Haiti, Essential Oils & Synthetic Biology

Potential Impacts on Haiti's Farming Communities

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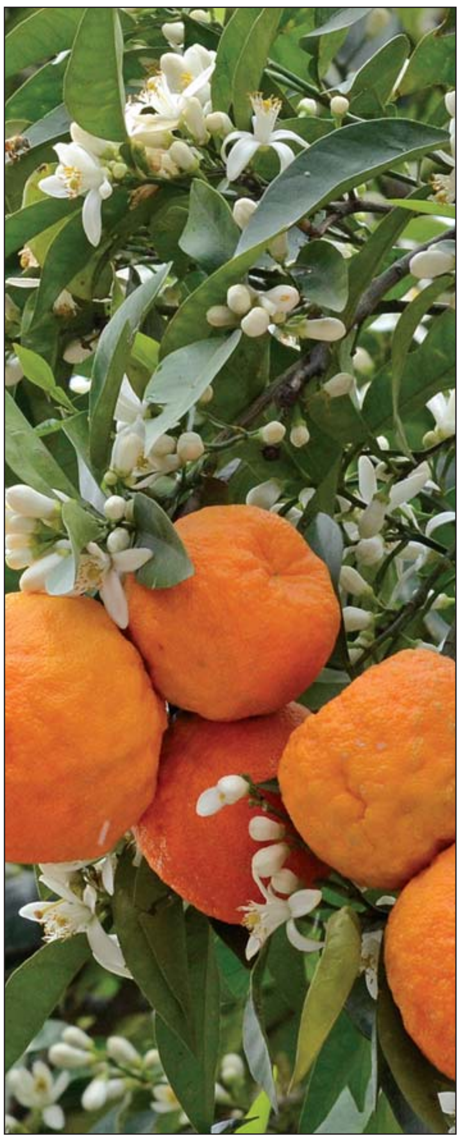

A Case Study

September 2016

Haiti, Essential Oils & Synthetic Biology:

Potential Impacts on Haiti's Farming Communities

A case study July 2016

ETC Group

...works to address the socioeconomic and ecological issues surrounding new technologies that could have an impact on the world's poorest and most vulnerable people. We investigate ecological erosion (including the erosion of cultures and human rights); the development of new technologies (especially agricultural but also other technologies that work with genomics and matter); and we monitor global governance issues including corporate concentration and trade in technologies. We operate at the global political level. We work closely with partner civil society organizations (CSOs) and social movements, especially in Africa, Asia and Latin America.

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Executive Summary:
Haiti, Essential Oils and Synthetic Biology

Synthetic biology is being used to develop a manufacturing platform for the production of so-called "natural" flavors & fragrances including essential oils that are sourced from plants in Haiti. Synthetic biology companies aim to produce high-value, low-volume flavor/fragrance compounds in engineered microbes as a market alternative to costly botanical imports or chemically-derived synthetics. Our fact-finding report attempts to answer the following key questions: Is the market for Haiti's essential oils threatened by current R&D on synthetic biology? Are the livelihoods of Haitian farming communities jeopardized by these developments?

Essential oils are Haiti's most valuable agricultural export—accounting for US$16 million in 2012.[1] Among essential oil exporting countries, Haiti ranks 30th, but its global ranking belies the critical importance of essential oils to Haiti's small farm economy—and to the flavor/fragrance industry. For example Haiti is the world's single most important source of high-quality vetiver oil, accounting for 50% of the estimated 120-150 tons produced worldwide per annum. Some 30,000 farmers in Haiti's southwest region cultivate vetiver grass on small plots of land—and many more livelihoods depend on its production/processing.

Our report examines the current status of synthetic biology R&D and potential impacts on Haiti's most important essential oils, including: 1) Vetiver; 2) Bitter Orange; 3) Amyris (West Indian sandalwood).

Synthetic biology-derived flavors/fragrances refer to compounds produced by engineered microorganisms via new industrial fermentation technologies.

Synthetic biology-derived flavors / fragrances refer to compounds produced by engineered microorganisms via new industrial fermentation technologies.

Synthetic biology is a proven technology to produce some high-value compounds. For example, Amyris Inc.'s artemisinin, Evolva's vanillin and Isobionics/DSM's valencene are already commercially available—and many more compounds are in the pipeline. Existing regulations in the EU and US allow these products (derived from fermentation and other microbiological processes, which are considered process aids for regulatory purposes) to be labeled as "natural" ingredients/products, positioning them to compete with botanically-derived compounds as well as with their synthetic (chemically derived) counterparts.

If commercially successful, synthetic biology's designer organisms have the potential to de-stabilize traditional flavor/fragrance markets, disrupt trade and eliminate jobs. Agricultural workers in countries like Haiti, where alternative income sources are scarce, could be severely affected if the market for essential oils is up-ended by a synthetic biology manufacturing platform. These communities don't have social safety nets and aren't prepared to respond to sudden demands for new skills or different crop commodities.

Photo(cc) RDECOM

In the case of vetiver, we have identified only one company, Evolva, that currently holds patents related to the use of synthetic biology to produce compounds that are structurally-related to vetiver. In the course of our investigations Evolva told ETC Group that it was not currently conducting R&D to commercialize its proprietary vetiver-related compounds, and that it is unlikely that it will do so in the future. We believe that Evolva is backing down due to combined pressures, including: the visibility of the Haitian earthquake and high-profile initiatives by the Clinton Foundation and others that focus on vetiver-growing projects to support small farmers in Haiti; ongoing inquiries by ETC Group about Evolva's position, as well as consumer campaigns (initiated by Friends of the Earth, with support from ETC Group), raising awareness of and opposition to Evolva's biosynthetic vanillin due to its potential effect on small farmers. As a result of these pressures, Evolva might have reconsidered its association with vetiver-related compounds a public relations liability and a distraction from the company's more strategically important products. (It is also possible that the technology, though patentable, did not succeed in producing a marketable vetiver-like fragrance.)

Although it is not currently under active R&D, there is no certainty that vetiver-related fragrance compounds will not be the target of Evolva or other synthetic biology researchers in the future.

At the very time flavor & fragrance industry giants (e.g., Givaudan, Firmenich) are supporting high-profile sustainability initiatives to help farming communities grow flavor/fragrance crops (including vetiver in Haiti), they are also bankrolling R&D in the field of synthetic biology. At least five of the world's top 10 flavor & fragrance corporations have entered R&D partnerships with synthetic biology firms (and it is likely that some alliances have not been made public).

The synthetic biology manufacturing platform is real, growing rapidly, already disruptive and a serious economic threat to economies and livelihoods of producers of many natural plant products.

This does not mean that flavors and fragrances from "syn bio" (sometimes referred to as metabolic pathway engineering or advanced microbial fermentation) will be technically or economically viable for all flavor/fragrance compounds. And it does not mean that markets for natural, botanically-derived flavors/fragrances will be eliminated. Because of the notorious secrecy of the flavor & fragrance industry, a number of synthetic biology companies have not publicly disclosed the specific flavor/fragrance compounds that are the subject of current R&D.

The synthetic biology manufacturing platform is real, growing rapidly, already disruptive and a serious economic threat to economies and livelihoods of producers of many natural plant products.

Under current labeling regulations in the EU and US, consumers of essential oils and natural flavors/fragrances have no way of knowing if the natural ingredient they seek is derived from botanicals or biosynthetic organisms. **There is virtually no consumer awareness that the definition of "natural" extends to flavors/fragrances excreted by engineered microbes produced via industrial fermentation.**

Part I. Background: Synthetic Biology and the Global Flavor & Fragrance Industry

What is Synthetic Biology?

Synthetic biology, dubbed "genetic engineering on steroids," broadly refers to the use of computer-assisted, biological engineering as well as geen editing techniques to design and construct new synthetic biological parts, devices and systems that do not exist in nature; it also refers to the redesign of existing biological organisms using these techniques. Synthetic biology attempts to bring a predictive engineering approach to genetic engineering using genetic 'parts' that are thought to be well characterized and whose behavior can be rationally predicted.

"The overall aim of synthetic biology is to simplify biological engineering by applying engineering principles and designs—which emanate from electronic and computer engineering—to biology."[2]

Over the past decade, before world oil prices plunged, fledgling syn bio start-ups (with the financial backing of fossil fuel corporations) made grandiose claims about using designer microbes to produce plentiful, low-cost biofuels in giant fermentation tanks. Manufacturing petrochemical substitutes at commercial scales proved elusive, however. Now with energy markets sputtering, most syn bio companies are giving up on biofuels and turning to high-cost, low volume flavor & fragrance molecules that can be economically produced in smaller batches.[3]

Biodiversity—especially exotic plants and animals—has been the source of natural flavors and fragrances for millennia. Plants, animals and microorganisms are prolific generators of bioactive flavor/fragrance compounds (known as secondary metabolites) that, once extracted, are widely used in food, feed, cosmetics, chemicals and pharmaceuticals.

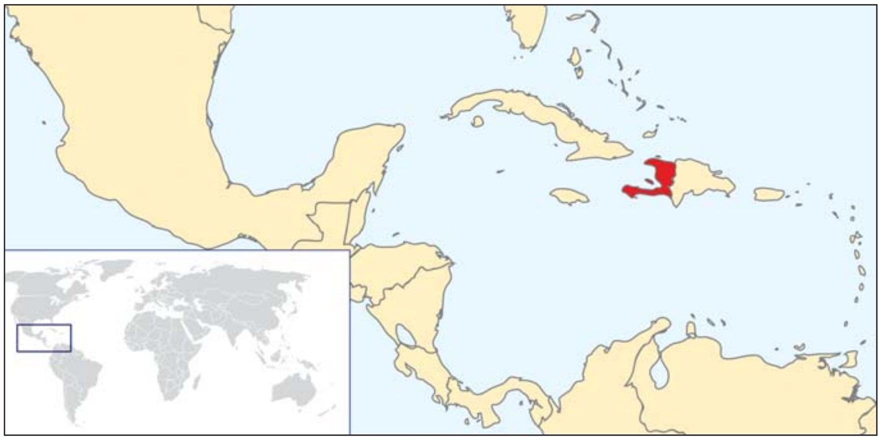
"There is potential for biosynthetic routes to completely replace any natural sources."

– Kalib Kersh, Lux Research, quoted in Chemical & Engineering News[4]

The world's largest flavor & fragrance corporations are eager to partner with synthetic biology companies because of the increasing production uncertainties caused by climate change and the potential to secure cheaper, uniform and more accessible sources of expensive natural ingredients. With synthetic biology, the goal is to produce high-value flavor/fragrances in engineered microbes instead of relying on costly botanical imports or conventional chemical synthesis. The biosynthetic manufacturing platform involves the engineering of genetic pathways in microorganisms to produce molecular compounds that have historically been extracted from plants. Scientists and software engineers are tweaking the DNA of existing microorganisms as well as designing new ones from scratch.

In the words of one industry analyst: "There is potential for biosynthetic routes to completely replace any natural sources." – Kalib Kersh, Lux Research, quoted in Chemical & Engineering News.[4]

With advances in molecular biology and engineering, researchers are attempting to pinpoint the precise biochemical instructions in the cells of a living organism that result in the production of bioactive molecular compounds. Plant natural product metabolism is exceedingly complex. For instance, in one well-studied plant, Arabidopsis thaliana (a.k.a. mouse-ear cress or thale cress), at least 20% of the genes are thought to play a role in the biosynthesis of secondary metabolites.[5] The complex interaction of genes and catalytic enzymes all play a role in the plant's "metabolic pathway"—the means by which it produces a useful chemical compound.



Haiti and its neighbours Map (cc) Wikipedia

"Our technology fundamentally takes what exists in nature, makes it via fermentation in a sustainable and consistent way, and allows us to give a flavor and fragrance company a whole new platform to innovate around [...] as long as we can put it in our microbial platform and use sugar as a feedstock, reliability is not an issue." – Ena Cratsenburg, V.P. of Business Development, Amyris, Inc., quoted in Chemical & Engineering News, July 2012.[8]

Using "metabolic pathway engineering," synthetic biologists are turning microbial cells into "living chemical factories" that can be induced to manufacture substances they could never produce naturally. To date, synthetic biology firms are honing in on the best-known metabolic pathways such as terpenoids, polyketides, alkaloids—these pathways are the keys to producing tens of thousands of natural product families at the molecular level. To scale up the production of a desired compound, the novel biosynthetic pathway (constructed with synthetic DNA) is inserted into a microbial host (yeast, bacteria, fungi or algae strains, for example) that feed on plant sugars in giant (e.g., 200,000-litre) fermentation tanks.

The engineering of microbes for industrial purposes is nothing new, but synthetic biology start-ups are accelerating the process with computer engineering principles and highly-automated, robotic systems. In a mostly random process, software-directed robotic systems design, build, test and analyze DNA sequences and active compounds to identify promising candidates and optimize biomolecular pathways in microbes. Despite the staggering complexity of biological systems, synthetic biologists compare themselves to industrial product designers: "This design strategy can be likened to building millions of variants of a chemical factory, selecting or screening for control system variants that yield the most product and discarding all but one or two of the most productive designs."[6] One synthetic biology company refers to its employees as "organism designers" who work in a "foundry," not at a lab bench.[7]

In the words of one venture capitalist, Bryan Johnson, founder of the OS Fund, the ultimate goal of syn bio is to control biology and make it predictable: "We aren't there yet with biology—I can't just sit down and program biological code to create a particular outcome on a more complex scale. In my estimation, biology is the largest most significant code base we have in humanity. What's standing between us making good use of that is our ability to make it predictable."[9]

Despite the techno-rhetoric, the design and control of synthetic organisms is far from routine, simple or inexpensive. Biosynthetic pathway engineering is highly complex. Just two examples of this complexity:

- Researchers at Amyris, Inc. (California) successfully engineered the metabolic pathway of yeast to produce artemisinic acid, a precursor of artemisinin, an effective drug to treat malaria, which is typically sourced from the Chinese wormwood plant.[10] The biological engineering involved at least 12 new synthetic genetic parts[11] (and more than $53 million in research grants[12]).
- Evolva (Switzerland) commercialized a proprietary yeast biosynthesis platform for the production of vanillin—a key flavour compound in natural vanilla. In 2009 researchers disclosed that construction of the *de novo* pathway in yeast incorporates bacterial, mold, plant and human genes.[13]

Both products are now commercially available.

Box 1: Flavor and Fragrance Industry's Syn Bio Advantage

For the industrial flavor/fragrance industry, the synthetic biology platform could offer two major advantages:

1) The potential to secure more uniform, uninterrupted supplies of high-value raw materials in factory-based fermentation tanks. In other words, companies would be unencumbered by climate, weather, crop failure, price and political volatility or the logistical complexity of sourcing raw materials from farmers and other suppliers in remote locations.

2) The ability, under current regulations in the USA and Europe, to market biosynthesized flavors and aroma compounds as "natural" products.[14] In other words, biosynthetic products manufactured via microbial fermentation are deemed "natural" or "substantially equivalent" to a botanically-derived product. In contrast, chemically synthesized flavors/fragrances derived from petroleum cannot be labeled "natural."[15] Research shows that consumers have a strong preference for the "natural" label—despite the murkiness that surrounds it. One survey indicates that almost 60% of consumers in the United States look for the word "natural" when they shop for food products.[16] Because regulations governing "natural" products specifically permit "fermentation" and "microbiological" processes, the biosynthesis of flavor/fragrances in engineered microbes is not only positioned to compete with natural, botanically derived counterparts—they will also have an advantage over synthetically derived flavors/fragrances.[17] The bottom line: consumers will have no way of knowing if a "natural" flavoring or scent is derived from industrial, genetically engineered microbes or from a traditional botanical source.

The Global Flavor & Fragrance Industry

In 2016 the global flavor and fragrance market is expected to top $26.5 billion,[18] and is expected to grow to over $35 billion by 2019.[19] This figure reflects the value of ingredients for processed foods and fragrances only, and does not include the value of crop commodities such as coffee and cacao beans, which are commonly used to flavor processed foods. The industry is increasingly concentrated in the hands of four multinational firms[20]: Givaudan, Firmenich, IFF and Symrise accounted for 56.7% of the global flavor and fragrance (F&F) market in 2015.[21] In 2015 the top 10 companies collectively accounted for an estimated 74% of total industry sales (compared to 64% in 2000).[22] **At least six of the top 10 companies have entered R&D agreements with synthetic biology firms or have their own synthetic biology R&D activities.**[23]

F&F giants are pursuing every feasible route to secure cheaper and more accessible raw ingredients, both natural (sourced from biodiversity) and synthetic (chemicals synthesized from petroleum).

Although the flavor and aroma industry likes to emphasize the use of "natural" ingredients, the vast majority of flavors and fragrances are the product of chemical synthesis: an estimated 95% of the compounds used in fragrances are synthesized from petroleum, not sourced from plants, animals or microorganisms.[24] Even so, the giant F&F firms source thousands of plant and animal-derived ingredients from dozens of countries worldwide.

Flavors and fragrances are essential ingredients in the manufacture of household cleaning products, perfumes, cosmetics, pharmaceuticals, food & beverages, aromatherapy and more. For example, the soft drink industry is the major consumer of natural flavors/fragrances, especially essential oils of citrus origin.[25] In fact, 'cola' soft drinks cannot be produced without essential oils like lemon or lime.[26]

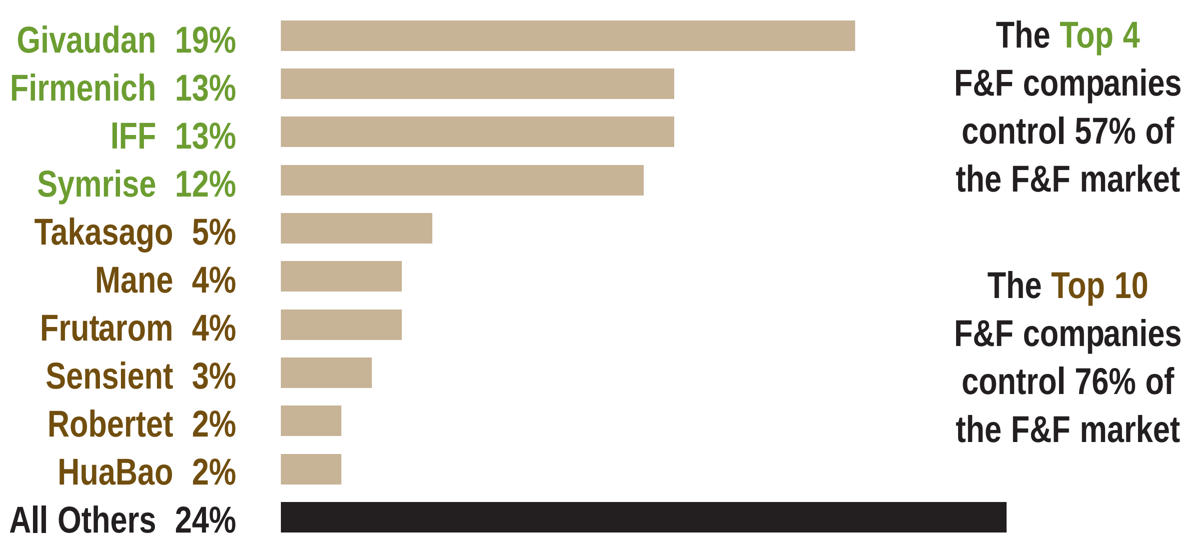
The F&F industry currently sources 200 to 250 different botanical crops grown on an estimated 250,000 hectares worldwide. Around 95% of these crops are grown by small-scale farmers and agricultural workers, mostly in the global South.[27] An estimated 20 million small-scale farmers and agricultural workers depend on botanical crops sourced for natural flavors and fragrances.[28] (This is a low estimate and does not include common flavors such as cocoa or coffee.)

Flavor & fragrance industry trade groups acknowledge that these botanicals are "highly important in terms of their socio-economic impact on rural populations and may also have important environmental benefits within agricultural systems."[29] Although "essential oils are typically categorized as 'minor crops,' they are of major economic social and environmental importance to the communities that are involved in their production and frequently represent the key cash crop (family income generator) in their farming mix that supports improvement in social indicators—notably health and education."[30]

Although the industry is notoriously secretive about its complex supply chains, raw materials are sourced globally. For instance:

- **Givaudan** – Switzerland (2015 sales: $4.58 billion): spends roughly CHF 1.6 billion per annum to buy 11,000 ingredients "to enrich the creative palette of our perfumers and flavorists."[31]
- **Firmenich** – Switzerland (2015 sales: $3.14 billion): buys and processes over 1,000 natural products every year that come from 170 botanical families supplied by growers in over 50 countries.[32]
- **International Flavors and Fragrances** – USA (2015 sales: $3 billion): sources over 9,000 raw materials from more than 2,200 companies.[33] Half of these materials are natural ingredients derived from flowers, fruits and other botanicals as well as from animal products (purchased in processed or semi-processed form).[34] In turn, IFF sells its flavoring/fragrance products to over 4,000 companies in around 80 countries.

Chart 1: Flavor & Fragrance Industry: Market Share by Company, 2015



Source: Perfumer & Flavorist 2016

Table 1: Synthetic Biology Firms and Flavor & Fragrance Targets

Syn bio Company	Target Flavor / Fragrance and Partner (if disclosed)	Other Partners
Amyris (US) "22 molecules under contract with the world's leading companies"[35]	Patchouli; farnesene; Biofene (Givaudan)	Firmenich; IFF; Givaudan Takasago[36]
Celbius (UK)	2-phenylethanol (2PE), an aromatic alcohol with rose-like odour widely used in the food, drink and cosmetic industry	
Evolva (Switzerland) Founded 2004	Stevia - Cargill; Vanillin - IFF; Saffron; Valencene; Nootkatone; Sandalwood (Alpha- and beta-santalol); Saffron; Agarwood – Universiti Malaysia Pahang *"Tourmoline" (undisclosed product);* Vetiver – based on Allylix's previous R&D	BASF; Roquette; Ajinomoto; L'Oreal; Takasago
Ginkgo Bioworks (US) Contracts to create 20 customized microbes	Rose oil - Robertet	Robertet
Isobionics (Netherlands)	Valencene; Nootkatone; Beta Elemene (extracted from ginger root); Sandalwood under development	DSM Nutritional Products
Oxford Biotrans UK)	Patchouli oil – under development	De Monchy Aromatics (Dorset, England)
Pareto Biotechnologies (US)	Nootkatone via bioconversion of orange-derived valencene; Unspecified flavor compounds, "with novel and enhanced properties" based on the polyketide pathway.	DNA 2.0
PhytoMetaSyn Project (Canada) Public-private initiative focusing on synthetic biosystems for the production of high value plant metabolites	75 plant targets – including opium poppy	4-yr. (2009-2013) now expired. $13.6 million project involving 7 public research institutions; supported by Canadian government & industry
P2 Science, Inc. (USA) has also entered into a renewable F&F molecule development agreement with Bedoukian (Danbury, Connecticut).	F&F ingredients; Source: Perfumer & Flavorist, Vol. 39, September 2014	Symrise, Bedoukian Research, Inc.

Source: Compiled by ETC Group

Part II. Haiti: Essential Oils Trade

Essential oils are Haiti's most valuable agricultural export, accounting for US$16 million in 2012 (just 1.7% of the country's total export earnings). On the list of Haiti's top export commodities (by value), essential oils rank ninth.[37]

Globally, essential oil exports were valued at US$3.6 billion in 2012.[38] Among essential oil exporting countries, Haiti ranks 30th, accounting for a tiny fraction of global essential oil trade (0.44%). But Haiti is the only Caribbean country among the world's top 50 exporters,[39] and its global ranking belies the importance of essential oils to Haiti's small farm economy—and to the flavor & fragrance industry.

When it comes to Haiti's role in botanically-sourced flavors & fragrances, the dichotomy is striking: Ingredients for many of the world's highest-dollar luxury goods (perfumes, essential oils, liqueurs, cosmetics) are sourced from poor farmers living in one of the world's most impoverished nations.

What is an essential oil?

An essential oil is a concentrated liquid containing volatile aroma compounds that are extracted from plants using a distillation process. The oils are used to make perfumes and cosmetics, for flavoring foods and drinks, and for scenting household cleaning products. Note: "volatile" aroma compounds refer to molecules that easily transform into gases at room temperature.

Haiti: Geopolitical Background to Essential Oils Trade

Haiti is both an LDC [Least Developed Country] and a SIDS [Small Island Developing State], the poorest country in its region and one of the poorest in the world. Current and reliable statistics on Haiti's economic sectors are rare, and statistics on Haiti's essential oil industry are rarer still. Recent export statistics for Haiti, from UN Comtrade for example, are, out of necessity, based on "mirror statistics," that is, statistics from developed countries reporting on sources of their own imports; mirror statistics are known to be unreliable.[40] Nonetheless, mirror statistics suggest that in 2014, Haiti's essential oil exports were valued at US$21.1 million.[41]

Other reasons for uncertainty about Haiti's essential oil production, particularly bitter orange and amyris, include:

1) The highly-secretive nature of the fragrance and flavor industry, the buyers of Haiti's essential oils;

2) The informal nature of Haiti's workforce—estimates in 2012, at the launch of the Haitian government's first-ever business census, were that 80% of Haiti's economy is in the informal sector;[42]

3) The dominance of vetiver oil production in Haiti: bitter orange and amyris are minor contributors to Haiti's exports in comparison. Haiti is the world's largest exporter of vetiver oil and it is generally accepted that 60,000 people in Haiti depend on vetiver for their income; the number of people currently involved in bitter orange and amyris production is unknown;

4) The OAS trade embargo (1991-1994), which devastated Haiti's export capacity. Decades old truisms about Haiti's essential oils industry no longer held true in the period after the embargo. Lime oil, for example, had been a mainstay export since the 1950s, with the USA being the largest importer of Haitian lime oil; production was virtually eliminated during the embargo and is now in the "revitalization" stage with projects launched by NGOs and philanthropic foundations (e.g., Hugh Locke's Smallholder Farmers Alliance and the Clinton Foundation) partnering with companies interested in raising their sustainability profile (e.g., Swiss perfumer Firmenich's project to diversify crops grown by small farmers by planting lime, bitter orange and ylang-ylang seedlings in Haiti's South Department / le département du Sud);[43]

5) The earthquake in January 2010, affecting 3 million people and further disrupting Haiti's industrial capacity in all sectors. Statistics on Haiti's essential oil industry that pre-date the earthquake may bear little resemblance to the reality of Haiti after the earthquake.

Though vetiver accounts for the majority of Haiti's essential oil production, essential oils from bitter orange and amyris remain, apparently, income-generating commodities. "West Indian" lemongrass *(Cymbopogon citratus)*, lime *(Citrus aurantifolia [Christman] Swingle)* and ylang-ylang *(Cananga odorata)* are currently minor crops.

Box 2: A Note on the Impacts of the OAS embargo of Haiti 1991-1994

Elizabeth Gibbons, former head of UNICEF's office in Haiti and now at Harvard University,[44] attempted to assess the impact of economic sanctions against Haiti (1991-1994) in response to the coup d'état that ousted newly elected President Jean-Bertrand Aristide.[45] The embargo instated by the Organization of American States (OAS)—backed by the muscle of the United States under Bill Clinton—blocked fuel and arms imports and froze Haiti's exports. In Gibbons's estimation, the embargo cost Haiti 200,000 jobs and its toll on Haiti's exports totaled $15 million in coffee and cocoa exports, $12 million in mangoes and $14 million in essential oils. The embargo decimated the lime oil industry in Haiti—the USA was the biggest importer of Haitian lime oil at the time of the embargo. The Clinton Foundation is now focusing its philanthropy on Haiti. One of the "Partners in Haiti's Future," Firmenich—the world's second largest flavor & fragrance company—explains that it had sourced lime oil from Haiti in the 1980s, but "over time" the lime industry in Haiti disappeared. Its disappearance is one direct casualty of the trade embargo of the 1990s.[46]

Table 2: Haiti's top ranking exports in 2012

Rank	Export Product	Value (US$) million	% of total exports
1	Knit T-shirts	360	38.8
2	Knit Sweaters	222	23.9
3	Non-Knit Men's Suits	122	13.1
4	Scrap Iron	35	3.7
5	Non-Knit Men's Shirts	21	2.2
6	Knit Women's Undergarments	20	2.1
7	Knit Women's Suits	18	2.0
8	Non-Knit Women's Suits	16	1.8
9	Essential Oils	15.9	1.7
10	Scrap Copper	12.5	1.3
11	Tropical Fruits	11.4	1.2
12	Non-Knit Active Wear	10.1	1.0
13	Cocoa Beans	8.6	0.9
14	Crustaceans	4.5	0.4
15	Coffee	3.5	0.3
16	Non-Knit Women's Shirts	3.3	0.3
17	Scrap Aluminium	3.0	0.3
18	Knit Men's Suits	2.9	0.3
19	Non-Knit Men's Coats	2.9	0.3
20	Tanned Goat Hides	2.2	0.2
30	Citrus and Melon Peels	1.1	0.1
33	Perfume Plants	1.0	0.1
134	Vanilla	.015	–

Total export earnings: = US$929 million

Source: MIT's Observatory of Economic Complexity[47]

Vetiver

Vetiver plants Photo (cc) Josuah

Haiti's most important essential oil product, by far, is vetiver oil, a fragrance widely used in perfumes and cosmetics that is extracted from the aromatic roots of a perennial grass *(Chrysopogon zizanioides)*, commonly known as vetiver. Vetiver grass is native to India and mainland southeast Asia, but Haiti is the world's single most important source of high-quality vetiver oil. Haiti accounts for 50% of the estimated120-150 tons of vetiver oil produced worldwide per annum. An additional 25% of the world supply is produced in Indonesia. China, Madagascar, Brazil, Paraguay and India also export vetiver oil.

The crop (harvested for its aromatic roots) is extremely labor intensive and thrives in harsh environments. Vetiver grass can be cultivated on steep hillsides, which makes it well-suited to Haiti's terrain (i.e., over half the land in Haiti has a slope of more than 40%.[48]

Environmental Risks & Benefits: Because of the plant's exceptionally deep roots, vetiver grass is used as a tool for erosion control and water purification in many areas of the world (including Haiti). When harvested for oil production, however, the deep-penetrating vetiver roots can strip all vegetative cover from the soil and cause debilitating soil erosion. In Haiti, when appropriate harvesting and re-planting practices are used, the vetiver root crop can reportedly be cultivated and harvested sustainably. Farmers can and do take preventive measures to counter soil depletion. However, when farmers are under severe economic pressure, premature harvesting and lack of resources for re-planting can lead to environmentally damaging practices. A 2011 report, *Vetiver in Southwest Haiti,* prepared by Scott Freeman and published by the United Nations Environment Programme (UNEP), describes the pressures faced by Haiti's vetiver farmers:

The environmental impact of the vetiver plant is dependent on its context. While it has remarkable possibilities in terms of environmental conservation, the impact of vetiver must be framed in light of the context in which it is utilized. In the process of essential oil production, vetiver 'digging' can damage the limited quantity of top soil on the hillsides cultivated by farmers. While farmers recognized this damage and may make concerted efforts to repair or limit the soil erosion, the economic necessities of many Haitian families places pressure to harvest at environmentally and economically inopportune times. [49]

Vetiver oil is a major ingredient in many brand-name perfumes. Dubbed "the androgynous anchor of the fragrance world," vetiver is used in fragrances marketed for both men and women.[50] In fact, the majority of the world's perfumes contain some vetiver oil.[51] In addition to perfumes, vetiver oil is used in lotions, air fresheners, household products, ice creams, cosmetics and food preservation.

Industry noses describe vetiver:

Vetiver oil is an amber to grayish brown, olive brown or dark brown viscous liquid with an odor that is sweet and very heavy woody-earthy, reminiscent of roots and wet soil, with a rich undertone of precious wood notes. [52]

It smells like a perfume unto itself, with a lemony opening, a green-rosy heart, and a peppery-woody base. At its best it is both wild and refined. It provides the sunny effervescence in CHANEL's Cristalle, the raw green of Christian Dior's Eau Sauvage, and the star power of Vetiver by Guerlain, the men's fragrance most frequently co-opted by women.[53]

An estimated 60,000 people in Haiti's southwest region depend on vetiver as their primary income source.

In the Les Cayes region, where farmers cultivate vetiver on small plots of land, the aromatic root crop traditionally provides more income-generating potential than any other farm product. Approximately 13 distillers of vetiver operate in the Les Cayes region. But the harvesting of vetiver roots is back-breaking work that requires digging up dense clumps of roots and removing the hard-packed soil. The roots are then transported to local distillers where the vetiver oil is extracted by steam distillation. It takes about 150 pounds (68 kg) of roots to make 1 pound (0.45 kg) of oil.[54]

A 2011 report, *Vetiver in Southwest Haiti,* prepared by Scott Freeman and published by the United Nations Environment Programme (UNEP), describes Haiti's vetiver supply chain as "secretive and extractive."[55] The farming communities that grow and harvest vetiver in southwest Haiti are the hardest working but least powerful link in a global supply chain that includes: growers/ harvest labor; intermediaries; distillers; oil producers; exporters; perfumers/flavorists. The UNEP report estimates that the average Haitian vetiver farmer had gross annual income of just US$130 in 2011, and despite the money-making potential, the farmers' situation is precarious:

> *Farmers of vetiver were rarely content with their occupation. There was a pervading sense of frustration with the system they worked in. While vetiver provides the most cash of any income generating strategy the farmers and their families had, it most often did not provide a sufficient income for their cash related needs.*[56] *The harvest of vetiver is physically taxing, time consuming, and can be potentially damaging for topsoil. Because the oil produced by the vetiver plant is contained only within its root structure, the plant must be completely dug up in order to harvest the roots. This involves cutting off the tall grass, digging up and removing the roots. This practice leaves the harvested hillside with loose, upturned soil. The already mostly treeless hillsides are then particularly vulnerable to erosion should rain fall. The tools used for the harvest are simple: often a pick and/or machete. Given the minimal tools, terrain, and the nature of the harvest, vetiver work has a reputation for being extremely physically taxing.*[57]

Haitian Vetiver and the Flavor & Fragrance Industry

Even before the 2010 earthquake that killed more than 300,000 Haitians and left millions homeless, vetiver production in Haiti was unstable and experiencing a slow decline. [See geopolitical background, above.]

Operating under severe economic pressures, some vetiver farmers were forced to sell vetiver roots for whatever price they could get. Premature harvesting of the roots (especially in the rainy season) led to worsening soil erosion, lower yields and lower prices. The problems intensified because farmers didn't have the resources they needed to harvest and re-plant the crop sustainably. As a result, exports of Haitian vetiver oil reportedly dropped by half over the past 30 years.[58]

The 2010 earthquake focused worldwide attention on the devastation in Haiti. Following an influx of humanitarian aid, vetiver was identified as one of the few cash crops that could bring income to small farmers in southwest Haiti.

Since 2011, Haitian vetiver has become a cause célèbre. The flavor & fragrance industry not only recognized that its vetiver supply chain was endangered, but the spotlight on Haiti also provided a public relations-friendly backdrop for public-private initiatives espousing "fair trade," "sustainability" and "ethical sourcing." Even former US President Bill Clinton championed the cause of vetiver farmers and in 2013 the Swiss CEO of Firmenich traveled to southwest Haiti to tour vetiver-growing communities. These and other public/private initiatives (see below) claim to support rural communities in southwest Haiti by enabling small farmers to adopt socially and ecologically responsible production of vetiver oil.

Although vetiver oil can be sourced from other countries, perfumers consider Haitian vetiver the highest quality. Over the past four years the leading flavor & fragrance firms as well as many other industry players (perfumers, aromatherapy companies, etc.) have launched high-profile initiatives to support sustainable vetiver sourcing in Haiti.

For example:

Firmenich: In 2010, Firmenich made a commitment under the Clinton Global Initiative platform to work with farmers in Haiti to ensure the sustainable production of vetiver oil.[59] In partnership with the Swiss Development and Cooperation Agency (SDC), Firmenich is reportedly investing $1 million in its sustainable vetiver program, including building roads, a primary school, supporting renewable energy for distilling operations, and focusing on economic opportunities for women.[60] Firmenich's program focuses on the farming community of Débouchette (pop. ~6,300) in the Les Cayes region (southwest Haiti). According to Firmenich, Débouchette has been certified by ECOCERT, a sustainable development organization that certifies environmentally friendly standards for agriculture.

In July 2016 **IFF** and **Unilever** announced Vetiver Together, a "new partnership with leading non-governmental organizations to enhance the livelihoods of smallholder vetiver farmers in Haiti."[61] Unilever uses vetiver oil in their Axe and Impulse brands. The project is supported by the Enhancing Livelihoods Fund, a partnership between Unilever, Oxfam Great Britain, and the Ford Foundation. The initiative will focus on "sustainably improving food security, increasing yields and diversifying income, as well as working to support women's empowerment and environmental conservation."[62]

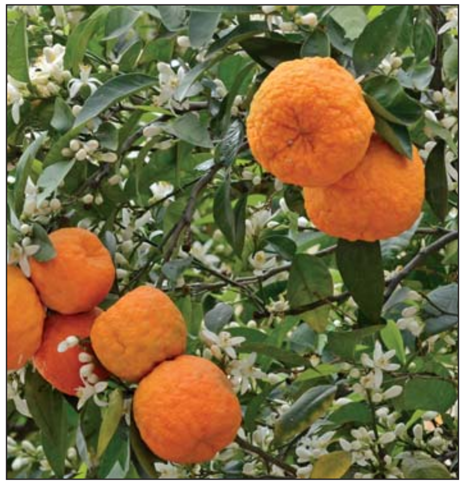
Givaudan also supports a sustainable vetiver sourcing initiative in Haiti in partnership with a Les Cayes distiller, Agri-Supply, reportedly the largest producer and exporter of vetiver oil in the world.[63] Since 2013, Givaudan has supported a cooperative of 160 vetiver growers from three villages, Massey, Faucault and Bazelais, that produce an exclusive, certified vetiver oil for Givaudan perfumers.[64] [Firmenich also partners with Agri-Supply.]

Industry supported non-profits/foundations have also been formed to support "ethical sourcing" and "fair trade" of vetiver, among other raw materials. Founded by a consortium of beauty, fragrance, and flavors companies, **Natural Resources Stewardship Circle (NRSC)**, is a non-profit organization based in France that promotes "responsible sourcing" of natural ingredients, including vetiver. The organization supports six cooperatives in Haiti with the objective of increasing the production capacity of traced vetiver oil to 15-20 tons. Notably, NSRC has developed a 26-page document that details specifications for all actors in the vetiver supply chain. The aim is "to assure the economic, ecologic and social sustainability of the Haitian vetiver chain."[65] The specifications—which apply to cooperatives of small producers, individual producers, distillers, exporters, industry/manufacturers, finished-product companies—set minimum best practices.

Although NSRC encourages actors to respect the specifications, it does not monitor compliance and they are non-binding—that is, they are voluntary.[66] However, a joint UNCTAD/WTO Session on Private Standards points out that the term "voluntary" may be misleading in the context of supply chains that are tightly concentrated: "Although not legally binding in a regulatory sense, private-sector standards are, *de facto,* increasingly becoming mandatory because of the market power of certain large, globally acting retailers and importers."[67] "Private voluntary standards" are becoming a key element of many global supply chains for food and agriculture. Although the vetiver "specifications" aim to support sustainable practices, the top-down approach to standard-setting raises many questions, especially for the most vulnerable actors in the supply chain: Will record-keeping and "internal tracking" practices imposed by NSRC specifications (e.g., GPS coordinates, notes on yields, storage requirements) benefit some farmers and disadvantage or exclude others?

Compliance with environmental standards may improve the management of natural resources and result in better conditions for farmers, but it may also encourage consolidation and concentration within the farming/processing community. A 2009 report by the Human Rights Council's Special Rapporteur on the Right to Food warns that "the development of private standards has worked against smallholders."[68]

It's not clear how many vetiver farmers are now involved in cooperatives and how much they are directly benefiting from the new initiatives. These are important questions for on-the-ground researchers in Haiti.



Bitter oranges   Photo (cc) Zeynel Cebeci

According to an April 2014 article by Reuters on new vetiver initiatives in Haiti: "The cooperative farmers have seen as much as a 30 percent rise in income, as well as improved yield and root quality, said Rene Louis Maurice, 69, a cooperative member. Perfumers working with the distillers now offer a 15 percent premium to farmers who follow best practices, as well as a guaranteed minimum price. That includes leaving the vetiver roots alone for at least 12 months and not harvesting them during the rainy season (August to November)."[69]

It's not clear how many vetiver farmers are now involved in cooperatives and how much they are directly benefiting from the new initiatives. These are important questions for on-the-ground researchers in Haiti.

Virtually all of the major industry players, as well as public-private initiatives, are putting heavy emphasis on the establishment of farmer cooperatives, sustainable sourcing and fair trade of vetiver. New initiatives are called a "win-win" partnership for Haiti's farmers and for the flavor & fragrance industry. The Reuters article reported that farmers who belong to vetiver cooperatives now account for 30% to 50% of the vetiver processed by the big distillers, but it's difficult to tell how many farmers are benefiting from the new initiatives.[70]

Bitter Orange

Botanical name: *Citrus aurantium,* family: *Rutaceae;* French: *orange amère* or *orange bigarade;* Creole: pye zoranj sure*;* also known as Seville orange and sour orange.

The bitter orange tree is the source of several indispensable ingredients for the flavor & fragrance industry. According to Mark Blumenthal of the American Botanical Council: "In the fragrance industry, the products from the bitter orange tree include neroli oil, bitter orange flower absolute (an absolute is a concentrated flower oil used in the fragrance industry), bitter orange flower water absolute, bitter orange petitgrain oil (bitter orange leaf oil), bitter orange leaf water absolute, bitter orange petitgrain absolute and other petitgrain oils.

In the food industry, bitter orange oil, which is usually expressed from the fresh peels, is widely used as a flavoring agent. Bitter orange oil is used as flavorings for beverages, particularly liqueurs and to intensify the orange character of soft drinks."[71]

According to The Aromatic Plant Project: Blossoms of the true bitter (sour) orange tree…on being distilled yield Neroli bigarade oil. If, on the other hand, the leaves and petioles (leaf stalk) are distilled, oil and hydrosol of Petitgrain Bigarade is obtained.[72]

Bitter orange also contains the protoalkaloid, p-synephrine. Flavonoids, including limonene, hesperidin, neohesperidin, naringin, and tangaretin, are present in bitter orange peel, flowers, and leaves; bitter orange also contains the furocoumarins bergapten and oxypeucedanin.[73]

Haiti's bitter orange trees are mostly grown in the Département du Nord / North Department in the communes of Ranquitte, Bahon, Grande Rivière du nord and St-Raphael.[74]

A technical analysis of agriculture in the North Department published in 2010 estimated that 66,000 producers grow some citrus, but this figure includes both sweet and bitter oranges, as well as lime and "chadèque" (i.e., pomelo).

Due to the secrecy of the flavor & fragrance industry, it is difficult to know which companies buy Haiti's bitter orange peels and oils and for what purposes. However, in the early 2000s, two French companies producing high-end orange liqueurs—Société des Produits Marnier-Lapostolle, which makes Grand Marnier, and Rémy Cointreau Group, which makes Cointreau—were the targets of workers' rights campaigns, organized by the Haitian labor union Batay Ouvriye. Haiti's bitter orange is used in both liqueurs, and news of the workers' struggles garnered international attention and unveiled some details about the work and working conditions:

An article by Charles Arthur in *International Union Rights* [75] describes "...a spirited—and significantly—successful struggle for improved pay and conditions waged by workers at an orange tree plantation owned by the French liqueur company, Marnier-Lapostolle.

In 1999, workers at the plantation just outside Cap-Haïtien organised themselves into a union to demand protective clothing and an increase in a daily wage that was equivalent to less than one US dollar. When the Haitian management refused to discuss a realistic settlement, international campaigners bombarded the main office of the French parent company with emails and letters of protest. In August 2000, Marnier-Lapostolle, fearing for the public image of their prestige brand, the Grand Marnier liqueur, authorised a 25% wage increase and improved working conditions..."

A related article in *The Guardian* from 2002 described the work involved in the processing of bitter oranges:

"The 16 women workers here [at the Madeline processing plant in Cap-Haïtien] cut the oranges in two and feed them into a machine that extracts the oil. They are paid per 42-kilo box, so they need to work quickly. They hold three or four oranges in a hand at one time and, inevitably, some workers have parts of their fingers missing. The citric acid also damages their skin, but they say the fumes from the oranges are worse. On long days they sometimes faint, and many say they have respiratory illnesses. For each box they cut, they earn 4.5 gourdes (11p). On a good day, they'll do 40 or 50. The work is seasonal: 20 weeks last year, but less than eight weeks this. At Marnier-Lapostolle [plantation] the work is harder. About 300 people process the oranges in two ways. The women cut some into quarters, pulling out the bitter pulp by hand before sending the peels to the dryer. Other workers laboriously grate the zest by hand, and this is then processed to extract the oil. They, too, are paid per 42-kilo box: 32 gourdes (83p) for cutting and extracting the pulp, 45 gourdes (£1.16) for grating by hand. None of the women I met had recognisable fingernails: the citric acid had burned them down to gnarled stumps. Sometimes, they say, their hands are so painful that they can't wash their family's clothes. They too report respiratory problems: 'Sometimes if we cough, blood comes out..." [76]

Amyris / "West Indian Sandalwood"

Sandalwood
Photo (cc) Kinshuk Sunil

Botanical name: *Amyris balsamifera,* family: *Rutaceae,* Creole: bwa chandèl [bois chandelle], bwa chandèl vèt

According to the web site of Albert Vieille,[77] a French fragrance company:

Amyris is a small tree that forms dense clusters, native to the Caribbean and Gulf of Mexico...Though its fragrance has a woody dimension similar to sandalwood, the plant does not belong to the genus Santalum and should not be confused with Indian sandalwood, Santalum album.

Indigenous peoples traditionally called amyris wood 'candlewood' because of a high essential-oil content that caused it to burn longer. Haitian fishermen used it to make 'torches' that they used by night to catch sea crabs. Country-dwellers also used it when they had to go to the market before sunrise. The scent of the essential oil of amyris wood has a characteristic woody, sweet heart that develops and ultimately becomes a bottom note with a slightly smoky facet.

Production areas for this wood are very hard to reach. The gathering and cutting is done by indigenous farmers and takes a great deal of physical effort. The harvested branches and trunks are then routed to the distilleries, mainly via Les Cayes and Port-au-Prince. The wood must dry for at least a year, ideally for two or three years, before distillation. It is coarsely crushed and then steam-distilled using water. The resulting essential oil is then refined for several months or even a year to ensure optimal olfactory quality.

According to Bernard P. Champon Sr., owner of the Haiti Essential Oil Company, writing in 2001, "Only the wood from trees that have died naturally is used. Collection of wood is carried out by 'speculators', who transport the material to the distilleries for sale. Some distillers carry a wood stock that is equivalent to many tens of drums of oil."[78]

Exports of Haitian amyris oil first began in 1943-44 from a production plant located at Chalons outside of Miragoâne, according to an agricultural assessment of Haiti produced by USAID in 1987.[79] At the time of USAID's report, the main supply areas of amyris wood were Tortuga Island and Môle-St.-Nicolas. According to USAID citing a 1983 study of Haitian essential oils by Leslie Delatour, only trees from certain areas are appropriate for processing, and the wood requires at least 6 months of drying before processing [note the difference from Albert Vieille's timeline, above]; then the wood is chipped by hand and mechanically ground into sawdust. Because it is very corrosive, only stainless steel can be used for processing, with a distillation time of up to 168 hours. According to a 2003 study, amyris distilleries are located in Ducis, Maniche, Miragoâne and Jacmal—those cities are in the southern peninsula (now) in the Départements of Sud, Sud-est and Nippes.[80]

According to Perfumer & Flavorist magazine, throughout the first decade of the 21st century, Haiti's annual production of amyris oil was 60 metric tonnes (Note: This estimate was published in 2009, one year before the earthquake).[81] Though Haiti may still be distilling some amyris oil, the supply of native amyris wood is often described as depleted. A 2004 proposal from an essential oil company (Texarome, Inc.) for a biomass energy project (from vetiver) to the government of the Dominican Republic reports that all the Amyris balsamifera in Haiti comes from the Dominican Republic and is smuggled across the border into Haiti.[82] In 2001, Bernard Champon wrote: "From time to time, there are rumors to the effect that there is a shortage or potential shortage of raw material in Haiti. However, I have specialized in Haiti oils for 50 years and have heard such rumors many times. There always seems to be sufficient wood and I am certain that more would be forthcoming if the demand for the oil increased."[83] However, Gilbert Assad of Arome et Essence d'Haïti, reported to ETC Group in April 2015 that, currently, amyris production is virtually non-existent in Haiti due to depleted supply of native wood and to changes in export regulations in the Dominican Republic.[84]

Part III. Haiti's Essential Oil Crops & Synthetic Biology

Vetiver and Synthetic Biology

Is it possible to produce aroma compounds that are structurally related to vetiver in engineered microbes? Is biosynthesis of vetiver-related compounds commercially viable? Is it a threat to small farmers in Haiti?

Background: In March 2012 California-based synthetic biology company, Allylix, Inc., announced that it had successfully engineered a metabolic pathway in yeast to produce a key fragrance compound found in vetiver oil. Allylix said that its new biosynthetic fragrance—dubbed "Epivone™"—is structurally related to beta-vetivone, one of the key components of vetiver oil. According to the then-CEO of Allylix: "Epivone™ is a highly valuable compound and because we own the patents claiming the fragrance and its novel production method, we expect to be the only commercial supplier."[85] Allylix claimed that beta-vetivone had not previously been commercialized because chemical synthesis of the compound is too expensive. The company projected that its biosynthetic Epivone™ fragrance would generate revenues of $20 million to $200 million.[86]

Allylix Inc. has engineered yeast that produces a key fragrance compound found in vetiver oil dubbed 'Epivone™'

Evolva Acquires Allylix: Although Allylix had announced plans to commercially launch its Epivone™ fragrance in the third quarter of 2012,[87] no subsequent information about the product launch was disclosed by the company, and the vetiver-related fragrance was not commercially released.

In November 2014, Allylix was acquired by another synthetic biology company, Switzerland-based Evolva.[88] Like Allylix, Evolva has its own "proprietary, fermentation-based platform" for the production of biosynthetic flavors/fragrances in yeast.[89]

With the acquisition of Allylix, Evolva added 100 patents and two marketed flavor/fragrance products: valencene (flavor/fragrance from sweet oranges) and nootkatone (a flavor/fragrance from grapefruit). Evolva's IP portfolio includes four US patents related to beta-vetivone and additional patent applications.

Industry analysts suggest that Evolva's acquisition was motivated primarily by the acquisition of Allylix's patented technology that reportedly enables higher-yields for biosynthetic compounds in yeast, especially stevia.[90] Stevia is a high-intensity, natural sweetener produced by the stevia plant. Since 2013, Evolva has partnered with Cargill to jointly develop and commercialize biosynthetic production of steviol glycosides in yeast. (Steviol glycoside is the primary compound responsible for the sweet taste of stevia plant leaves.) Under the agreement, Evolva has the option to form a joint venture (owning up to 45%) with Cargill to market the stevia products, which the company expects to launch in 2016. According to Evolva, the high-intensity sweetener market for beverages alone is worth an estimated $4 billion.[91]

Table 3: Allylix (now Evolva) Patents Related to Biosynthesis of Vetiver

Patent #	Pub. Date	Title
1. US 8,642,815 B2	4 Feb. 2014	Fragrance And Methods For Production of 5-epi-beta-vetivone, 2-isopropyl-6,10-dimethyl-spiro[4.5]deca-2,6-dien-8-one
2. US 8,362,309 B2	29 Jan. 2013	Fragrance And Methods For Production of 5-epi-beta-vetivone, 2-isopropyl-6,10-dimethyl-spiro[4.5]deca-2,6-dien-8-one, And 2-isopropyl-6,10-dimethyl-spiro[4.5]deca-1,6-dien-8-one
3. US 8,124,811 B2	28 Feb 2012	Fragrance And Methods For Production Of 5-epi-beta-vetivone, 2-isopropyl-6,10-dimethyl-spiro[4.5]deca-2,6-dien-8-one, And 2-isopropyl-6,10-dimethyl-spiro[4.5]deca-1,6-dien-8-one
4. US 7,622,614 B2	24 Nov 2009	Methods For Production Of 5-epi-beta-vetivone, 2-isopropyl-6,10-dimethyl-spiro [4.5]deca-2,6-dien-8-one, And 2-isopropyl-6,10-dimethyl-spiro[4.5]deca-1,6-dien-8-one

What is the current status of Evolva's R&D on Epivone—the compound related to vetiver?

Since the 2014 acquisition of Allylix, Evolva has not publicly disclosed plans for further research, development or commercialization related to beta-vetivone (i.e.,"Epivone™"), one of the key components of vetiver. The company's website does not mention "Epivone™" or the potential market for a vetiver-related fragrance.

ETC Group contacted Evolva's CEO, Neil Goldsmith, to find out about the company's plans to commercialize its proprietary Epivone™ product. [Note: Goldsmith is one of the few representatives of the synthetic biology industry working on flavors/fragrances who is willing to answer questions posed by ETC Group, and his cooperation is appreciated. Numerous other syn bio companies working on flavors/fragrances were contacted (repeatedly) during our research for this report, and most did not respond.] According to Neil Goldsmith: *"No we are not developing Epivone™. Allylix decided not to commercialize it, and we have no plans to revisit that decision. Is that a "no, never"? No it is not. But I think it is highly unlikely."* [92]

Contrary to statements made by Allylix's CEO, Goldsmith explains that his company's product cannot be compared to vetiver because Epivone™ does not contain the key aroma compound found in vetiver:

> *Vetiver oil is a complex mixture with Alpha-vetivone (not Beta) being the main aroma molecule, though there is some Beta in it. Epivone™ does not smell, blend or perform in the same way as vetiver, nor was it intended to. Yes there are some aspects in common, but that is like saying humans are the same as mice, just because they both eat cheese. In reality they are not the same...* [93]

Fragrance chemists do not agree that Alpha-vetivone is the "main aroma molecule" in vetiver oil. Writing in the February 2012 issue of *Perfumer & Flavorist*, one chemist observes that there is "a controversy regarding what specific molecules contribute to vetiver odor."[94]

According to Günther Ohloff *et al.*, in *Scent and Chemistry: The Molecular World of Odors* (2012), vetiver oil consists of a complex mixture of more than 150 sesquiterpenes (a class of organic compounds—a type of terpene).[95]

The sesquiterpenes *alpha*-vetivone, ß-vetivone, and khusinol always occur in vetiver oil in amounts up to 35%, and "they are considered to be fingerprints of the oil even though they do not possess the typical odor characteristics associated with vetiver."[96]

Chemists and perfumers believe that the chemical compound, khusimone, plays an important role in "the odorous principle of vetiver" even though khusimone is only present in small amounts (about 2%) of vetiver oil.[97] Although khusimone was first chemically synthesized in 1979,[98] the goal of chemically reproducing a synthetic vetiver oil remains elusive: "the holy grail of a synthetic vetiver odorant has still not been found and remains…one of the major challenges for the fragrance chemist."[99] According to a 2013 interview with Givaudan's senior fragrance chemist, Philip Kraft, "a 100% copy seems impossible, or at least extremely difficult."[100]

> *"Because vetiver oil contains a complex mixture of sesquiterpenoids with complicated structures, it is unlikely that an economical reconstitution of the oil will be feasible in the near future."* [101]

Will synthetic biology succeed where organic chemistry has failed? Chemists have thus far failed to replicate vetiver oil in the laboratory. Will synthetic biologists be able to engineer microbes that can manufacture molecules that mimic vetiver oil? If so, will it threaten the market for botanically-derived vetiver and the livelihoods of ~30,000 farming families in Haiti? Given the complexity of biological systems, it won't be easy.

Fragrance experts agree that the composition and odor quality of vetiver oil is tied to its geographic origin and the environment in which it is grown[102]—a factor that may be advantageous to Haiti as the preferred source of botanically-derived vetiver. A study by Italian researchers reveals that the quality of vetiver oil is affected by the composition of microbial communities present in and around the roots of the plant.[103]

Vetiver root cells produce certain oil precursors that are then metabolized by the root bacteria and ultimately affect the odor quality of vetiver oil extracted from plant's roots.[104] According to a 2015 study by a team of Indian scientists: "This opens up the possibility of using these bacterial colonies to directly manipulate the oil composition. This can be done either by in vitro method using specific bacterial strains to convert the raw material into the desired composition or secondly by in vivo method by manipulating the bacterial colonization of the plant root."[105]

> *"Bacteria seem to promote the production of essential oils, but also they change the molecular structure of the oil, giving it different odor qualities and properties."* [106]

Why did Evolva/Allylix move away from commercializing Epivone™? We do not know why Evolva decided not to pursue commercialization of Epivone™. Evolva told ETC Group that the decision to halt commercialization had already been made by Allylix before it was acquired by Evolva. We suspect that the high profile support for Haitian vetiver by philanthropic organizations and concerns already raised by ETC Group and our allies about Epivone™ impacting vetiver farmers was seen as a public relations liability and a distraction from Evolva's most strategically important products (especially stevia, in partnership with Cargill).

Bitter Orange and Synthetic Biology

Bitter orange trees *(Citrus Aurantium)* are the source of three major flavor and fragrance ingredients: bitter orange oil (bigarade) is expressed from the peels of the fruit and is used to flavor beverages and liqueurs;[107] petitgrain oil is distilled from the leaves and small branches and is used widely in perfumes; neroli oil is steam-distilled from the blossoms/flowers.

Neroli oil is a classic example of a high-value/low-volume ingredient, the salient characteristic of current synthetic biology R&D targets.

Steam distillation of 850 kg of carefully picked orange flowers yields just 1 kg of neroli oil.[108] Global annual production of neroli oil is between 2 and 3 tons, with the major producers in North Africa.[109]

Bitter orange oil contains the protoalkaloid, p-synephrine. Flavonoids, including limonene, hesperidin, neohesperidin, naringin, and tangeritin, are present in bitter orange peel, flowers, and leaves; bitter orange also contains the furocoumarins bergapten and oxypeucedanin.[110] Nootkatone, a target molecule of at least two syn bio companies, is not found in neroli or petitgrain.[111]

We have not identified a syn bio company that has publicly disclosed it is targeting bitter orange. (Celbius [UK] has developed a syn bio-derived 2-phenylethanol, an aromatic alcohol used in food, fragrances and cosmetics, which is also found, apparently, in neroli oil, but in small concentrations.) Because bitter orange essential oil has been used traditionally to treat digestive ailments (and as a weight loss aid)[112] due to the protoalkaloid component, p-synephrine, it may well be (or become) an attractive target for use as a flavoring ingredient, especially in "nutriceutical" products. (This is speculation on our part, but the secretive nature of the flavor and fragrance industry cannot be overemphasized; in so many cases, we don't know what ingredients companies are targeting. Evolva, for example, uses "code words" to refer to products in the pipeline that the company is not ready to disclose—Evolva's 2014 annual report lists six undisclosed products in its pipeline, with a note claiming that "additional undisclosed ingredients are in internal development."[113])

Amyris balsamifera ("West Indian Sandalwood") and Synthetic Biology

Amyris oil is rich in sesquiterpene alcohols. As reported in *Perfumer & Flavorist,* a 1989 analysis of a sample of amyris oil, "presumed to be of Haitian origin," contained valerianol (21.5%), 7-epi-a-eudesmol (10.7%), 10-epi-y-eudesmol (9.7%).[114] Note: Haiti's sandalwood does not contain santalols, sesquiterpene alcohols that are thought to be the main odor vectors in East Indian sandalwood.

Haiti's sandalwood has no botanical relation to the East Indian sandalwood *(Santalum album)*, which is the world's most expensive tropical hardwood; East Indian sandalwood oil now commands more than $2000/kg. "West Indian" sandalwood oil is described as having a less potent, but similarly woody fragrance than its more valued/valuable Eastern counterpart. (The retail price of amyris oil is ~$100/kg.) Because India's sandalwood trees have been dangerously over-harvested, western Australia has become a major source of sandalwood oil—derived from a different tree *(Santalum spicatum)* as well as from non-native *Santalum album* trees grown on plantations. There are already synthetic commercially available sandalwood fragrances (e.g., Sandalore) that are widely used in perfumes—some of them high-end fragrances[115]—but there is market demand for a sandalwood fragrance that can be labeled "natural" and "sustainable."

While we have not been able to identify a syn bio company specifically targeting *Amyris balsamifera,* we know that Allylix/Evolva are developing a syn bio-produced sandalwood-like fragrance, which may (or may not) indirectly affect the market for Amyris from Haiti.

The situation is complicated, however, because we do not know if there is any *Amyris balsamifera* wood left in Haiti. In the first decade of the 21st century, Haiti's annual production of amyris oil was estimated to be 60 metric tonnes, but no more recent statistics are available. In 2010, post-earthquake, the Haiti Essential Oil Company reported that "inventories are sufficient to meet all normal demand," but without details of the size of the demand or the source of the wood. An industry source in Haiti reported to ETC Group that there is no more Amyris wood left in Haiti.[116] Are there efforts afoot to revitalize Haiti's amyris industry in Haiti? Could these efforts be undermined by R&D in synthetic biology? The situation must be clarified by on-the-ground research before we can attempt to predict the effects of a syn bio-derived sandalwood fragrance on the market.

Box 3: How could farmers be impacted by synthetic biology developments? A Historical Perspective

History shows that the introduction of new technologies can have profound and devastating impacts on the livelihoods of farmers, agricultural workers and national economies. Distinct waves of technology transfer can be identified. In the colonial era, for example, European expansion accelerated the flow of food plants and livestock between continents and peoples. In most cases, colonial powers controlled the flow of crops and germplasm and also monopolized the production and processing technologies important to commercialization (e.g., cotton, rubber, coffee, tea and spices). As a result, the technology transfers often created patterns of long-lasting economic dependence in the colonized countries.

Developments in chemistry toward the end of the 19th century—particularly in Germany France and the United Kingdom—propelled a new technology wave that reduced and/or eliminated the demand for a wide array of raw materials once sourced in the global South. Chemically-synthesized dyes from Germany, for example, quickly replaced natural dyes such as the madder root. Between 1850 and 1870 Turkish farmers exported 15,000 tonnes of madder root a year to British textile firms. By 1900 Turkey's natural dye market disappeared due to a chemically synthesized substitute: alizarin. Liberia's valued export, a red dye from camwood, became commercially irrelevant almost overnight—as did Mexico's carmine dye (from the cochineal beetle). When blue synthetic dyes went into large-scale production in Germany in 1897, Indian farmers were cultivating 574,000 hectares of indigo in Bengal and Bihar.

By 1920, the crop had virtually disappeared. Following World War II, synthetic petroleum-based fibers quickly eroded the global market for not only textiles (silk and cotton), but also for hard fibers customarily used in everything from carpets to car mats, ropes and baling twine. In the 1930s, polymer science spawned the plastics "revolution." Less than a century later, we are beginning to comprehend the social, environmental and health legacies of petrochemicals and synthetic polymers.

The first beneficiaries of sudden technology shifts have historically been those who develop and/or control the new technology. The "losers" tend to be the producers of primary commodities who were unaware of the imminent changes and/or those who could not make rapid adjustments in the face of new demands.

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In order to assuage concerns that synthetic biology could result in the same winners/losers scenario, some advocates have argued that the transfer of field production to vat production could benefit local ecosystems and local food security. Amyris, Inc. in Berkeley, CA has suggested that the elimination of the field production of the Chinese wormwood shrub for a pharmaceutical compound (artemisinin) could allow farmers to grow more potatoes. This, in fact, is not economically or ecologically plausible. Farmers not only benefit substantially from wormwood shrub production, but also the antimalarial tea they brew at home is directly beneficial to their families and communities. Potatoes, on the other hand, are notoriously destructive to soils, and farmers are often obliged to make extensive use of crop chemicals with all the attendant economic, health and environmental damages.

In another case, undercutting natural vanilla production in Madagascar (and its replacement with vat production in Switzerland) would immediately damage the livelihoods of family producers and oblige them to cut back the wonderfully diverse and valuable forests that safeguard the vanilla plants.

Theoretically speaking, however, synthetic biology could stimulate demand for more of a given natural product. The development of synthetic rubber in the USA during World War II and after led, within a couple of decades, to synthetic rubber occupying more than 60% of the global market. At the same time, post-World War II affluence and the demand for tires also increased the demand for natural rubber and the producer countries in Southeast Asia have benefited. Likewise, the discovery of a bacterium in Thailand in the 1950s that led to the introduction of high fructose corn syrup (HFCS) in the 1960s could have been expected to wipe out demand for sugar cane and sugar beet. In reality, the explosion in consumer demand for sweeteners—and cars for ethanol—meant that the demand for both corn and sugarcane boomed, for better or worse.

Might this be so for natural flavors in fragrances? 95% of the market has already lost to chemical synthetics. The remaining 5% still sustains tens of millions of farm families around the world. They are worth fighting for. In the past few weeks, major food processors and even fast food companies (including Pizza Hut and Taco Bell) have announced that they are going back to "natural" flavors in the face of widespread consumer disaffection. This is a battle that can be won.

Schumpeter's dictum on "creative destruction" still dominates, however. Not just change—but also the threat of change—can be highly destructive, even if it may turn out to be beneficial in the long run. Simply the possibility that a crop could be grown in a vat can disrupt supply chains and damage producer prices causing farmers to abandon their best opportunities for fear that there will be no one to sell to at harvest time. In such cases, synthetic biology doesn't have to be technologically successful to be commercially successful if the competition has been persuaded to retreat. The bottom line is creative destruction is always devastating to marginalized peoples and even longer term changes shouldn't be considered before those affected are able to be full participants in the political and economic negotiations involved in any technological change.

Conclusion

Synthetic biology's quest to engineer microorganisms that synthesize flavors/fragrances via large-scale industrial fermentation is a proven technology for some high-value compounds—and many more are in the pipeline. Existing regulations in the EU and US allow these products (derived from fermentation and microbiological processes) to be labeled as "natural" ingredients/products, positioning them to compete with botanically-derived compounds as well as their synthetic (chemically derived) counterparts.

The synthetic biology manufacturing platform is real, expanding rapidly and a serious economic threat to economies and livelihoods of producers of high-value natural plant products.

Synthetic biology is already commercialized and is already undermining wormwood prices (from which the antimalarial compound, artemisinin, is made), especially for small farmers in East Africa. Nevertheless, the development of each synthetic biology product varies in complexity and, therefore, cost and time. Metabolic pathway engineering and microbial fermentation may not be technically or economically viable for all flavor/fragrance compounds, despite the comprehensive lists found in patents and patent applications. That the technology exists doesn't mean that the commercial logic exists. Startup companies inevitably exaggerate the speed and impact of their innovations.

There is no assurance that vetiver-related fragrance compounds will not be the target of Evolva or other synthetic biology researchers/companies in the future.

In the case of vetiver:

- We have identified only one company, Evolva, that currently holds patents related to synthetic biology and the production of compounds that are structurally-related to vetiver.
- Evolva claims that it is not currently conducting R&D to commercialize its proprietary vetiver-related compounds, and that it is unlikely that it will do so in the future. (The patents were issued to Allylix, a company acquired by Evolva in 2014.)
- Evolva claims that its proprietary compounds (related to beta-vetivone) are not the ones associated with vetiver's key aroma compounds. However, we don't have the technical expertise to verify this statement. We contacted numerous flavor/fragrance chemists in academia and industry to ask for their opinion on this issue, and we surveyed available patents and literature. One industry consultant agreed to look at our questions related to the molecular components of vetiver for a minimum fee of $2000. (In the end, we were not confident that his expertise would sufficiently answer our questions.) Chemists have so far been unable to achieve chemical synthesis of vetiver essential oil—although key aroma compounds (such as khusimone) have been synthesized[117]
- There is no assurance that vetiver-related fragrance compounds will not be the target of Evolva or other synthetic biology researchers/companies in the future.

Although major industry players in the flavors/fragrance industry (e.g., Givaudan and Firmenich) currently invest in high-profile initiatives for sustainable production of vetiver in the Les Cayes region, the same companies are supporting R&D related to synthetic biology (though R&D is not related to vetiver, to our knowledge).

In the case of Haiti's bitter orange, no company has revealed that it is specifically targeting Haiti's *Citrus aurantium.* Because bitter orange essential oil has been used traditionally to treat digestive ailments and as a weight loss aid, it would seem to be an attractive target for a synthetic biology-derived substitute, particularly as a "natural" ingredient in so-called nutriceutical foods. Other known citrus-derived targets of syn bio R&D (e.g., valencene and nootkatone) could provide precedent.

The case of Haiti's sandalwood, derived from the wood of *Amyris balsamifera,* is unclear due to at least two factors: 1) Amyris production in Haiti seems to be at a standstill due to a scarcity of native wood and the difficulty of bringing wood into the country from the Dominican Republic for processing and 2) While no company has announced it is targeting amyris, at least two companies are focusing R&D efforts on producing an East Indian sandalwood oil fragrance using synthetic biology: Netherlands-based Isobionics and Swiss-based Evolva. Cost of the syn bio ingredient may ultimately determine whether it affects the market for West Indian sandalwood.

At the current time we believe that Haiti's essential oil crops are not in immediate danger from competition by synthetic biology substitutes but that could change in the future – especially if a company (eg Evolva) decided to resume work on vetiver fragrance. It is possible that developments in synthetic biology will not significantly affect Haiti's essential oil exports, but will affect Haiti's other important agricultural exports, including coffee and cocoa. It also bears repeating that the flavor and fragrance industry is notoriously secretive: in so many cases, we don't know what ingredients synthetic biology companies are targeting. Evolva's use of code words for flavors and fragrances under development is typical."[118]

An anecdote reported in a 2009 *New Yorker* article describes the culture:

> *Several years ago, a Givaudan employee attending a convention accidentally let slip to a reporter for Beverage World that the company had made a vanilla flavor for Coca-Cola. After the comment was published, Givaudan executives acted as if a state secret had been breached: they investigated the leak, restricted all information about their business with Coke to employees working directly for the company, and flew to Atlanta to visit the Coca-Cola headquarters and apologize in person. In the world of flavor, it is not enough to keep secret a chemical formula. (Typically, these formulas are not patented; hence the obscuring use of "natural flavoring" as an ingredient—and an omnipresent riddle—on food labels.) The Givaudan employee who attended the convention had broken a more fundamental rule. Few of the companies that sell processed foods or drinks want the public to know that outside laboratories supply them with flavors.*[119]

This secrecy extends to the "natural" ingredients produced via synthetic biology. **There is virtually no consumer awareness that the definition of "natural" extends to flavors/fragrances excreted by engineered microbes produced via industrial fermentation.**

Flavor & Fragrance industry executives suggest that their companies' choice to use a plant-derived natural ingredient, a syn bio-sourced ingredient or a chemically synthesized ingredient will be a pragmatic decision based on price and market. In a recent "sustainability" roundtable discussion with representatives of flavor & fragrance firms investing in syn bio-sourced ingredients (IFF, Firmenich and Bedoukian Research), Firmenich's David Shipman explained, "Customers want naturals for some reasons and synthetics for other reasons, so we have to cater to the customers for both…So I think the name of the game is going to be to listen to our customers, to watch our customers, and to watch the trends going on and be ready for the number of products 10 years from now, which are going to be very different from what we're using today."[120]

No one disputes that flavor & fragrance companies are watching their customers, but their hope is to pass off cheaper syn bio-derived ingredients as “natural” by exploiting weak labeling regulations in order to (appear to) satisfy customer demand.

This will have relevance for advocates of Haiti’s small farming communities whose livelihoods depend on essential oil crops, as public resistance to synthetic biology’s engineered foods is real and growing. A 2014 survey of public attitudes about synthetic biology indicates that one of the applications of synthetic biology that generates “a lot of criticism and concern” for consumers is the development of synthetic flavors to replace natural flavors and ingredients such as vanilla and citrus in foods that are intended for human consumption. According to the researchers: “The discussions reveal that participants are not so much concerned about developing synthetic ingredients for paint as they are about developing synthetic food additives that humans would ingest.[121] When it comes to vanilla, there is a sense that ‘we have what we need’ and so a synthetic version is not needed—it would create a potential risk for no good reason.”[122] Will the public concern about food ingredients translate to flavor/aroma compounds? Will the public have enough information to exercise choice?

Potential Next Steps

- **Further monitoring:** While the future impacts of syn bio developments on Haitian flavor/fragrance commodities are uncertain, advocates of Haiti’s small farmers who are dependent on essential oil production should be aware of, and keep tracking, these developments and what it might mean to them. Other essential-oil dependent Caribbean countries should also keep syn bio on their radar and investigate potential threats to their economies
- **Time to hand over Patents:** At this time, for example, we believe Evolva when they tell us they have no immediate plans to commercialize this vetiver-related compound. However, we are concerned that they (or a company that may acquire them in the future) hold the cards (including the patents) to commercialize at any time, which could have significant effects on Haitian livelihoods. Vetiver growers and others in Haiti may wish to request that Evolva relinquish their patents on the production of Epivone™. It would be reasonable for Evolva (and other companies) to surrender intellectual property related to biosynthesis of flavor/fragrance compounds that threaten the livelihoods of small farm producers.
- Public resistance to syn bio products is growing. Given the high profile of the flavor & fragrance industry’s initiatives to source sustainably-grown vetiver from small farmers in Haiti, **flavor/fragrance buyers (especially small buyers) should pledge not to use, develop, or buy compounds produced via biosynthesis that disrupt or destroy the livelihoods of small farm economies.**

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