. states are currently considering mandatory labeling initiatives, like the one in Washington state, where 500,000 citizens signed a petition last year to move the initiative the next step to their state legislature for consideration. Whole Foods Market supports that ballot measure in Washington and hopes it and other such state initiatives will finally lead to one uniform set of rules in support of the consumer's right to know … To ensure a growing supply of non-GMO options for our customers, we are stepping up our support of organic and certified products, and we are growing the non-GMO supply chain with our supplier partners."

Food Science Foes See GMO as Inherently Unstable

Who are the opponents of GMOs? And are they really, as Slate's Keith Kloor called them in a 2012 article, "the Climate Skeptics of the Left"?

More than 75% of conventional processed foods contain GMOs, said Courtney Pineau, assistant director of the Non-GMO Project, which advocates against GMO products and conducts non-GMO verifications for its own branded Non-GMO seal. Major crops currently available as GMOs include corn, soy, sugar beet, canola, alfalfa, Hawaiian papaya (a GMO solution that, it was later pointed out, was introduced to save the local industry), zucchini, summer squash and baby corn.

Pineau opened her presentation with the Non-GMO Project's definition of GMO (emphasis *P&F*'s):

> Genetically modified organisms (GMOs) are plants or animals created through the process of genetic engineering. This **experimental** technology **forces** DNA from one species into a different species. The resulting GMOs are **unstable** combinations of plant, animal, bacterial and viral genes that cannot occur in nature or in **traditional** breeding.

Far from being a neutral descriptive elucidation, Pineau's GMO definition comes loaded with alarming code words. In her eyes, GMO is an "unstable" and "experimental" technology. (When, exactly, a technology stops being "experimental" was not mentioned.) Furthermore, the definition implies violence with the verb "forces," while invoking "traditional" breeding as a presumably safer alternative without offering up a sliver of evidence.

Pineau followed up her definition by claiming, contrary to the available scientific evidence, "None of the genetically engineered traits in commercial production offer increased yields, drought tolerance or nutritional superiority." She also employed the image of a rat and invoked the widely discredited 2012 study from Seralini et al., "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize," noting that GMO can cause serious health defects several generations down the line and stating that humans reflect a first-generation experiment. In fact, the Seralini paper failed to present any evidence of harm to multiple generations of rats.

Peter van der Schaft, Axxence Aromatics GmbH, provided insights into biotech-generated aromatic ingredients.

When asked if the Non-GMO Project stood by the discredited study, Pineau said the Non-GMO Project's "technical advisors" determined there were "aspects of the study of good quality … and revealed there was definitely more research to be done." She added, "We are aware there are aspects of the study that have been under scrutiny." Despite this, she said, "I think there's more research that needs to be done."

Thus emerged three major themes for the day: 1) If the parties can't agree on the basic scientific facts, how can industry and NGOs stop speaking past one another in the GMO debates? 2) In the minds of anti-GMO crusaders, how much research is "enough"? 3) If, as some claim, anti-GMO fears are based primarily on belief, as opposed to facts, what tools does food science have at its disposal to break through?

> "This is the next big technology. The best engineers in the world are going to get into this and do great things."
>
> —Jason Kelly, Ginkgo Bioworks

When asked if, hypothetically, it was proven beyond a shadow of a doubt that GMO posed no risk to consumer safety, would she would still advocate for GMO labeling, Pineau would only say, "I don't think that's a plausible question. I don't know that that's possible at this time." She quickly turned away from a scientific argument to something more theological, stating, "I think ultimately there's a lot of ethical questions for people not just [on] the science, but for some people it's the consumption of food that crosses the natural species barrier. I know for myself, I would continue to have some concerns."

(As presenter Jason Kelly of Ginkgo Bioworks noted later, such barriers do not exist on the tree of life, as outlined by N.R. Pace in 2009.[a] More on that in a moment.)

"Consumers need to be able to walk into a grocery store and know what they're buying," said Pineau.

She added that, in response to strong consumer demand and backlashes, conventional brands and private labels are showing increased interest in Non-GMO Project certification. However, she did acknowledge the huge challenges in ramping up non-GMO supply chains that are both stable and affordable. Notable growth has also been observed in specialty gourmet and natural supermarket segments, in part driven by the Just Label It, GMO Inside and Moms Across America projects that are aligned with the Non-GMO Project. Many of these groups are driven by social media outlets, a major focus for John Roulac, an anti-GMO activist and founder and CEO of organic food supplier Nutiva.

Opposing labeling is bad for brand reputation, said Roulac, who compared the battle for California's Prop 37 to the Arab Spring and the U.S. battle for marriage equality. The United States is the top GMO producer as measured by hectares, said Roulac, followed by Brazil and Argentina. And so it makes sense that Roulac and other anti-GMO advocates see the U.S. state of California as an incubator for right-to-know initiatives. Even when such measures fail, activists move the efforts to more friendly venues, such as Washington State. In Washington, the push is centered on GMO salmon, including AquaAdvantage fish from AquaBounty Technologies, GMO apples and GMO wheat. Unlike California, farmers in Washington State are generally anti-GMO. By Roulac's count, more than 20 states are considering anti-GMO legislation.

"This issue is not going to go away," Roulac said of the anti-GMO movement. He went on to accuse the food industry of ignoring "the facts" surrounding GMO, despite never citing a single scientific study backing up his anti-GMO stance. In fact, as Roulac's talk went on, it became clear that he considers GMO harmfulness as settled fact unworthy of further discussion, declaring GMOs full of "toxic chemicals and unknown risks."

"We can debate all we want around the science of GMO, the safety, you can hire 100 scientists and 50 or 80 of them will say 'these are safe,' but the bottom line for people like myself and a growing number of people is we want a food system that doesn't pollute the earth in the way it's being grown," said Roulac. "GMOs use more toxic chemicals than non-GMO crops. If you really understood what happens to the soil, you understood what goes on when you eat that food, generation after generation, you would probably not eat so much GMO food."

As evidence, he repeatedly referred to the documentary *Genetic Roulette*, an anti-GMO film produced by Jeffrey Smith, who, despite being called a scientist by Dr. Oz on his popular daytime talk show, holds "no scientific degree from any institution" and has "no experience in genetics or agriculture," according to Michael Specter's 2013 profile of Oz, "The Operator," in *The New Yorker*. In fact, Smith's background consists solely of a business studies stint at the Maharishi University of Management and time spent as a dance instructor at the University of Iowa. This, in Roulac's view, is the person who should be telling the global food industry and consumers how to operate. Roulac's second thread of proof involved repeated negative insinuations about Monsanto, condemning the safety of GMOs by stating the company's involvement in the production of Agent Orange and polychlorinated biphenyls—guilt by association.

Roulac noted that the Just Label It movement, with which he is aligned, collected about 1.2 million signatures demanding that

[a] NR Pace, Mapping the tree of life: progress and prospects. *Microbiol Mol Biol Rev*, 73(4), 565–576 (2009)

Courtney Pineau of the Non-GMO Project provided a look into the reasoning and motivations behind anti-GMO.

the U.S. Food and Drug Administration label GMO-containing foods. Another allied group, GMO Inside, has more than 37,000 *Facebook* likes as of press time. (Among other things, the page's commenters blame GMOs for autism.) These and other groups have hired professional publicists and social media directors, which have launched attacks on the social media pages of top food and beverage brands. Yet later Roulac claimed NGOs did not have enough funds for studies.

"A lot of people feel there's a concern about [GMO] but they're not quite sure why," he said. "The epidemic of health issues has been off the charts in the past 30 years. Is it all GMO [related]? It's really hard to show where it's all coming from. We don't have $5 million or $10 million studies because it's not so easy to fund this. Part of the challenge is we're a small group, this is just getting going."

Modesty aside, assuming a $10 million study was necessary to solve the safety questions surrounding GMO, each GMO Inside fan would need to contribute about $270.27; each Just Label It supporter, on the other hand, would need to pitch in just $8.33.

Natural Flavoring Substances, Biotech and GMOs: an Industry Perspective

Taking a decidedly more scientific approach to food science, Peter van der Schaft, technical director of Axxence Aromatics GmbH, discussed the definitions of flavoring substances under EC 1334 in Europe. The categories include flavoring substance, natural flavoring substance, flavoring preparation, thermal process flavoring, smoke flavorings (which has its own regulation), flavor precursors and "other" flavorings. Only natural flavoring substances and flavoring preparations can be declared natural under the European Union regulations. All others are considered synthetic, though some can be considered natural in the United States. Annex II of the regulations also outlines what traditional cooking practices and temperatures may be applied while retaining a natural status. Fermentation is included, particularly enzymatic conversions, as well as microbiological processes, and solvent extractions (in accordance with a positive list of approved solvents for food ingredients). Physical processes that don't convert the chemical makeup of natural flavoring substances are allowed. In lay parlance, natural flavoring substances should not be produced using harsh chemical substances.

"There is a great resistance to GMO in Europe," said van der Schaft.

How strong is it? Just this past January, BASF halted the development of Fortuna, Amadea and Modena GMO potato projects due to the uncertain regulatory environment in Europe.

In the EU, GMO food and feed is covered by regulation (EC) No1829/2003 of the European Parliament. It states:

> *Flavourings falling within the scope of Council Directive 88/388/EEC of 22 June 1988 on the approximation of the laws of the Member States relating to flavourings for use in foodstuffs and to source materials for their production which contain, consist of or are produced from GMOs should also fall within the scope of this Regulation for the safety assessment of the genetic modification.*

The regulation also addresses labeling:

> *Additional requirements for the labelling of genetically modified foods are laid down in Regulation (EC) No 258/97, in Council Regulation (EC) No 1139/98 of 26 May 1998 concerning the compulsory indication, on the labelling of certain foodstuffs produced from genetically modified organisms, of particulars other than those provided for in Directive 79/112/EEC(14) and in Commission Regulation (EC) No 50/2000 of 10 January 2000 on the labelling of foodstuffs and food ingredients containing additives and flavourings that have been genetically modified or have been produced from genetically modified organisms.*

Van der Schaft noted that this labeling requirement did not pertain to products produced *with* a GMO organism; processing aids such as GMO enzymes are not covered. The enzymes allowed are listed on the EU Community list.

The limit of GMO allowable in non-GMO products is 0.9%; this small allowance compensates for categories in which 100% GMO-free options are not technically possible. The labeling's intent is to allow consumers to make an informed choice. Individual member states can restrict or prohibit the use or sale of GMO products on its territory in the interest of human health or the environment, which has occurred, for instance, in France and Germany. This has caused a large inhibitory effect on GMO introductions in the EU, which maintains an approved list of about 50 species that are GMOs. Only a few are allowed to be produced in the EU, while the remainder can be imported from markets such as the United States. While attitudes toward GMO in Europe could change, van der Schaft said the time line was unpredictable, making innovation a risky investment. As scandals such as the unlabeled horsemeat debacle in Europe continue to occur, the consumer population maintains a strong mistrust of the food system.

Why GMOs Matter

"People expect [genetic engineering] not to work and say, 'oh, they're crossing the species barrier, it's an abomination," said Jason Kelly of Ginkgo Bioworks, referring to Pineau's earlier comments. "How can you take a human gene and move it into a bacteria? How could that work? How could that bacteria make human insulin?" Pointing to a map of the Tree of Life, Kelly said, "We're all descended from the same point. Everything originated from the same organism at some point. As a result we all kind of work the same way. Bacteria don't make enzymes any differently than I make enzymes. We make different kinds of stuff, but we all have the same mechanics, the same operating system. That's what genetic engineering is all about."

While the day's presentations certainly presented a sense that GMOs face an uphill battle with consumer and regulatory acceptance, Kelly's talk presented strong evidence of the promise and safety of GMO technology in flavor and fragrance. Ginkgo's work, he explained, centers on the engineering of microorganisms (processing aids, in van de Schaft's terminology) to produce specific flavor and fragrance ingredients. Since 1982, when biotech processes were used to create the biosynthetic insulin Humulin for diabetes sufferers, microorganism technology has grown increasingly sophisticated. The production of Humulin replaced less ideal sources derived from pig pancreases, which had presented allergenic, sourcing and performance issues. This, in a nutshell, is GMO biotech's promise: targeted, highly refined outcomes.

So, how does it work? Kelly described every organism as "digitally encoded" with DNA that defines it. Each portion of DNA accounts for certain enzymes. These enzymes in turn affect chemical reactions among molecules. "That's true across all biology," he added, echoing Pineau's earlier concerns about crossing so-called species barriers. To take that basic knowledge and apply it to genetic engineering requires several steps, according to Kelly:

- Find the required genes;
- Get physical copies of the required genes using polymerase chain reactions that allow biologists to make thousands or even millions of copies of specific segments of DNA;
- Transfer the genes into an industrial microbe via conjugation so that the microbe takes on the desired DNA encoding; and
- Feed these microbes into a bioreactor for fermentation to produce the final desired product, whether it's Humulin or an aromatic material.

Since the completion of the Human Genome Project, the work of finding the required genes and obtaining physical copies has become enormously cheaper and faster. Gene copies can be produced in a matter of weeks. These copies can be recombined to produce desired activities.

Applying this technology in flavors and fragrances is an obvious fit, according to Kelly: "For a lot of extracted products there's a good opportunity now to apply fermentation as an alternative means of production." The benefits include:

- Better land usage that avoids growing large acreages of aromatic plants to extract materials that are present in tiny amounts, such as santalol in sandalwood: "You're going to get a much more stable outcome with fermentation," Kelly said.
- Unlimited supply: This would relieve producers of the uncertainties of weather or geopolitical events.
- Product consistency: Moving fermentation in-house allows producers total control over the outcome of products end-to-end. "You're getting out what you expect to get out every time," said Kelly
- Reduced cost of production: Total process control and reasonably priced inputs create price controls and stability; in addition, as processes are continuously refined, costs are expected to drop exponentially. "Eventually you're going to get very competitive with the [biotech] products," said Kelly

(*Continued on Page 30*)

(*Continued from Page 27*)

Donald Wilkes (Blue Pacific Flavors) introduced the day's talks.

Biotech continues to make significant inroads in the flavor and fragrance space. Kelly noted that the range of products produced using fermentation—including many non-GMO—is ever-increasing: raspberry ketone from betuloside catalysis, vanillin from ferulic acid, pyrazines from threonine, γ-dodecalactone from oleic acid, etc. Publicly announced partnerships include IFF-Evolva for vanillin; BASF-Allylix for nootkatone, valencene and β-vetivone; Cargill-Evolva for stevia, DSM-Isobionics for nootkatone and valencene; Firmenich-Amyris for patchoulol and santalol; and Ginkgo and an unnamed partner, which is pursuing the production of two ingredients.

In a typical scenario, a fermentation provider delivers feedstock and fermentation, delivering a final ingredient to the flavor or fragrance customer. (Ginkgo engineers the microbes that perform the fermentations and does not actually produce any ingredients.) As processes are refined and costs decrease, flavor and fragrance palettes may adopt more and more biotech ingredients, Kelly said. If the cost gets to a low enough point, Kelly believes biotech ingredients could dominate some ingredient categories.

Opposing labeling is bad for brand reputation, said Roulac, who compared the battle for California's Prop 37 to the Arab Spring.

In the case of Ginkgo, the company's organisms are considered genetically modified microorganisms (GMM)—not GMO—under Directive 2009/41/EC. These GMMs are applied under "contained use": "any activity in which micro-organisms are genetically modified or in which such GMMs are cultured, stored, transported, destroyed, disposed of or used in any other way, and for which specific containment measures are used to limit their contact with, and to provide a high level of safety for, the general population and the environment."

As such, the materials produced with GMMs are considered made "with," not made "from" GMOs since the microorganisms are in no way present in final products. In such cases, no labeling is required.

The Future

As food science's critics push on with their populist message of fear and mistrust, genetic engineering continues to break new ground. For instance, several years ago at iGem, a synthetic biology competition for undergraduate students, participants engineered *E. coli* that smelled of mint. This, said Kelly, is just the beginning of genetic engineering's possibilities.

"This is like the computer industry," he said. "This is the next big technology. The best engineers in the world are going to get into this and do great things. It's easy to make a boogeyman out of Monsanto, but these people are just trying to do good things."