

# Vanilla & Synthetic Biology

## A Case Study

**PRODUCT:** Natural vanilla flavor/fragrance is sourced from the cured seed pod of the vanilla orchid.

**STATUS:** Switzerland-based synthetic biology company, Evolva, is partnering with industry giant, International Flavors & Fragrances (USA), to engineer metabolic pathways in microbes to produce key flavor compounds found in vanilla.

**AFFECTED COUNTRY/REGION:** An estimated 200,000 people are involved in the production of cured vanilla beans per annum. Madagascar, Comoros and Réunion historically account for around three quarters of the world's vanilla bean production. Other producers include: Indonesia, China, Mexico, Uganda, Democratic Republic of Congo, Tanzania, French Polynesia, Malawi, Tonga, Turkey and India.

**MARKET:** The global vanilla market, both natural and chemically-derived (vanillin), is valued at about \$650 million. The value of worldwide trade in vanilla beans is forecast at \$150 million in 2013. At the consumer end natural vanilla sells for thousands of dollars per kilogram, synthetic vanillin sells for only tens of dollars.

**COMMERCIALIZATION:** Evolva and IFF are now scaling up and are “on target” to commercialize a bio-synthesized vanillin flavor in 2014.<sup>1</sup>

Despite high-profile corporate pledges to source raw materials ethically and sustainably, the world's largest brokers of flavor and fragrance ingredients (e.g., Givaudan, Firmenich & IFF) are partnering with synthetic biology companies to develop a new manufacturing platform – “microbial cell factories” – for the biosynthesis of high-value flavor/fragrance molecules, a move that could dramatically reduce botanical imports and banish hundreds of thousands of small-scale farmers, especially in the tropics, from commodity supply chains.

*“There is potential for biosynthetic routes to completely replace any natural sources.”*

Kalib Kersh, industry analyst, cited in *Chemical & Engineering News*, 16 July 2012<sup>2</sup>



If government regulators permit companies to market new, biosynthesized products as “natural” – consumers may never know if their flavor/fragrances are sourced from small farmers in the tropics or giant fermentation tanks in Northern factories. The synthetic biology platform offers the potential to secure uninterrupted supplies of high-value, flavor/fragrance/ pharmaceutical compounds in industrial-scale fermentation tanks instead of sourcing plant materials from millions of South-based farmers. So-called microbial cell factories are less constrained by geography, extreme weather, crop failures, price volatility – or the farm families whose livelihoods depend on cultivation of high-value botanical exports.

<sup>1</sup> Evolva website:  
<http://www.evolva.com/products/vanilla#sthash.x0PLnUHO.dpuf>  
Accessed on October 2, 2013.

<sup>2</sup> Melody Bomgardner, “The Sweet Smell of Microbes,” *Chemical & Engineering News*, July 16, 2012, p. 26.



Farming communities in the global South could be affected by biosynthesis-based production of high-value flavors and fragrances. For example: One of the world's largest corporate brokers of flavor & fragrance ingredients, Swiss-based Firmenich, buys over 1,000 natural products every year that come from 170 botanical families in over 50 countries.<sup>3</sup> Givaudan (Switzerland), the world's largest flavor/fragrance company, annually sources more than 10,000 ingredients from around the world.<sup>4</sup> Germany-based Symrise, the fourth-largest supplier of flavor/fragrances, purchased 202,000 tons of raw materials for processing in 2012 from over 100 countries.

Natural vanilla – extracted from the cured seed pod of the vanilla orchid (*Vanilla planifolia*) – is a complex flavor made up of more than 150 flavor compounds. “Vanillin” is the most important one. Due to the high cost of vanilla beans, flavor/fragrance companies have long used chemistry to develop a cheaper, chemically synthesized vanillin. Although chemically-synthesized vanillin now accounts for 97% of all vanilla flavor used commercially,<sup>6</sup> the artificial product has not come close to duplicating the complex flavor profile of natural vanilla – which is still in high demand.

Natural vanilla extract from the cured beans of the vanilla orchid is expensive, ultimately selling to the consumer for thousands of dollars per kilogram. By contrast, synthetic vanillin, made from lignin-containing wood pulp waste or from phenol, typically costs \$10-20 per kg. The global market for chemically-synthesized vanillin is about 15-16,000 tons per year, while vanilla derived from vanilla beans represents just 50 tons a year.<sup>7</sup> Synthetic biologists are now using a complex genetic engineering process to modify the metabolic pathway of yeast to produce biosynthesized vanillin in industrial fermentation tanks.<sup>8</sup> The artificially constructed gene sequences involve not just yeast genes, but bacteria, mold, plant and human genes.

3 Firmenich News Release. “Firmenich CEO Confirms Long-Term Commitment To Farmers In Haiti,” April 4, 2013. <http://www.firmenich.com>

4 Anonymous. “2013 Flavor and Fragrance Leaderboard.” *Perfumer & Flavorist*, Vol. 38, June 2013.

5 *Ibid.*

6 Synthetic vanillin is typically made from lignin-containing wood pulp or from phenol.

## Livelihoods at Stake

An estimated 200,000 people are involved in the annual production of cured vanilla beans worldwide.<sup>9</sup> Industry analysts predict that the market for vanilla beans exports worldwide will reach an estimated \$150 million in 2013 – with African producers accounting for approximately 64% of the total export market.<sup>10</sup>

Production of natural vanilla from vanilla beans is extremely labour intensive: 1 kg of vanilla requires approximately 500 kg of vanilla pods and hand-pollination of approximately 40,000 flowers.<sup>11</sup> Madagascar and other island nations in the Southwest Indian Ocean (Comoros, Réunion) historically account for around three quarters of the world's vanilla bean production – and continue to dominate the market today. Vanilla bean production and processing is a vital cash crop in agroforestry systems where there are few alternative income sources.

In Madagascar, an estimated 80,000 families cultivate vanilla orchids on approximately 30,000 hectares. In Comoros, about 5,000-10,000 families depend on vanilla bean production. Approximately 10,000 farm families in Mexico cultivate vanilla orchids, the geographic center of origin of vanilla.<sup>12</sup>

**In 2012, the global market for flavors & fragrances (F&F) was \$23 billion. The top 4 companies control 56% of the global F&F market.<sup>5</sup>**

7 Robin Wyers, “Bringing Sustainability to Vanillin,” *The World of Food Ingredients*, September 2011. [www.foodingredientsfirst.com](http://www.foodingredientsfirst.com)

8 Hansen, E. H., B. L. Møller, G. R. Kock, C. M. Bunner, C. Kristensen, O. R. Jensen, F. T. Okkels, C.E. Olsen, M. S. Motawia and J. Hansen., “De novo biosynthesis of Vanillin in Fission yeast (*Schizosaccharomyces pombe*) and Baker's yeast (*Saccharomyces cerevisiae*),” *Applied and Environmental Microbiology*, 75, 2009, pp. 2765-2774.

9 Personal communication with Michel Grisoni, CIRAD (Centre de coopération internationale en recherche agronomique pour le développement), based in Réunion. All estimates for vanilla production and agronomic practices provided by Michel Grisoni.

10 Parker, Philip M. (2013). *The World Market for Vanilla Beans: A 2013 Global Trade Perspective*, INSEAD. [www.icongrouponline.com](http://www.icongrouponline.com)

11 Hansen *et al.*, “De novo biosynthesis of Vanillin”

12 According to information compiled by ETC Group, this number includes at least 4,000 farm families in Veracruz, 4,000 in Puebla and at least 1,000 in Oaxaca. Beyond commercial producers, this number includes farm families who are dedicated to growing and conserving vanilla orchids as part of their traditional identity, culture and sustainable agroforestry practices.



The vanilla cropping system in these countries is vital for the maintenance and sustainability of agroforestry areas (mainly organic). The vanilla orchid vines rely on tropical forest shade and support, and require labor-intensive cultivation, harvest and processing.

About 8,000 families in Central Africa (Uganda, Democratic Republic of Congo, Tanzania) depend on vanilla bean production. In recent years Indonesia and China have become major vanilla bean producers; other vanilla bean producers include French Polynesia, Malawi, Tonga, Turkey and India.

## Current R&D

In 2009 researchers working with Switzerland-based synthetic biology company, Evolva, described the creation of a de novo pathway to produce vanillin from glucose in two yeast strains; a pathway involving bacterial, mold, plant and synthetic versions of human genes.<sup>13</sup>

- 2010 – Evolva enters a 4-year agreement with the Danish government’s strategic research council to develop an environmentally sustainable production route for biosynthetic vanillin.
- January 2011 – Evolva and International Flavors & Fragrances (IFF) launch partnership to commercialize a biosynthetic route for production of vanillin.
- February 2013 – Evolva and IFF announce they are scaling up production of biosynthetic vanillin and “on-target” to launch commercially in 2014.

13 Hansen *et al.*, “De novo biosynthesis of Vanillin”

14 Personal communication with Evolva CEO, Neil Goldsmith, October 5, 2011.

15 Personal communication with Evolva CEO, Neil Goldsmith, October 5, 2011. Email communication from Neil Goldsmith on October 10, 2013 confirms that this information remains accurate.

16 Email communication with Neil Goldsmith, CEO Evolva, October 10, 2013.

17 Personal communication with Evolva CEO, Neil Goldsmith, October 5, 2011. Email communication from Neil Goldsmith on October 10, 2013 confirms that this information remains accurate.

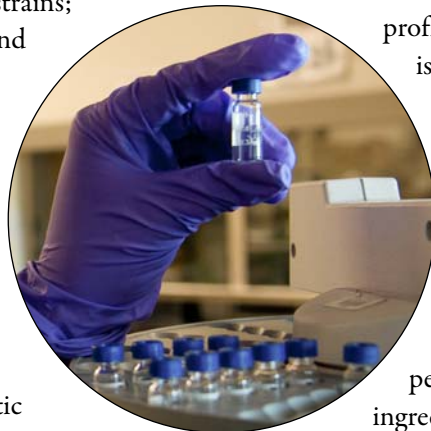
In 2009 the global vanilla/vanillin market, including natural, synthetic and artificial sources, was valued at approximately \$650 million. Evolva believes that its fermented vanillin can capture up to \$360 million of the total global market.<sup>14</sup>

The company’s yeast-based fermentation route is producing vanillin at a price that is competitive with the most expensive artificial vanillin on the market today.<sup>15</sup> According to Evolva CEO Neil Goldsmith: “99% of the vanillin that we all eat comes from petrochemicals or chemically treated paper pulp. If we can offer an alternative that is more sustainable and higher quality then we believe that to be beneficial.”<sup>16</sup>



Photo: (CC) Brocktopia

Photo: (CC) RDECOM



Evolva acknowledges that the flavor of the company’s biosynthesized vanillin is not equivalent to the flavoring derived from the cured vanilla bean, but claims that the taste profile of vanillin produced by engineered yeast is more complex and closer to the natural vanilla flavor than artificial vanillin.<sup>17</sup>

The commercial success of biosynthesized vanillin ultimately depends not just on competitive price and flavor, but labeling. Will IFF’s customers – the food companies that use vanillin in bakery/confectionary /dairy/beverages – be permitted to label a biosynthesized vanillin ingredient as “natural”? IFF’s director of R&D recently told the *New York Times*, “The need for natural is the key driver.”<sup>18</sup> Recent precedent suggests that biosynthesized vanillin produced via fermentation may win the natural label: Chemical giant, Solvay (Belgium), already makes a vanillin ingredient via fermentation of ferulic acid derived from rice bran. Government regulators permit Solvay’s bio-fermented vanillin to be labeled “Natural flavoring/Flavor/Vanilla flavor” (EU) or “Vanillin derived by a natural process” (US).<sup>19</sup>

18 Andrew Pollack, “What’s That Smell? Exotic Scents Made From Re-engineered Yeast,” *New York Times*, October 20, 2013.

19 [http://www.rhodia.com/en/binaries/Rhovaniil\\_Natural\\_Highlight\\_2013.pdf](http://www.rhodia.com/en/binaries/Rhovaniil_Natural_Highlight_2013.pdf)



Evolva plans to make several molecules involved in the complex flavor profile of natural vanilla. While Evolva insists that its biosynthesized vanillin is not designed to compete with farmer-grown vanilla beans, if the company succeeds in producing a vanillin flavor that can be marketed as “natural” and scaled-up at a fraction of the cost of botanically-derived vanilla, it has the potential to provide a bio-based substitute that will inevitably capture some portion of the natural vanilla bean flavor market.

## Real or Artificial?

### Flavor & Fragrance Industry Pledges Corporate Commitment to Sustainable and Ethical Sourcing of Vanilla

**International Flavors & Fragrances:** Within months of announcing that it is “on target” to commercialize its biosynthetic vanilla, IFF released its 2013 sustainability report, pledging the company’s commitment to “Natural Ethics Vanilla” – the purchase of vanilla from farmers who adhere to strict sustainability guidelines.<sup>20</sup> IFF wants to ensure that the farmers who supply the company’s natural vanilla beans are using sustainable production practices. But the company is simultaneously bankrolling (and claiming monopoly patents on) the development of a new biosynthetic process that will potentially disrupt or destroy the livelihoods of hundreds of thousands of small-scale farmers – literally overnight.

**Givaudan:** “The sustainable sourcing of raw materials is an integral part of our operations and is one of our strategic pillars as well as being part of our Sustainability programme.” Our ethical vanilla sourcing programme in Madagascar involves improving traceability, helping farmers certify their organic produce and supporting school building projects.”<sup>21</sup>

**Firmenich:** Firmenich has begun commercializing Bourbon vanilla that has been sourced from Rainforest Alliance Certified™ farms. Firmenich has worked with a local partner in Madagascar to help a vanilla bean co-operative of more than 1,300 farming families from 38 villages earn Rainforest Alliance certification.<sup>22</sup>

## Intellectual Property Related to Biosynthesis of Vanilla

Company	Patent/Application #	Title	Date Published
International Flavor & Fragrances/Evolva	WO2013022881 A8 (application)	Composition and Methods for the Biosynthesis of Vanillin	21 March 2013
Evolva SA	US8105786	Method of producing a low molecular weight organic compound in a cell	31 Jan 2012
Evolva SA	EP2388333A3	Method of producing a low molecular weight organic compound in a cell	4 April 2012

20 IFF. 2013. *Moving Forward, our sustainability report 2012*. <http://www.iff.com>

21 Givaudan – 2012 Annual Report: <http://www.givaudan.com>

22 Firmenich News Release. “Firmenich Becomes the First Flavor House to Offer Rainforest Alliance Certified™ Vanilla,” March 27, 2013. <http://www.firmenich.com>



### Further information:

ETC Group’s online resource on Synthetic Biology:  
[www.etcgroup.org/issues/synthetic-biology](http://www.etcgroup.org/issues/synthetic-biology)