Genetic Engineering and the Law—Past, Present and Beyond: 20+1 Criteria to Help Focus the Path to Our Common Future

Margarida Silva

Abstract

Genetic engineering (GE) is a powerful molecular tool deployed daily in life sciences labs everywhere. When taken out into the world complex issues arise, many unanswered to this day. Three moments in time are considered in this analysis: the past, with the first generation of genetically modified (transgenic) crops, the present, focusing on the current generation of new breeding techniques, and the future, looking into what synthetic biology and cell manufacturing have promised. Twenty criteria that have shown promise in winnowing sustainability from failure, drawn from history, ecology and the law, are applied as tests to help understand whether society is moving towards the right outcome. An additional 21st criterion is suggested and an urgent call for change is issued.

Keywords

Genetic engineering · Sustainability criteria · Science vs. Society · Public policy · Solidarity

1 Introduction

In his compelling essay on (un)sustainability, the Laudato Si' Encyclical Letter, Pope Francis states one of the requisites quite clearly: "We require a new and universal solidarity." Could solidarity help science and society find the elusive path towards our common food future?

In the very broadest sense humankind has been genetically modifying plants and animals since before there was even a *Homo sapiens*. By choosing the juiciest fruit to eat, for instance, and unwittingly spreading the seeds, breeding had effectively begun. With the advent of agriculture and increased understanding of biological phenomena a more intentional approach developed over many generations, with crops and livestock carefully scrutinised to make sure carriers of the prized characteristics were chosen and multiplied.

The cumulative impacts of such efforts cannot be overstated: hundreds of thousands of varieties of humanity's most important food staples were crafted into our collective survival insurance. Corn is a case in point: the wild ancestor (teosinte) has many more branches, with dozens more ears. Teosinte ears are about 5 cm long, with just ten (very hard) grains or less, while corn ears grow up to 30 cm and can hold over 500 soft (hence easy to eat) grains. There are many other differences, and their common genealogy was at first all but obvious. Many hundreds of genes changed over time, but all these modifications

---

M. Silva (✉)
Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Porto, Portugal
e-mail: msilva@ucp.pt

M. d. G. Garcia, A. Cortês (eds.), *Blue Planet Law*, Sustainable Development Goals Series,
https://doi.org/10.1007/978-3-031-24888-7_22

and benefits were brought about within the confines of Nature's rules and limits.

The leading thread in the history of corn, and agricultural biodiversity, is that coevolution was allowed to happen over time—not out of some deep reverence for Nature but simply because no tools were available to do otherwise. It wasn't just the germplasm that evolved—plant seeds, animal breeds—but the cultural wealth accumulated as well: how to grow, how to use products for food, fuel, clothing fibres, shelter or medicine, and indeed how to keep all of it coevolving and meeting basic human needs alongside the rhythm of inevitable change.

Enter molecular biology after World War 2. For the first time ever genetic approaches allowed researchers to go into and directly rewrite life's inner sanctum: DNA. So a brand new technology, interfering with a newly reached dimension of our core infrastructure, came into being and rapidly developed to the point where it is now "do it yourself" for those with basic molecular training.

If society is to have a say in how technologies are run, namely regarding their environmental footprint, criteria must be established. In 2001, expanded later in 2013, the European Environment Agency (EEA) published the ultimate history lesson: what went wrong with technological debacles in previous decades and how they could have been prevented (European Environment Agency 2001; European Environment Agency 2013). In order to avoid repeating history the 12 late lessons the EEA uncovered would do well to be heeded today. These will form the first 12 criteria considered in this chapter.

Other rules must be obeyed, however, if health and the environment are to be protected. Not least among them are the principles embedded in Article 191 of the Treaty on the Functioning of the European Union (Precaution, Prevention, Polluter pays and Rectification at source). These are four additional criteria to be considered throughout the chapter.

It could be argued, however, that the decisive rule is Nature's. Whether modern society is to transform and survive or crash into oblivion like many civilizations prior comes down to how well we integrate into the web of life. Which rule is that? Perhaps Barry Commoner put it best when he enunciated his Four Laws of Ecology in the book "The Closing Circle": Everything is connected to everything else, Everything must go somewhere, Nature knows best, and There is no such thing as a free lunch (Commoner 1971). These constitute the final four criteria considered.

These 20 criteria are first detailed below then applied to genetic engineering's three main evolutionary stages (conventional transgenesis, new breeding techniques and synthetic biology) through relevant examples in order to evaluate overall (un)sustainability.

2 Twenty Sustainability Criteria

2.1 From the EEA's Late Lessons From Early Warnings

Respond to ignorance as well as uncertainty (LL1)—How can governments legislate and regulatory agencies set standards to deal with the unknowns of human activity? It's hard enough to make sure all relevant available knowledge is taken into account. And yet the need to avoid or at least approximately anticipate disruptions stemming from unexpected connections within the extremely complex, dynamic and seemingly chaotic system we live in is real and urgent. Ways to safeguard against unpleasant surprises are not failproof but ignoring these smacks of foolhardy arrogance.

Research and monitor for 'early warnings' (LL2)—Looking for the first signs that something is amiss means that research may start looking for trouble when no such trouble is detectable or even out there. However, waiting until it is obvious means protective action is delayed and wellbeing not maximized in instances where things do go wrong. It may take a long time before trouble becomes apparent to the naked eye and when it does that may still be insufficient for decisive action. At any rate the lack of early solid evidence aids and abets potentially destructive early inaction.

Search out and address 'blind spots' and gaps in scientific knowledge (LL3)—Being willing to look for weaknesses in current knowledge and act according to the gained insight is a sign of humility in the light of intrinsic human limitations and an essential condition when dealing with powerful new technologies, assuming health, the environment and the global future are to be secured. Political and business cycles, however, are seldom conducive to such reflection.

Identify and reduce interdisciplinary obstacles to learning (LL4)—Availability of knowledge does not guarantee the information will be put to use, particularly where fields of expertise must be bridged. A focused intention is required, which is not customary.

Ensure that real world conditions are fully accounted for (LL5)—The requirement that real life should be taken into consideration seems rather extraordinary in that it is obvious. And yet it became a late lesson precisely because of a widespread oblivion regarding the gap between theory and practice, between laboratory and field, between controlled conditions and the fallibility of the human condition.

Systematically scrutinise and justify the claimed 'pros' and 'cons' (LL6)—The decision to (dis)approve a particular technology requires the full evaluation of all its negative impacts, as well as its purported benefits. Evaluation must cast a wider net than usual and avoid the bias in prioritising some features over others.

Evaluate alternatives and promote robust, diverse and adaptable solutions (LL7)—Finding society's best path forward requires a full comparison within the options palette. Only when all opportunity costs are taken into account may the overall best choice become clear.

Use 'lay' and local knowledge as well as all relevant specialist expertise (LL8)—Nobody disputes the need to consider expert knowledge, but many forget it is not the only useful type of knowledge and could benefit from complementary sources, empirical or otherwise.

Take account of wider social interests and values (LL9)—Even if, hypothetically, a technological approach is (apparently) safe and stakeholders agree on its comparative effectiveness, it may still be widely unacceptable culturally, which should be reason enough for rejection.

Maintain regulatory independence from economic and political special interests (LL10)—Any manner of conflicts of interest will taint the most democratic decision-making process. It also corrupts science itself, to the point where independent scientists risk becoming extinct.

Identify and reduce institutional obstacles to learning and action (LL11)—In an ideal world the same evidence would result in the same technical understanding across countries or government agencies. The fact that it does not serves to prove institutions can develop their own inner resistance to acting as needed.

Avoid paralysis by analysis (LL12)—Institutional stalling is one particular type of political obstacle and results in appropriate action being delayed. It frequently stems from an unwillingness to confront whoever stands to lose from the intervention. It is always possible to know more, but this should not stand in the way of action.

2.2 From the Treaty on the Functioning of the European Union

Precautionary principle (EUP1)—This is one of the most overarching guiding principles in the European Union when it comes to protecting the environment and health, and it is certainly among those that private economic concerns most fight against. It is both surprisingly self-evident and deceptively simple to apply. It is directed at a precise moment of the scientific process pertaining to any technology evaluation or monitoring: when there is some evidence of harm (but not enough proof or understanding that allows for a regular science-backed decision) while at the same time a holistic perspective points towards potentially significant impacts as a consequence of inaction. This effectively states that societies should act to curtail activities and incur economic losses even if later (when science has come up with a fuller explanation) the issue turns out to be a false positive—because these are not as problematic as false negatives.

Prevention principle (EUP2)—Whereas the precautionary principle deals with uncertain threats, the prevention principle focuses on activities where there is sufficient knowledge of the negative outcomes to calculate their probability and determines that they should be avoided rather than remedied.

Rectification at the source principle (EUP3)—Something of a corollary to the previous principle, this one establishes that prevention should happen where the problem originates rather than down the pipeline.

Polluter pays principle (EUP4)—If prevention was not or could not be applied then the perpetrator must be held liable for damages. This does not mean a polluted environment is necessarily returned to its previously pristine condition, but rather that crime should not pay.

2.3 From Barry Commoner's The Closing Circle

Everything is connected to everything else (BCLE1)—The respected American naturalist John Muir put it clearly when he wrote, "When we try to pick out anything by itself, we find it hitched to everything else in the Universe." Ecosystems work through interactions, an unfathomably large number of them, creating a web of interconnectedness through which cascades of consequences ripple arguably forever. Even if reactions are not endless, they are also never zero and can outnumber our expectations.

Everything must go somewhere (BCLE2)—It would be interesting if we could make trash or pollution disappear. Alas, when they are gone from sight they have just taken up another form elsewhere. Nature deals with this requirement by turning one population's waste into another population's food. Industrialised society, however, has yet to make the transition which means currently many unhealthy accumulations occur.

Nature knows best (BCLE3)—This thesis runs counter to dominant western worldviews by stating that it is really hard to improve on Nature. Commoner posits, "any major man-made change in a natural system is likely to be detrimental."

There is no such thing as a free lunch (BCLE4)—The extraction of natural resources and the usage of ecosystem services may seem free for the taking but there is always a hidden cost. This includes the loss of opportunity for future generations, the health impact for the population at large or a cumulative long-term impact, among many others.

3 The First Generation

The year 1973 marks the beginning of conventional genetic engineering with the creation of the first genetically modified organism (GMO), a bacterium that incorporated added DNA containing an antibiotic resistance gene. Recombinant DNA had been made possible by the discovery of a special group of enzymes a mere five years prior. These enzymes can cut DNA at specific locations, as defined by the linear sequence of the four nucleotides that make up the genome. There are hundreds of such restriction enzymes available that vary according to the sequence recognised.

According to the World Health Organization a GMO has been changed at the gene level through a method that Nature does not use (WHO 2014). The European Directive 2001/18/EC additionally excludes humans and establishes some exceptions as to methods. The result is typically the presence of one (or more) additional gene (s) coding for a specific protein that in turn results in some added functionality for the host plant, animal or microbe. Target genes can originate in a closely related species or be transferred across different kingdoms, since the genetic code is universal across life-forms.

China was the first country to allow introduction of a GMO onto commercial markets, with tobacco in 1992 (James and Krattiger 1996). In 1994 a genetically modified (GM) tomato was put on sale in the United Sates. The European Union began approving GM products in 1994 with a GM tobacco strain, and GM food was first approved in 1996 (James 2001).

There are hundreds of genetically modified food varieties currently on the market in different countries, from species such as soy, corn, canola, rice, apple, papaya, eggplant, potato, sugar cane and sugar beet. Industry estimates that in 2019 about 190 million hectares were grown with GM crops, with soy and corn together representing 80% of the total (ISAAA 2019).

Some other species where GMO varieties have been approved include flowers, trees, beans and cotton. The United States remains the world's largest producer, with the top five countries (USA, Brazil, Argentina, Canada and India) growing over 90% of the world's GM area. In the European Union GM crops have been banned in a number of countries and from 2016 onwards only two countries have farmed GM products (with a single GM corn crop): Spain (30% of maize produced in 2019 was GM) and Portugal (6% was GM).

The technical procedure for GMO production is a sophisticated one. The gene of interest is isolated from the donor cells and cloned in the laboratory. It must be combined with support sequences that allow for adequate functioning in the target genome, including a selectable marker. The composite is inserted into the target cells which, for plants, normally involves shooting fine DNA coated particles into the cell culture or using a bacterial vector. Then cells are recovered by cultivation in a growth medium containing the selection agent, frequently antibiotics, and finally tissue culture techniques complete the regeneration process. At this point the GMO obtained are studied to determine which of them adequately expresses the desired trait.

The two traits that have dominated GM farming for 20 years and occupy over 99% of all hectares grown are herbicide tolerance (HT: where the transgene helps the plant survive herbicide applications that would otherwise kill it) and insect resistance (IR: where the transgene codes for a protein that kills insects that would otherwise eat the crop). These traits are frequently merged together into the same plant (stacked traits). SmartStax corn is one such stacked GMO: it carries two HT transgenes and six IR transgenes and is marketed for food and feed in the European Union, United States, Brazil and Canada, among others.

3.1 What Alternatives?

It is hard to imagine that humankind's food supply would ever be doomed had genetic engineering not been uncovered and developed. So what are the other options and how do they compare? There's organic farming, permaculture, agroecology, polyculture and small scale family farming—to name just a few concepts—besides the mainstream intensive farming option that uses conventional (non-GM) seeds. According to criterion LL7, any major decision should take all options and opportunity costs into account. However, this is notably absent from official GMO approval procedures on both sides of the Atlantic. The European Union (EU) has a stronger framework in place and does require pre-market authorisation. However the stated objective is narrowly focused on environmental and health risks. The approval procedure does not weigh strategic alternatives. If little or no problems are detected lawmakers give themselves no option but to approve. This is precisely the opposite of what criterion LL7 prescribes.

3.2 Alertness or Head Buried in the Sand?

With a technology that, for the first time in history, allows people to massively and irreversibly alter heredity directly at the DNA level, the need to be mindful of any unintended surprises might seem logical. And indeed there are some post-market monitoring requirements laid down in Directive 2001/18/EC but these are weak and incomplete. Two examples should be mentioned, among many more: in the case of HT crops no attention is given to the inevitably associated increase in herbicide use and, for stacked crops, there is no requirement to assess the combined (and potentially synergistic) effects of the various herbicides and insecticides.

In the USA crops are often deregulated before hitting the market which translates into zero monitoring or oversight for their full commercial life cycle. Pre-market approval exemptions for most GMO are now available and allow companies to decide whether their GMO falls within the exempt or the regulated category.

Although different in scale, the European and American stances unveil the same underlying callous indifference to the need for immediate problem detection. Clearly no early remedial action can be expected from the highest echelons of these governments, which is exactly what criterion LL2 tells us is a bad idea, carrying poor prognoses.

3.3 What Voice for the People?

In 2010, the last year Eurobarometer surveyed Europeans regarding biotechnology, 67% of Europeans from 27 countries did not support GMO in food, 73% considered them unsafe and 78% saw them as unnatural. With 2021 hindsight, "the acceptance of GE by European people has not changed significantly over the past 20 years and remains at a relatively low level (Woźniak et al. 2021)." The "unnatural" epithet is not a scientific construct, nor does it have to be. It relays a feeling of unease towards what is seen as not fitting in with Nature. Notorious food scandals (mad cow disease being one among many) have likely shaped this position.

Public distrust notwithstanding, including an EU-wide petition for a ban on GM crops that collected over a million signatures and was the first submitted to the European Commission under the Citizens' Initiative provision (giving citizens a direct say in the bloc's legislative decisions), there are about 100 GM plant varieties approved for food consumption in the EU.

Labelling—meant to give sceptical Europeans the right to choose—is in place but its half-hearted reach means most GMO go where consumers do not see them (animal feed is labelled but it is not up to consumers to choose) and hence cannot avoid them (animal products are not labelled even when the animals were fed GMO for their entire life), among a number of other limitations.

American consumers, however, have it much worse. Even though 89% support mandatory package labelling (TMG 2015), there have never been federal requirements in place. In fact, even those companies that made sure their ingredients were GM-free were stopped from saying so. The federal government has recently published labelling requirements, due to go into force at the beginning of 2022, but these have been challenged in court because the information may not be visible (accessed through QR code only), the terminology has been changed ("bioengineered"), the symbol is nondescriptive and most GMO are excluded from the mandate, while States are banned from enforcing any additional requirements.

These examples illustrate the deep divide separating people from power. Had criterion LL9 been followed, reality would be better aligned with society's preferences and principles. The fact that it is not points to history repeating itself due to a failure to learn the appropriate lessons.

3.4 Who Pays?

What happens if GM seeds contaminate that which should be protected at all costs: heirloom seeds? These old, patent-free, adapted and adaptable open pollinated gems contain food germplasm diversity, the most precious of human survival tickets.

Examples abound of the difference a broad genetic base makes. Ireland's Great Famine in the 19th century resulted in the death of over a million people and originated in the genetically uniform potato stock that made the whole island (and beyond) susceptible to a fungal disease. On the other hand, in India and Indonesia, when a new virus ravaged rice production, agronomists spent years testing about 7000 different rice varieties looking for a gene that might help:

which they found, a single one in a single population from Uttar Pradesh (Brikell 2003).

The Portuguese laws (Decree-Laws 160/2005 and 387/2007) regulating coexistence—the set of rules governing the relationship between GMO and other crops because of GM contamination—offer a uniquely clear window into how genetic pollution is being handled in the brave new gene world. According to these rules contamination is not to be prevented, only minimised. And compensation is available only when commercial seeds are used. Seed saving and traditional varieties are specifically excluded from reparation.

In addition, by determining that only a small flat fee be paid by GM farmers these are effectively insured against any additional real costs. Overall either the polluter does not pay (where peasant seeds are concerned) or the payment covers just a very buffered amount of whatever might be due. At any rate, criterion EUP4 could not have been more profoundly ignored.

3.5 Science Speaks or Fake News Wars?

Over 80% of the GMO on the market are specifically engineered to withstand herbicide applications, which warrants a closer look at these chemicals. Even though various active principles (the main chemicals) are deployed, glyphosate held a virtual monopoly for over a decade and is still the dominant weedkiller option for HT GMO. Over time such agronomical choices rolled out two major unintended, interconnected and nefarious consequences that slowly became painfully clear: herbicide overuse and superweeds.

Although many promises were made about GM ushering in a new, cleaner agricultural era, between 1996 and 2011 US farming applied an additional 239,000 tons of glyphosate because crops were GM (Benbrook 2012). The reasons for this trend have not gone away.

As for the weeds targeted by glyphosate, faced with the immense selective pressure created by the widespread repeated use of a single control mechanism, it can be said that life happened. Resistance was first detected in 1996 and it grew slowly at first, then faster. In the US, according to the International Herbicide-resistant Weed Database at weedscience.org, resistance in GM soy fields, first detected in 2000, has now been detected in 7 separate weed species across 24 states. Ian Heap, one of the world's top weed experts, minces no words (Heap and Duke 2018):

> Although glyphosate-resistant weeds have been identified in orchards, vineyards, plantations, cereals, fallow and non-crop situations, it is the glyphosate-resistant weeds in glyphosate-resistant crop systems that dominate the area infested and [show] growing economic impact. Glyphosate-resistant weeds present the greatest threat to sustained weed control in major agronomic crops [. . .].

Rather than take objective science at face value the agrochemical industry has seized on the chance to turn the debacle into a business opportunity—and this is the reason why there are stacked GMO. Bayer recently announced in 2020 it has developed a new variety, tolerant to five herbicides at once. It is just a matter of time before weeds with the appropriate resistance genes conquer these new GMO fields. The impossible endgame, where we end up eating food modified by an ever larger number of transgenes dowsed with an ever increasing toxic cocktail somehow fails to be acknowledged.

The two examples above show that criteria EUP2 and EUP3 are far from being institutionally respected.

3.6 One Report, Two Reports, How Many Reports?

Few people and fewer administrations would question the legitimacy and the reports of the IPCC—International Panel on Climate Change of the United Nations as regards climate science. A similar type of body was created for agriculture: the IAASTD—International Assessment of Agricultural Knowledge, Science and Technology for Development ran for six years, starting in 2002, at the behest of the World Bank together with other international agencies. The reports (Abate et al. 2009) produced involved around 400 experts, two rounds of peer review and many hundreds of stakeholders and were approved in 2008 by dozens of governments. This represented an inclusive, multidisciplinary, exhaustive and visionary attempt to model the best future for agriculture globally. Robert Watson, director of the IAASTD, famously said, “Business as usual is not an option.” The documents emphasised agroecology, smallholder farming and agriculture’s multifunctionality beyond mere food production, while criticizing GM crops in particular for being expensive with little benefit.

The IAASTD reports had little to no impact. Just some short months after their publication the FAO—Food and Agriculture Organization of the United Nations launched a debate forum with an almost identical focus. The World Bank itself had released another major document in 2007. Since then a number of multilateral initiatives with similar scopes have taken place and the rate shows no sign of abating. They all recognise the urgency of the situation and yet nothing happens.

Information being generated with no real action is a typical case of paralysis by analysis: precisely what criterion LL12 admonishes against. Another late lesson still unlearnt.

3.7 Who’s to Judge?

No one wants a thief to sit as judge at his own trial. No one expects an oil company to be upfront about climate change. And no one should expect scientists to be independent when their work ties them in any way to the GM industry. Not surprisingly, when a GM researcher is financed by a GM concern results tend to be more favourable to the company’s interests (Diels et al. 2011). This virtually means unless scientists are strictly independent their results cannot be trusted and should not be admissible. Yet industry studies on their own products form the basis of the European Union’s GM safety evaluations.

How careful are European institutions regarding conflicts of interest? A 2017 review (CEO 2017) of the European Food Safety Authority (EFSA), the scientific focal point for GMO evaluations, showed that in the science panels 46% of the members had conflicts of interest. This is not a fluke; a similar analysis in 2013 had put that number at 59%. The situation has been so consistently dire that the European Ombudsman formally ruled that the EFSA should “revise its conflict of interest rules, and the related instructions and forms it uses for declarations of interests”. The culture of undue influence by vested interests forced the European Parliament to send the EFSA several yearly demands on this subject between 2014 and 2020 (most of which were ignored by the agency).

If criterion LL10 had been taken seriously none of this would have happened. Since it did happen, this is yet another invitation for late lessons to surface in the future.

3.8 Real Life? What Real Life?

Substantial equivalence (in the United States) and comparative safety assessment (in the EU) are different phrases that embody the same concept—a politically charged, legally unacceptable and scientifically baseless decision to assume that ill-defined chemical similarity is synonymous with toxicological risk. The result is a safety testing waiver for most GMO. The incongruousness of such an approach is brought into sharp focus by mad cow disease. There is absolutely no chemically discernible compositional difference between a healthy and a sick animal, meaning they are 100% substantially equivalent. Nevertheless the risk clearly varies.

The adoption of substantial equivalence is a disingenuous way for GMO to be approved without any significant scientific oversight and the fact that some scientists acquiesce and participate in the farce can only be understood in the light of the previous lesson. It is also clear evidence that criterion LL5 currently has no bearing on GMO approvals in most of the world.

4 The Second Generation

As genetic engineering progressed, so the original transgenesis recipe—isolating a gene from a host, processing it and then inserting it into a target organism—evolved from 2001 onwards into a multitude of technological options. These new breeding techniques (NBT) ushered in the GMO 2.0 era, where direct genome edition of the target creates the desired variation.

According to the European Commission's Joint Research Centre there are currently four major approaches among the numerous genomic techniques available:

- Both DNA strands are cut then edited at the repair stage
- The genome is edited without breaking the DNA strands (or only one is cut)
- The DNA sequence is not altered but the way it is read into RNA is changed
- The RNA is targeted, rather than the DNA

The most widely used technique is by far the CRISPR-Cas9 method (from the first group above) which resulted in the 2020 Nobel Prize in Chemistry being awarded to the two researchers that discovered it. One of them co-authored a paper in a leading scientific journal anticipating a number of major well intentioned applications:

- Solutions for human diseases, such as those stemming from genetic disorders
- New antimicrobials, both against bacteria and viruses
- Improved crops and livestock, including improved yield in water- and nutrient-depleted environments
- Increased ease and versatility in the engineering of bacteria for industrial use
- Gene drives, that have the potential to eradicate malaria and other diseases

This brand new world of infinite genetic possibilities for biotechnologists has led Paul Knoepfler, from the faculty of the University of California Davis School of Medicine, to muse that it is akin to being a "kid in a candy store" (Plumer et al. 2018).

4.1 Precaution: It Would be a Good Idea

The European Academies' Science Advisory Council (EASAC), composed of representatives from 29 national academies of sciences in Europe, issued a statement on NBT (European Academies' Science Advisory Council 2015) that was supportive of the precautionary principle (PP). . . apparently. Based on a United Kingdom House of Commons Science and Technology Committee report, the EASAC argued with its full institutional weight that the circumstances that justify a PP intervention, such as uncertainty, do not apply to NBT. This was stated even though it recognises that NBT "are emerging rapidly from advances in genomic research", which translates to: we are just beginning to grasp them, have yet to amass significant experience, do not fully understand the whole area yet and have no way of knowing if we ever will.

This conspicuous failure to recognise the internal inconsistencies points in equal measure to hubris and recklessness and does not bode well for the influence of scientists in decision making. At any rate this is but one among an unfortunately very large example pool of what can only be understood as a broader and recurrent pattern among life's technologists: an entrenched inability or unwillingness to self-reflect. At the very least it shows how criteria EUP1 and LL1 have yet to percolate through critical stakeholders.

4.2 Innovation: A Decision Was Made

Genetic engineering in general and NBT in particular represent a top-down approach to agricultural innovation. In the European Union research and innovation policies are guided by the Research and Technology Directorate of the European Commission (RTD), most visibly through its Framework Programmes that determine priorities and fund advanced knowledge institutions. This effectively defines who innovates, what is innovated upon and who benefits.

One of the targets and measures of success of RTD programmes is the generation of intellectual property (IP), but not all innovation is amenable to IP protection. Therefore those submitting grant proposals for products that can be "bottled and marketed" will stand a better chance of receiving EU funding (even more so when industry partners are brought into the team) and also, subsequently, large scale commercial success (because market outcomes depend on zeroing in on customers who can pay).

It follows that less wealthy niches and less protectable approaches (such as management strategies rather than products) are neglected or even undermined, which in fact creates a social bias that does not stem from sustainability potential, needs of the poor, efficacy, democratic choice or any other desirable criterion. Each path leads down to a very different food system (Quist et al. 2013).

The above can be summarised as a type of obstacle to learning, as defined in criterion LL11, reducing society's chances at a future.

4.3 Consultations: Knowing What You Want

In 2018 the European Court of Justice ruled that NBT fall within the scope of existing EU laws on GMO. This spelled bad news for the industry, as companies had been arguing that NBT do not create GMO, in order to avoid compliance with a law that says GMO should be safe and labelled. When Member States asked for a study on how to implement the ruling, the Health and Food Safety Directorate defined a methodology that included an invitation-only consultation of EU stakeholders. Of those chosen, 74% represented industry whereas only 14% were civil society organisations.

There is nothing wrong in asking vested interests what they think, but planning for misrepresentation that can skew the outcome ("capture") goes specifically against the Commission's own rules. Clearly not all contributions were equally welcome. This involves both non-professionals and experts from various fields and is an example where two criteria are breached: LL4 and LL8.

4.4 Connections: It's Who You Touch

Gene drives have raised particular attention since they bypass the Mendelian laws of inheritance and ensure genetic change takes hold of the entire population in a number of generations independently of (dis)advantages or external selection pressures. Thus the evolutionary arc of the population is altered and even planned extinctions could be possible. To expect that a modification of such magnitude will not create a tsunami-like wave throughout the web of life with any number of unforeseen consequences can only be seen as childish, goes against Commoner's BCLE1 and BCLE2 criteria and defies basic common sense.

5 The Third Generation

Genetic engineering's next frontier, as perceived by Todd Kuiken, a faculty member at North Carolina State University and previously with the Synthetic Biology Project at the Woodrow Wilson International Centre for Scholars, is undoubtedly synthetic biology.

Synthetic biology (synbio) was born at the crossroads of genetics, engineering and a Lego-like view of Nature. Taking advantage of powerful software tools, the life engineers (better still, synbioneers) aim at shaping DNA in their own image: the genetic code and a programmer's code become one, aligned with a specific technological worldview. Tom Knight, widely regarded as the original synbioneer, sees great advantage in the streamlining of biological systems into something "as predictable and free from complexity as possible" (Coghlan 2012).

In the synbio world upcoming food innovations include cell agriculture (e.g. meat from in vitro animal cell production), yeast farming (e.g. cow free milk, where milk proteins are produced individually then mixed in the right proportion), designer proteins for Mars outpost rations and many more.

Already on the market are mostly high value-added molecules aimed at the additives market for the food, feed, cosmetic, chemical and pharmaceutical industries. According to one expert, "There is potential for biosynthetic routes to completely replace any natural sources (Bomgardner 2012)." And for those that see engineered cells as still not robotic enough, the path is now open to sidestep them: cell-free protein synthesis uses dead cell extracts to better control the process.

Fully synthetic cells built from scratch (using inorganic components only) have not been created (yet) but cell mimics, which emulate some functionality of a natural cell, are already possible. "Regular" genetic engineering seems almost naïve by comparison.

One common thread is a self-professed respect for Nature as existential justification. Amyris Inc, one of the top public synthetic biology companies in the world, proudly states on its website:

> As the world's leading manufacturer of sustainable ingredients made with synthetic biology, our technology allows millions of people, young and old, to enjoy environmentally-friendly products that are made with our sustainable ingredients. Using sugarcane fermentation, we convert basic plant sugars into rare bioidentical molecules, essential ingredients and clean, effective everyday products. We are passionately pioneering the future of clean chemistry where people and planet can prosper.

Life has become the starting point for a new generation of chemical factories in the express name of environmental protection. What could go wrong? Nothing, at least for the time being, according to Tom Knight.

5.1 Six Reasons It Could Go Wrong

We might be forgiven for thinking that, since synthetic biology is, for now, mostly a contained endeavour, environmental concerns can be postponed. But, first of all, things leak. Human error made Chernobyl explode and could easily let synbios escape. Genes and microbes are not radiation but in a sense are worse, since life grows and multiplies.

The second reason is that once the tools have been developed, the knowledge has spread and public distrust has been won over, nothing but an act of God can stop a rogue biology major from unleashing society's worst nightmares.

Thirdly, these synbiobeings need fuel and that comes from the environment. Usually sugar cane is used as the source, but sugar cane plantations are notorious for human rights abuses, large scale monocultures, agrochemical dependency, excessive water consumption and profound biodiversity impacts. This footprint is not noted on Amyris's website.

The fourth reason: there is a subtle conceptual warping of human ethos when technologies become the go-to solution for human-made problems, as if the issues become less critical since we have powerful tools to figure out solutions. Why care for the planet when you can board a ship and leave for Mars? Of course, Mars is no planet B.

Fifthly, once technological applications become widespread and foster significant economic activity, they will not be easily stopped or changed, even when the negative impact is duly acknowledged. This has happened dozens of times in the last hundred years, according to the EEA report.

The sixth and last reason is that people's views of risk change. In 1975, at the Asilomar conference, scientists discussing what was then a frontier topic were concerned about the ramifications of genetic engineering and recommended containment be made a central tenet of any such endeavour. Alas, 20 years later, environmental release had become the norm. It is true that evaluations were carried out, technical opinions published and options legitimised. However, the underlying parallel evolution of what is generally acceptable cannot be denied.

The above six (non-systematic) issues regarding the currently non-existent environmental assessments for synthetic biology are good examples of how criteria LL3, LL6, BCLE3 and BCLE4 have not been adequately internalised, to the detriment of our common future.

6 In Conclusion: More Solidarity, Less Corruption

Genetic engineering failed the test on all 20 counts. The examples detailed above are but that: examples. Many more could be expounded, space permitting. Of course, instances of good Earth keeping can also be found, but a nuclear bomb on an organic garden still returns a nuclear explosion.

Deeper reasons underlying most of the cases mentioned possibly range from misguided commitment to outright corruption: political, economic and the egocentric type. The fact that corruption is so prevalent (Transparency International 2021) speaks volumes about its power—and science/technology are not immune. So far society has been unable to come up with sufficient countermeasures.

Lawmakers, at least those that would rather their grandchildren lived, would do well to mandate a systematic review of technologies of concern under the 20 criteria discussed here. But one more criterion is in order: that of solidarity. As Pope Francis notes in the Laudato Si' plea for integral ecology, solidarity is key. Without it we are condemned to heartless individualism and ultimate failure as a species. In fact, it can be argued that estrangement lies at the center of what separates us from our common future.

How these 20+1 ideas could become mandatory central pillars of environmental protection to help us home in on the path to a common sustainable future is not at all obvious. The fact remains that this is a matter of urgency, as sustainability is simultaneously non-negotiable and, right now, non-existent—at least as it pertains to genetic engineering.

Acknowledgements This work was supported by National Funds from FCT - Fundação para a Ciência e a Tecnologia through project UIDB/50016/2020.

References

Abate T, Albergel J, Armbrecht I, Avato P, Bajaj S, Beintema R, Zid RB, Brown R, Butler LM, Dreyfus F, Ebi KL, Feldman S, Gana A, Gonzales T, Gurib-Fakim A, Heinemann J, Herrmann T, Hilbeck A, Hurni H, Huyer S, Jiggins J, Kagwanja J, Kairo M, Kingamkono RR, Kranjac-Berisavljevic G, Latiri K, Leakey R, Lefort M, Lock K, Herrmann T, Mekonnen Y, Murray D, Nathan D, Ndlovu L, Osman-Elasha B, Perfecto I, Plencovich C, Raina R, Robinson E, Roling N, Rosegrant M, Rosenthal E, Shah WP, Stone JMR, Suleri A, Yang H (2009) Executive summary of the synthesis report of the international assessment of agricultural knowledge, science and technology for development (IAASTD). International Assessment of Agricultural Knowledge, Science and Technology for Development, Washington, DC

Benbrook CM (2012) Impacts of genetically engineered crops on pesticide use in the U.S. -- the first sixteen years. Environ Sci Eur 24:24

Bomgardner M (2012) The sweet smell of microbes. https://cen.acs.org/articles/90/i29/Sweet-Smell-Microbes.html. Accessed 4 Dec 2021

Brikell BH (2003) Genetically modified plants: a north/south perspective in the Mediterranean region. In: Camarda D, Grassini L (eds) Local resources and global trades: environments and agriculture in the Mediterranean region. CIHEAM, Bari, pp 93–108

CEO (2017) Recruitment errors. https://corporateeurope.org/en/efsa/2017/06/recruitment-errors. Accessed 4 Dec 2021

Coghlan A (2012) What's more dangerous: biology or synthetic biology? https://slate.com/technology/2012/12/father-of-synthetic-biology-tom-knight-on-biobricks-igem-and-the-craziest-synthetic-biology.html. Accessed 4 Dec 2021

Commoner B (1971) The closing circle. Knopf Press, New York

Diels J, Cunha M, Manaia C, Sabugosa-Madeira B, Silva M (2011) Association of financial or professional conflict of interest to research outcomes on health risks or nutritional assessment studies of genetically modified products. Food Policy 36:197–203

European Academies' Science Advisory Council (2015) New breeding techniques. https://easac.eu/fileadmin/PDF_s/reports_statements/Easac_14_NBT.pdf. Accessed 21 Jan 2022

European Environment Agency (2001) Late lessons from early warnings: the precautionary principle 1896-2000. European Environment Agency, Copenhagen

European Environment Agency (2013) Late lessons from early warnings: science, precaution, innovation. European Environment Agency, Copenhagen

Heap I, Duke SO (2018) Overview of glyphosate-resistant weeds worldwide. Pest Manag Sci 74:1040–1049

ISAAA (2019) Global status of commercialized biotech/GM crops in 2019: biotech crops drive socio-economic development and sustainable environment in the new frontier. Cornell University, Ithaca

James C (2001) Global review of commercialized transgenic crops: 2000. ISAAA, New York

James C, Krattiger AF (1996) Global review of the field testing and commercialization of transgenic plants:

1986 to 1995: the first decade of crop biotechnology. ISAAA, New York

Plumer B, Barclay E, Belluz J, Irfan U (2018) A simple guide to CRISPR, one of the biggest science stories of the decade. https://www.vox.com/2018/7/23/17594864/crispr-cas9-gene-editing. Accessed 21 Jan 2022

Quist DA, Heinemann JA, Myhr AI, Aslaksen I, Funtowicz S (2013) Hungry for innovation: pathways from GM crops to agroecology. In: Gee D, Grandjean P, Hansen SF, van denHove S, MacGarvin M, Martin J, Nielsen G, Quist D, Stanners D (eds) Late lessons from early warnings: Science, precaution, innovation. EEA, Luxembourg, pp 490–517

TMG (2015) Voters want GMO food labels printed on packaging. http://4bgr3aepis44c9bxt1ulxsyq.wpengine.netdna-cdn.com/wp-content/uploads/2015/12/15memn20-JLI-d6.pdf. Accessed 4 Dec 2021

Transparency International (2021) Corruption perceptions index. https://www.transparency.org/en/cpi/2021. Accessed 4 Dec 2021

WHO (2014) Food, genetically modified. WHO, Geneva

Woźniak E, Tyczewska A, Twardowski T (2021) A shift towards biotechnology: social opinion in the EU. Trends Biotechnol 39:214–221