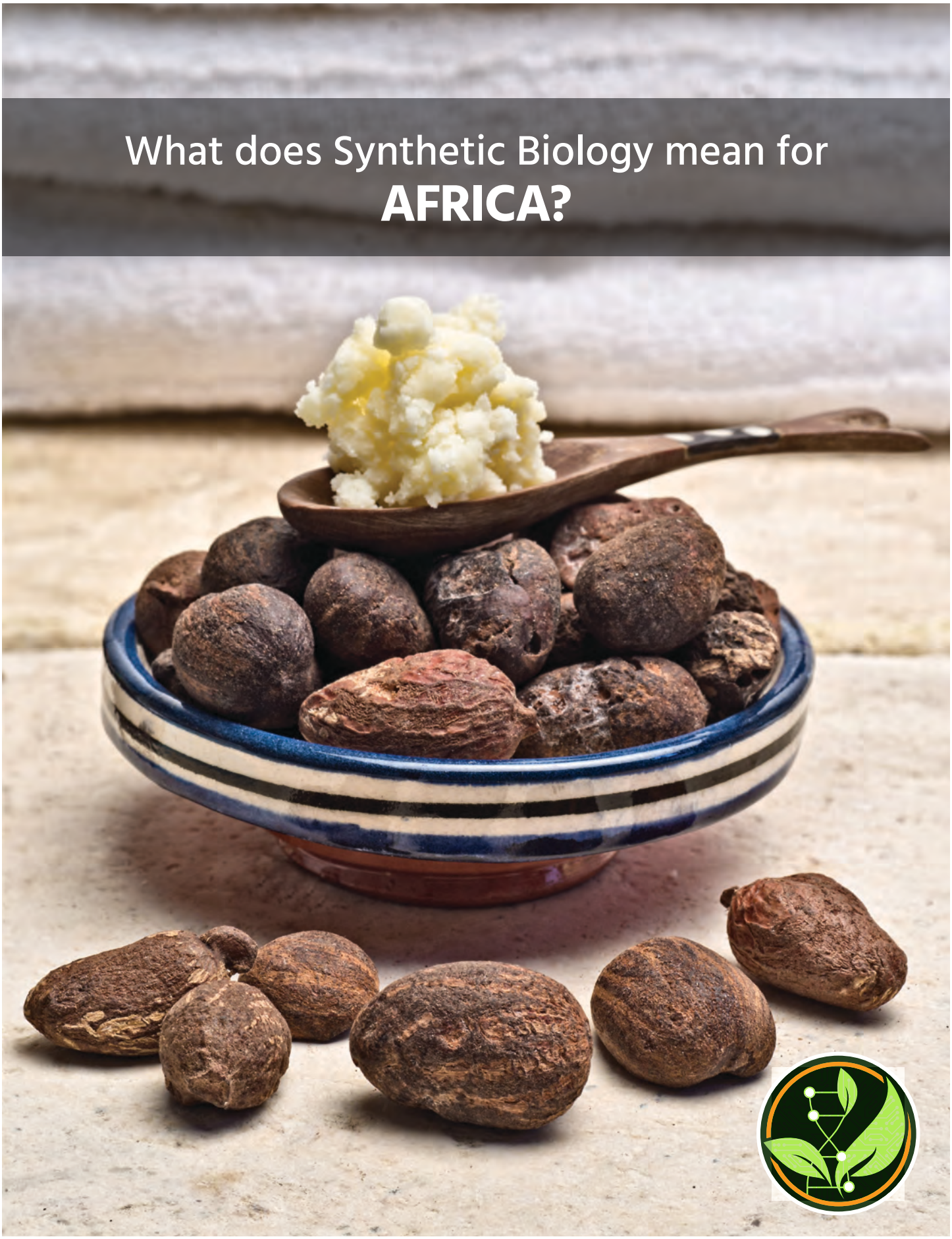
What does Synthetic Biology mean for **AFRICA?**



What Does Synthetic Biology Mean for Africa?

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Building International Capacity in Synthetic Biology Assessment and Governance

What does Synthetic Biology mean for Africa?

Introduction

Huge technical advances in molecular and big data biology have opened the door to a novel range of genetic engineering techniques now being employed by the global biotechnology industry. Such techniques are to be reviewed by the UN Convention on Biological Diversity, under the term 'synthetic biology.'

Synthetic biology is increasingly being referred to as part of the 'fourth industrial revolution,' encompassing the digitisation of biology, development of toolkits that enable rapid and effective translation, and the opportunities that are opening up as a result. Techniques incorporate DNA/RNA synthesis, sequencing, genome editing and gene drives to manufacture synthetic fragrances and ingredients, as well as modify living organisms with novel traits for agricultural or ecosystem changes.

Massive market growth is expected, with the biotech sector growing substantially faster than GDP in leading markets. Nations with large biotechnology industries see huge economic potential for synthetic biology, including next generation genetically modified organisms (GMOs), dubbed GMOs 2.0, and their products, many of which are intended for export to African nations. However, GMOs 2.0 are raising real environmental, health and socio-economic concerns, and their potential impact on the African continent requires a thorough review of existing regulations in order to address such concerns. While ostensibly the claimed modus operandi of many of the latest developments is to help Africa to feed itself, in the absence of domestic biotechnology expertise, it also conveniently provides the opportunity for the shaping of the biosafety discourse to suit the technologies' developers and others that stand to benefit from the use of the technology. This is exemplified by efforts to exclude GMOs 2.0, such as those developed using gene editing technologies, from GMO legislation.[1]

Lessons learnt from commercial growing of GMOs in Africa

Commercialisation of first generation GMOs has, to date, been limited on the African continent. Of the 50 African countries, only two (South Africa and Sudan) currently cultivate GMOs, with South Africa being the only one to cultivate GMOs that are food crops. Nonetheless, these limited experiences across the continent serve as a precautionary lesson for the potential consequences that synthetic biology and next generation GMOs 2.0 may have for food security, farmer livelihoods and social and cultural issues. Other global regions where GMOs have been more extensively cultivated, such as the United States, Argentina and Brazil also reveal negative impacts on health and the environment, where rises in pesticide as a result of GMO cultivation have coincided with rises in cancers, birth defects,

reproductive toxicity and abortion.[2,3] pesticide residues have been found in mother's breast milk, drinking water and citizens' blood and urine.

GMOs entering South Africa and Burkina Faso were sold as technologies that would benefit small-scale farmers, who provide up to an estimated 80% of food in sub-Saharan Africa. However, GM cotton cultivation in South Africa and Burkina Faso has failed to live up to those promises. In South Africa, GM cotton production in the Makhatini Flats in KwaZulu-Natal started in 1997, with Monsanto's GM Bt cotton. Within two years, almost 90% of small-scale farmers were growing GM cotton. However, this coincided with a subsequent collapse of small-scale farmers cultivating the crop, from over 3 000 in 2001/2002, to only 300 in 2009/2010.[4] This was caused by increased prices of seed and the required chemical inputs that forced farmers to take on loans that they were later unable to pay back, resulting in the crippling of the loan companies and a drop in credit available to farmers. Large-scale farming of maize has also suffered from expensive costs of GM agriculture, which has had a knock-on effect on food prices. The prices of yellow GM maize seeds rose by 35% from 2008 to 2011, while white GM maize saw a 30% rise during the same period. Maize production in South Africa exceeds the quantity needed to feed the population, yet, 11 years on from the start of GM maize cultivation, 24 % of the population still go to bed hungry, while the price of a five kilogram bag of mielie/maize meal in 2012 was 84% more expensive than it was in 2008.

Burkina Faso also has suffered damage to its cotton industry, following the introduction of GM cotton, which was phased out in 2015, only seven years after its introduction.[5] Cotton is the main cash crop in Burkina Faso, which is renowned for the high quality of cotton fibres, based on the long fibres that can be spun into high quality cotton, as well as its high fibre efficiency or ginning ratio, which allows for high quantities of lint per unit of cotton weight. However, after the first few years of commercialisation of Bt cotton, some undesirable characteristics of the fibre, particularly its length, were noted: the Bt cotton had

produced shorter fibre lengths and lower cotton fibre efficiency than conventional cotton. As a result, cotton companies from Burkina Faso began to lose international markets because of the poorer lint quality, leading farmers to seek compensation from Monsanto in the order of 84 million dollars.

Recent years have seen a renewed effort to expand GMOs across the continent, with additional focus on non-commercial crops, such as cassava, cowpea, pigeon pea, sorghum, millet and sweet potato. As of 2016, seven countries had conducted or were conducting trials (Egypt, Burkina Faso, Ghana, Kenya, Nigeria, South Africa and Uganda) on the following crops: cassava, pigeon pea, sorghum, sweet potato and rice. The latest push is being accompanied by efforts to change seed regulations, through initiatives like the G8 Alliance for Food and Nutrition in Africa, and establishing GM-sympathetic biosafety regulations that support transnational companies, threatening and even criminalising smallholder farmers for saving seed.

The experiences in Burkina Faso and South Africa, and the latest development initiatives presented as philanthropic ventures are instructive to the region, and serve as a precautionary tale for the next wave of GMOs 2.0 and other synthetic biology products that are again being presented as the next African saviour, especially as we enter a new era of climate change.

Synthetic biology and biosynthesis

Synthetic biology techniques are being employed to biosynthesise alternatives to natural ingredients and fragrances – that is, to synthetically produce these compounds in a living organism. Some of these are already on the market and present threats to existing livelihoods in industries that produce the natural counterparts, which are often highly prized and costly. Replacing the need for the natural botanical plant or substance has an impact on the sustainable use of biodiversity.

Techniques involve genetically engineering microbes such as yeast and algae, which feed on sugar, or other biomass that will extend the need for industrial agriculture of sugar crops. Despite purported claims of synthetic products being sustainable, environmentally friendly alternatives, these requirements will only extend the need for industrial monocropping for production of sugar or other biomass. This has potential negative effects on biodiversity.

The map illustrates where the following natural crops are produced in Africa. The current and near term biosynthetic production of numerous ingredients or chemicals to replace these crops has relevance for Africa. These include:

BURKINA FASO
Shea, cocoa butter

KENYA
Artemisia, stevia

BURUNDI
Stevia

MADAGASCAR
Vanilla, Artemisia, Silk

CÔTE D'IVOIRE
Shea, cocoa butter

MALI
Shea butter

SOUTH AFRICA
Artemisia, sandalwood

UGANDA
Vanilla, artemisia

GHANA
Shea, cocoa butter

NIGERIA
Shea butter

TANZANIA
Artemisia, vanilla, stevia

ZIMBABWE
Artemisia, vanilla

Stevia

A natural sweetener and medicine originating in Paraguay and Brazil, Stevia is increasingly on the demand as a healthy alternative to sugars. It is a leafy plant that grows with little need for agrochemicals and has a low carbon footprint. The whole leaf is typically used medicinally or added as a sweetener. It is now mainly produced in China (80%), but is also increasingly grown in East Africa, predominantly Kenya, but also Burundi and Tanzania. Stevia growing was introduced to Kenya by Malaysian Company PureCircle Inc., and acreage has rapidly grown since. PureCircle buys all 10,000 tonnes of Kenyan stevia leaf from five to six thousand Kenyan farmers based in 11 counties and hopes to scale up Kenyan growing of this crop to 10,000 farmers.

The sweet flavour is based on steviol glycosides, which include Reb (rebaudioside) A, Reb C, Reb F, Reb M, Reb D, Reb X and stevioside. These compounds can have up to 350 times the sweetness of sugar. Commercial use has largely focused on extracting these chemicals and adding them to food products, to allow for less sugar in processed

foods. The commercial market is growing rapidly, with predictions estimating that it may take up 15% of the global sweetener market by 2020. Companies such as Coca Cola already use it for some of their products.

Biosynthetic production is focusing on the production of the steviol glycosides, particularly Reb M and Reb B, which unlike Reb A, do not have a bitter aftertaste. Baker's yeast is used to convert sugars to glycosides via fermentation. As with biosynthetically produced vanillin, there is industry excitement around synthetic stevia, which can be labelled as 'natural' due it being manufactured via a fermentation process. Three companies, including Cargill in partnership with Evolva, as well as DSM, a Dutch chemical and ingredients company, are working on synthetic stevia production. Cargill recently launched production of its product in March 2018, called EverSweet™.

Shea, Cocoa Butter

Shea butter (shíyiri, shísu, nkuto, nku, kaɗe, karité) is an oil extract from the nut kernel of the shea tree, *Vitellaria paradoxa*, also known as karate-nut. Shea trees are native to the Sahel region of West Africa, although they grow in 21 countries across the African continent, reaching Sudan and Ethiopian highlands in the east. Estimates put the total area covered by shea trees at three million square kilometres. It is the second most important oil crop in Africa, after oil palm, but, as it grows in areas unsuitable for oil palm, where annual precipitation is less than 1,000 mm, it assumes primary importance in regions of West Africa. The tree is important for improving the microclimate and soil fertility, and, as such, is an important species in traditional agroforestry parklands.

The use of shea butter has been documented as far back as the fourteenth century. It is mainly used for cosmetics, skin emollients and pharmaceuticals. Shea butter is a complex fat, rich in oleic, stearic, linoleic, and palmitic fatty acids. It also contains high levels of triterpenes, tocopherol, phenols and sterols in the unsaponifiables. Its anti-inflammatory and antioxidant properties make shea butter a highly coveted product, both locally and with the international cosmetics industry.

Cosmetic products include skin and hair related products, such as moisturisers, hair conditioners, soaps and emulsions. It is a primary ingredient in some of the most expensive skin creams on the international market.

In pharmaceuticals it is useful as a base for medicinal ointments; for its anti-inflammatory, emollient and humectant properties; and as a sun-blocking lotion, due to its ability to absorb ultraviolet radiation.

Shea butter is also edible and often used in food preparation. Its low levels of trans fats and high levels of healthy fats are making it an increasingly attractive edible oil.

The shea butter industry is largely run by women, from harvesting to extraction and commercialisation. The UN Development Programme (UNDP) estimates that an average of three million African women work directly or indirectly with shea butter.

The shea tree is the major source of foreign exchange earnings in many cultivating regions, and it plays a significant role in food security, poverty alleviation and ecological services. In 2000, it represented Burkina Faso's third largest export after cotton and livestock. It is Ghana's third biggest cash crop. Other major exporters include Mali, Ghana, West Nigeria, Côte d'Ivoire, Benin, Togo and Guinea. Of the estimated 600,000 tons of shea nuts harvested in West Africa, around 350,000 tons are exported.

Cocoa butter, like shea butter, is also a vegetable fat used for both food and cosmetics. Though native to the tropical regions of Central and South America and the Caribbean, the Food and Agriculture Organization (FAO) of the United Nations reports that the African continent is the largest cocoa producer. Côte d'Ivoire accounts for 44% of global cocoa production alone, followed by Ghana, with African nations together accounting for 71% of the world's production. Unlike other major crop commodities, cocoa is largely grown on small farms.

Corbion (formally Terravia/Solazyme) genetically engineers microalgae that secrete 'tailored' oils. The use of microalgae is seen as attractive for industrial purposes, due to the already existing GRAS (Generally Recognised as Safe) status of numerous algae. Corbion is already commercially offering its AlgaWise algae butter, after receiving GRAS approval from the United States Department of Agriculture in April 2017.[6] Sold as a vegan, low saturated fat solution for bakery, spreads and confectionary applications, this synthetic biology butter mimics the properties of shea stearin and is one of many oils produced by Corbion for cooking, baking and dressing, as well as for a range of cosmetic products, including AlgaPūr™ High Lauric Oil for skin and hair.

Though the precise methods for the engineering process remain legally protected, a Food and Drug Administration (FDA) permit issued in 2016[7] for algal butter describes the use of standard genetic engineering approaches to alter the fatty acid production – including introducing a gene encoding the melibiase (MEL1) enzyme, and a hairpin RNA interference cassette targeting an endogenous algal gene to reduce triglyeride fat production – and to allow for the metabolism of sugar as an energy source, instead of sunlight. Bunge Limited, a large agribusiness, is partnered with Corbion to supply sugar to feed the algae, raising questions surrounding the purported environmental sustainability of this product.

Artemisia

Artemisia annua (sweet wormwood) is an annual shrub indigenous to China, but able to grow in a wide range of sub-tropical and temperate climates. It is well suited to small-scale plantation culture, requires relatively few inputs and suffers little from pest or disease problems. The average crop area per farmer is around 0.2 hectares. The shrub has been used for over 2000 years for the treatment of malaria, with the effects mediated by the active ingredient, artemisinin (or qinghaosu), derived from the leaves and flowers. Artemisinin-based combination therapies (ACTs) are recommended by WHO as the drug of choice. They combine an artemisinin derivative, such as artemether, artesunate or dihydroartemisinin with an effective antimalarial medicine. By 2009, ACT therapies were adopted by 80 countries globally as first-line treatment of uncomplicated *P.falciparum* malaria.

Global demand for artemisinin is growing, reflected in the increased cultivation of the crop in various regions, including various African nations. East Africa now grows an estimated 10% of the global supply, since the introduction of the crop in the 1990s, and is the third most important growing region in the world after China and Vietnam. From 2005, the commercial production of artemisinin in Africa has been concentrated largely in Kenya (65%), Tanzania (19%) and Uganda (19%), though it is also grown in Zimbabwe, Kenya, Mozambique, Nigeria, Niger and South Africa. In Kenya, commercial cultivation started in 2002 with just three to four farmers on 40 hectares, and by 2010 over 7,500 farmers were making their livelihoods from the crop.

A 2006 study by the Dutch Royal Tropical Institute concluded that it is possible to cultivate sufficient artemisinin to cure all the malaria patients in the

world and that an ACT could be made available at an affordable price within two to three years.[8] However, achieving this would require significant investment, as well as a complete overhaul of the supply and distribution chain. The pharmaceutical sector monopolises production, with only six companies owning a prequalified ACT. Nonetheless, the fact that ACTs are still not widely available in malaria endemic areas supports the position in developing countries that growing artemisia locally may be preferable to relying on synthetic imports, both for access to its medicinal benefits and the livelihoods its local cultivation sustains. The cultivation and extraction (with ethanol for example) of artemisia can already be done with relative ease in developing countries.

Synthetically derived artemisimin was first commercialised in 2013 by Sanofi Aventis and Amyris Biotechnologies, who introduced multiple transgenes encoding the biosynthetic pathway for artemisinin into yeast strains, resulting in the production of the artemisinin precursor artemisinic acid, which is later converted into artemisinin. This 'semi-synthetic' version was supported by 64 million dollars of philanthropic support from the Bill & Melinda Gates Foundation. Subsequent to its introduction, the market price for naturally-derived artemisinin crashed from more than $1,100 to $200 per kilogram, driving 80 processors and many small farmers out of business.[9] This exemplifies the threat of synthetic artemisinin to the livelihoods of small farmers. Though the initial plan by Sanofi to replace a third of the world's naturally derived supply has not come to fruition, the future of natural artemisia cultivation is uncertain and will likely be under increased pressure if synthetic production costs and yields can be improved. Currently, these issues have resulted in limited success for Sanofi, who failed to produce any synthetic artemisinin in 2015, due to a glut of the natural counterpart and subsequent low prices.

Vanilla

Vanilla is a flavouring derived from the cured seed pod of the vanilla orchid plants. The most widely known member is the flat-leaved vanilla (*V. planifolia*), native to Mexico, from which commercial vanilla flavouring is derived. According to the FAO,[10] Madagascar was the largest producer of commercial vanilla in 2016, harvesting 2,926 tonnes and contributing 37% of the total global supply. An estimated 80,000 families across 30,000 hectares cultivate vanilla in Madagascar. Its cultivation is also regarded as critical for maintenance and sustainability of agroforestry areas in the country. Central Africa (Uganda, Democratic Republic of Congo) and Tanzania are also major vanilla cultivators, produced by approximately 8,000 families, with Uganda as the seventh largest global producer.[11] The production of vanilla is labour intensive: 1 kg of vanilla requires approximately 500 kg of vanilla pods and the hand-pollination of approximately 40,000 flowers.

Vanilla is the second most expensive plant-derived flavouring in the world, after saffron. Recent gains in market share by China and Indonesia, and the rise of chemically synthetic vanillin (see below) caused a collapse in the market during 2004–14, leading to the curbing of production by farmers. Prices have since spiked again, driven by increased demand for the natural ingredient, but these examples serve as a warning to farmers of the potential threat to their livelihoods of synthetic biology-produced vanilla, especially when it is marketed as a 'natural' flavour.

Synthetic biology vanillin already on the market

Synthetically produced vanilla compounds have been on the market since 2014, sold by Evolva in partnership with International Flavours and Fragrances, a Swiss synthetic biology company. Evolva engineered yeast to produce key flavour compounds. Though it is thought that hundreds of compounds contribute to the distinct vanilla pod taste, only a few of those are being produced biosynthetically, primarily vanillin. Evolva's patent (WO 2013022881)[12] is based on the use of microbes genetically engineered to express five key enzymes that convert a carbon source to vanillic acid and then vanillin.

As stated in the patent application, synthetic vanillin currently produced from benzene-derived guaiacol "cannot be labelled as a natural flavouring and synthesis of vanillin from benzene-derived guaiacol is not environmentally benign ... it would thus be desirable to have a synthesized vanillin. It would further be desirable to provide a method for synthesizing vanillin which is economically attractive."

It is clear that there is great incentive to market a natural-labelled vanilla flavouring, despite the fact that it is biosynthetically produced. Further, the use of sugar as feedstock by the microbes will likely lead to increased demand for sugar cultivation, which is water-intensive and diverts land used for food production to producing yet more sugar.

Gene editing

Gene editing is being sold as a more precise form of genetic engineering, or even as a technique comparable to natural breeding, in terms of the modifications it induces and the claimed lack of risk associated with it. However, gene editing comes with a number of biosafety concerns that are also associated with current GMOs. Current biosafety regulations in the region are not adequate for assessing risks of gene editing techniques, such as CRISPR/Cas9 systems, which are associated with off-target modifications to the genome as well as additional unintended changes at the target site. Integration of genetic material has also been documented. This goes against the major selling point of these techniques: that no foreign DNA is theoretically introduced to the modified organism.[13]

Additional concerns surround the fact that gene editing opens up new opportunities to modify a wide range of crops, including orphan crops in Africa, also raising concerns surrounding biopiracy of African indigenous crops. One example is the development of cassava plants that are resistant to brown streak virus. Cassava, though not native to Africa, is one of the commonest staple crops in the region, with Nigeria as the world's largest producer. It is drought-resistant, highly productive, well adapted to various altitudes and can be successfully grown on marginal soils. New public/private partnerships, such as the DuPont Pioneer and Danforth Center collaboration intend to use CRISPR/Cas9 systems for this purpose. The collaboration also intends to develop gene edited versions of indigenous crops, such as teff, sorghum and millets.[14]

A similar public/private partnership has been established between CIMMYT (International Maize and Wheat Improvement Centre) and DuPont Pioneer to use CRISPR/Cas 9 systems to modify maize genomes, to make them resistant to maize lethal necrosis disease in sub-Saharan Africa. Again, maize is another important staple crop in the region.[15]

Digital sequences and biopiracy

Biopiracy by the global North of African plants and crops, as well as knowledge associated with them, has a long history. For example, the New World coffee industry was founded on a single tree from Ethiopia, which reached Amsterdam's botanic gardens in 1706, via Ceylon and Java. Coca-Cola's flavour also derives from the West African Kola nut and gum Arabic from Sudan. More recent cases of biopiracy include drugs and medicines (such as diabetes drugs and antibiotics) and cosmetics derived from plant medicines (e.g. aloe vera, pharaoh's wheat or farro, Bambara groundnut).[16]

With the advent of advances in digital sequencing and DNA synthesis, it is now extremely simple to synthesise whole genes and even genomes, based solely on digital sequence information that can be shared across borders electronically, without the need to transport seeds or an entire tree. This raises major concerns surrounding the benefits of sharing laws and policies, and agreements which are predicated on the transfer of physical material.

African Orphan Crops Consortium,[17] whose goal is to sequence 101 traditional African food crops to supposedly "improve their nutritional content," as well as to "train 250 plant breeders in genomics and marker-assisted selection for crop improvement over a five-year period" is one example of a project that raises biopiracy concerns. The project is being supported by GMO proponents, such as the Alliance for Food and Nutrition in Africa, and New Partnership for Africa's Development (NEPAD), with partners that include Google and Mars. Open access sequences open up important medicinal and nutritional crops to be mined for disease resistance, flavour ingredients and medicinal properties, and to be gene edited by agrochemical companies. Plants to be sequenced include highly nutritious and medicinal crops, such as moringa, okra, tamarind, cereal grains, macadamia nuts, amaranth and yams.

Gene drives

Gene drives are described as 'mutagenic chain reactions' that are designed to spread throughout a population, overriding Mendelian inheritance patterns to spread rapidly through a population. This means that a single trait introduced one time could spread throughout an entire species, and lead to that species becoming altered or extinct. Deployment of gene drives has been suggested as a mechanism for wiping out disease vectors such as mosquitoes, as well as pest species, such as rodents or weeds. Such technologies are designed to move across international borders, with potentially unstoppable cascades that pass down the generations. The spectre of Irreversible changes to entire populations present a new level of potential risks, the extent of which are currently unknown, as are the assessment and management measures required to control those risks.

GM and gene drive mosquitoes —Target Malaria project

Genetically modified mosquitoes were exported to Burkina Faso from Imperial College, London in November 2016. The mosquitoes are currently in 'contained use' facilities in Bobo-Dioulasso, as part of experiments by the research consortium Target Malaria. The mosquitoes have already received a permit from the National Biosafety Agency and an application is soon expected for release into the environment in 2018, likely in the village of Bana, by the Institut de Recherche en Sciences de la Santé (IRSS), part of the consortium. Target Malaria also works in Mali and Uganda and beginning to work in Ghana, but it appears that mosquitoes are yet to be sent there.

Target Malaria is a consortium of research institutes that receives core funding from the Bill & Melinda

Gates Foundation and the Open Philanthropy Project Fund, an advised fund of Silicon Valley Community Foundation. Individual laboratories also receive additional funding from a variety of sources to support their work, including the United Kingdom government (the UK Department of Environment, Food and Rural Affairs and the Medical Research Council), the Wellcome Trust (a UK-based charity), the European Commission, the Ugandan Ministry of Health, and the Uganda National Council for Science and Technology (UNCST).

Target Malaria's ultimate aim is the release of 'gene drive' mosquitoes, in a multi-phased approach that is starting with the proposed release of 10,000 GM 'male-sterile' (and non-gene drive) mosquitoes this year. The *Anopheles gambiae* mosquitoes have been genetically modified to be male-sterile by a construct that incorporates the I-PpoI Homing Endonuclease Gene (HEG), and subsequently bred with local, wild mosquitoes. This first phase however, is not expected to reduce the population of mosquitoes.

The final phase reportedly involves the use of a gene drive system to spread either male bias or female infertility, with the ultimate aim of reducing the target population of *Anopheles gambiae*. However, there is already scientific evidence that gene drive is unlikely to work, because resistance to the gene drive will likely evolve, preventing some mosquitoes from inheriting the modified genes. Thus, the benefits of the project overall are extremely speculative (see African Centre for Biodiversity, 2018[18] for details of the project).

This project also raises questions regarding biosafety implications for human and environmental health, and, most critically, the effects on the transmission of malaria. Several species of mosquito carry the malaria parasite, so, even if future releases are successful in reducing *Anopheles gambiae* numbers, this may create a niche that could be taken up by other disease-carrying vector species, such as the *Anopheles arabiensis* and *Anopheles funestus*. This scenario has already been documented in Panama, following programmes preferentially targeting *A.agyptae* that included fumigation methods as well as limited releases of Oxitec's GM mosquito. These programmes were followed by a rise in numbers of the Asian Tiger mosquito, *Aedes* (*Stegomyia*) *albopictus*[19]. The authors of the study stated that these findings serve as a cautionary tale for the use of GM depopulation strategies that may lead *A.aegypti* populations to "quickly rebound via recolonization after cessation of GM programs" and that "GM strategies might have only short-term effects on vector population size and may commit Panama to a repeated and costly program for long-term arbovirus control."

Biosafety considerations are even more important when considering that Burkina Faso's biosafety regulation does not have any specific guidance for conducting risk assessment for GM mosquitoes, or what public consultation is required. Questions

also remain with regards to the legality of the transboundary movements of these mosquito lines from the UK. There are yet to be any published risk assessments for the environmental release of these lines, and it remains uncertain if these will comply with EU regulations (EC) 1946/2003, regarding their export. Such a risk assessment has not been done for the lines that have already entered Burkina Faso, as they were intended for 'contained use,' though this interpretation of the law and the obligations of the Cartagena Protocol is questionable considering the mosquitoes are intended for eventual environmental release.

RNA interference crops

Crops utilising RNA interference have recently began to enter African nations, including commodity release of Monsanto's MON87411 maize, which carries a transgene encoding for a non-coding RNA molecule that is designed to target and silence a gene in a Western corn rootworm species.

Applications for field trials in Nigeria were also received in 2017 for GM cassava varieties, AMY3 RNAi Transgenic lines, which carry an RNA interference molecule that is designed to silence the gene encoding for α-amylase, an enzyme that breaks down starch, with the intention of prolonging the storage life of the roots, post-harvest. These lines were developed by a collaborative project between the International Institute of Tropical Medicine (ITM) in Antwerp and the ETHZ Plant Biotechnology Lab in Zurich.

Biosafety questions regarding RNA interference crops, as well the limitations of current risk assessment protocols to adequately test for unintended effects, have been raised by researchers[20] and civil society[21]. Recent studies have shown that not only do non-coding RNA molecules survive mammalian digestion, but they also go on to regulate the genes of mammals that have consumed them. They are also known to have off-target effects, with non-coding RNAs regulating unintended genes.

Conclusions

The advances in synthetic biology present clear risks to the environment, health and biodiversity of the African region, and threaten livelihoods. The current regulatory environment needs to be updated and reviewed to stay abreast of these advances, with particular attention to the environmental release of synthetic biology organisms. Of especial concern is the potential deployment of gene drive systems, where even regulations pertaining to contained use should be reviewed with extreme precaution. Benefits sharing, with regards to digital sequences, should also be reviewed, since open access to digital sequences is likely to facilitate further biopiracy and profit extraction of African plant resources.

Endnotes

1 ASSAf. 2016. The regulatory implications of new plant breeding techniques. http://research.assaf.org.za/handle/20.500.11911/29.

2 Avila-Vazquez M, Difilippo F, Lean B, Maturano E and Etchegoyen A. 2018. Environmental exposure to glyphosate and reproductive health impacts in agricultural population of Argentina. Journal of Environmental Protection 9:241–253. doi: 10.4236/jep.2018.93016.

3 Paganelli A, Gnazzo V, Acosta H, López SL, Carrasco AE. 2010. Glyphosate-based herbicides produce teratogenic effects on vertebrates by impairing retinoic acid signaling. Chemical Research in Toxicology. 23(10):1586–95. doi: 10.1021/tx1001749.

4 African Centre for Biodiversity. 2011. Genetically modified crops in South Africa: A failure for farmers. https://acbio.org.za/wp-content/uploads/2015/03/ACB-factsheet_Who_benefits_from_GM_crops.pdf.

5 López Villar, J. 2017. Bt Cotton in Burkina Faso: When theory does not match reality. Third World Network and African Centre for Biodiversity. https://bangmosnowdotcom.files.wordpress.com/2016/05/bt-cotton-burkina-faso.pdf.

6 www.fda.gov/downloads/food/ingredientspackaginglabeling/gras/noticei nventory/ucm431759.pdf

7 TerraVia website, accessed 30th March 2018: terravia.com.

8 Heemskerk W, Schallig H, de Steenhuijsn Piters B. The world of artemisia in 44 questions. http://www.kit.nl/health/wp-content/uploads/publications/879_The%20world%20of%20Artemisia%20in%2044%20questions.pdf.

9 The East African. 2015. Africa's farm products could be pushed out of global market by synthetic biology, 14 April. http://www.theeastafrican.co.ke/news/Why-Africa-is-worried-about-synthetic-biology/2558-2685452-y2cj7y/index.html

10 FAOSTAT – Food and Agriculture Organisation of the United Nations. www.fao.org/faostat/en/#data

11 Ojambo, F and Hill, M. 2018. Vanilla Production in Uganda Surges as Farmers Battle Thieves. Bloomberg. 7 March. https://www.bloomberg.com/news/articles/2018-03-07/vanilla-production-in-uganda-surges-as-farmers-battle-thieves.

12 International Flavors & Fragrances Inc., Evolva Sa. 2013. (WO 2013022881 A8). Compositions and methods for the biosynthesis of vanillin or vanillin beta-d-glucoside. https://encrypted.google.com/patents/WO2013022881A8?cl=it&hl=en&output=html_text

13 Braatz J, Harloff H-J, Mascher M, Stein N, Himmelbach A, Jung C. 2017. CRISPR-Cas9 induced mutation in polyploid oilseed rape. Plant Physiology. DOI: https://doi.org/10.1104/pp.17.00426.

14 Taylor, N. 2017. DuPont Pioneer and Danforth Center collaborate to apply cutting-edge technologies to improve crops for smallholder farmers. 17 October. https://www.danforthcenter.org/scientists-research/principal-investigators/nigel-taylor/lab-news/dupont-pioneer-and-danforth-center-collaborate-to-apply-cutting-edge-technologies-to-improve-crops-for-smallholder-farmers

15 DuPont Pioneer & CIMMYT Form CRISPR-Cas Public/Private Partnership. 29 September 2016. http://foodsecurity.dupont.com/2016/09/29/dupont-pioneer-cimmyt-form-crispr-cas-publicprivate-partnership/.

16 Edmonds Institute (USA) and African Centre for Biosafety. 2006. Out of Africa: Mysteries of access and benefit sharing. http://www.edmonds-institute.org/outofafrica.pdf.

17 African Orphan Crops Consortium website, accessed 31st March 2018. http://africanorphancrops.org/about/

18 African Centre for Biodiversity, Third World Network and Genewatch UK. 2018. GM Mosquitoes in Burkina Faso http://acbio.org.za/sites/default/files/2018/02/GM_mosquitoes_in_Burkina_Faso_ENGLISH.pdf .

19 Miller MJ, Loaiza JR. 2015. Geographic expansion of the invasive mosquito Aedes albopictus across Panama – Implications for control of dengue and chikungunya viruses in Harley D (ed.) PLoS Neglected Tropical Diseases. https://doi.org/10.1371/journal.pntd.0003383.

20 Heinemann JA, Agapito-Tenfen SZ, Carman JA. 2013. A comparative evaluation of the regulation of GM crops or products containing dsRNA and suggested improvements to risk assessments. Environment International. 55C: 43–55. 10.1016/j.envint.2013.02.010.

21 Third World Network. 2016. Risks of GM crops engineered to utilise RNA interference. https://www.biosafety-info.net/file_dir/8091600255844dcba0d9c4.pdf.

Further information

ETC Group. 2016. Synthetic biology, biodiversity & farmers. Case studies exploring the impact of synthetic biology on natural products, livelihoods and sustainable use of biodiversity. http://www.etcgroup.org/content/synthetic-biology-biodiversity-farmers.