

Societal and Ethical Issues in Industrial Biotechnology



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Abstract In this chapter we aim to give an overview of the main societal and ethical issues that are currently voiced around industrial biotechnology. We will illustrate this with some recent cases, such as the development of synthetic artemisinin, synthetic vanillin and vegetable oil produced by engineered algae. We show that current societal and ethical issues in industrial biotechnology centre on the following five themes: sustainability, naturalness, innovation trajectories, risk management and

economic justice. In each of these themes, clashing public opinions fuel the public debate on the acceptability of new industrial biotechnology. In some cases this has led to the failure of otherwise promising innovations. In the last part, we provide suggestions on how to deal with these ethical and societal aspects based on the approach of Responsible Research and Innovation (RRI).

Keywords Economic justice, Ethical and social issues, Naturalness, Responsible research and innovation, Sustainability

1 Introduction

Until now industrial biotechnology has not received the same kind of public scrutiny as plant biotechnology has, especially not in relation to genetic modification [1]. The societal and ethical issues which do emerge around industrial biotechnology are more broadly oriented to its role as enabling technology with its many claims on applications aimed at sustainability, such as biofuels and biochemicals. With industrial biotechnological applications becoming more abundant, these public concerns do increase within the broader debate on bio-based economy, sustainable development goals and climate change, but also towards specific technological issues.

In this chapter we aim to give an overview of the main societal and ethical issues that are currently voiced around industrial biotechnology. We will illustrate this with some recent cases, such as the development of synthetic artemisinin (see also Schürle, this volume), synthetic vanillin and vegetable oil produced by engineered algae. We do not include a case on biofuels, because the public debate on biofuels has already been documented extensively [2, 3]. Where relevant we will refer to this debate. We did not include pharmaceutical products, because that would make the chapter too wide ranging. We mainly focus on the development of a bio-based economy (or bioeconomy), here understood as an effort to derive high-quality and highly sustainable products from biomass [2]. We will also consider the wider societal debate on the bioeconomy as can be found in public reports, newspapers and websites.

We claim that current societal and ethical issues in industrial biotechnology centre on the following five themes: sustainability, naturalness, innovation trajectories, risk management and economic justice. In each of these themes, clashing public opinions fuel the public debate on the acceptability of new industrial biotechnology. These clashes in the public opinion bring out salient ethical and societal aspects for industrial biotechnology. In the last part, we provide suggestions on how to deal with these ethical and societal aspects based on the approach of Responsible Research and Innovation (RRI).

2 Some Recent Controversies in Industrial Biotechnology

Recent controversies in industrial biotechnology are here shortly described by using three examples, namely, the production of artemisinin, vanillin and algae-based oil. These cases can be taken as indicators for the social and ethical issues that are relevant for industrial biotechnology in general. They point out clashes in perceptions and underlying values. Based on the issues that are central in these cases, we arrive at five general societal themes relevant to industrial biotechnology, namely: (1) What is sustainability and how can it be measured? (2) What is natural? (3) How should risks of emerging industrial biotechnologies be managed? (4) How will industrial biotechnological trajectories develop? and (5) Who benefits from these new technologies?

In the cases mentioned, criticism is most clearly articulated by the ETC Group,¹ a Canadian NGO opposing specific technologies such as synthetic biotechnology (synbio). Although this might be seen as only one actor, the ETC Group often represents a broad group of NGOs and thereby a widely shared societal perspective. For instance, in the Ecover case discussed below, the ETC Group started a petition against the company Ecover which was signed by 17 other NGOs.

This is not to say that the ETC Group represents a view shared by all environmental NGOs. Other environmental NGOs often express a more nuanced view on new technologies, i.e. they do not categorically condemn technologies such as synthetic biology but remain open to see if they could possibly produce benefits and, if so, under what conditions. The England, Wales, and Northern Ireland division of Friends of the Earth (FoE EWNI) is an example of such an NGO. Greenpeace, however, is often taking a position comparable to that of the ETC Group, i.e. categorically rejecting genetic technologies.

The position of the ETC Group is very interesting because it represents a very outspoken position, diametrically opposed to those in favour of industrial biotechnology. Many other perspectives on synthetic biology and green chemistry can be expected to be somewhere in between those strongly in favour of industrial biotechnology and those vehemently opposing it. Focussing on these two positions as indicative for societal concerns brings out the most well-articulated concerns, assumptions and beliefs.

2.1 *The Case of Synthetic Artemisinin Production*

In 2005, supported by funds from the Bill & Melinda Gates Foundation, the US-based company Amyris achieved a 'breakthrough'² by developing artemisinic acid, a precursor to artemisinin, the main ingredient for antimalaria drugs. Malaria

¹www.etcgroup.org.

²<http://investors.amyris.com/news-releases/news-release-details/amyris-scientists-describe-break-through-development-anti>.

treatments are currently mainly based on the Chinese sweet wormwood plant, from which artemisinin is extracted. However, this process is costly and time-consuming, according to Amyris. The semi-synthetic artemisinin (SSA) provides a viable and cost-effective alternative, as the company states. The platform for producing SSA is yeast whose metabolic pathways have been engineered. Amyris partnered with the pharmaceutical company Sanofi to produce ‘cost-effective malaria treatments’, which became available in 2013.

At the time, SSA was hailed as the first triumph for synthetic biology. It showed it was possible to provide a viable alternative to naturally occurring substances, with great promise for combatting a persisting global health issue: malaria. However, not everybody was convinced of the merits of this innovation. The most vocal of the opponents of SSA is the Canadian-based ETC Group. Their main objection is that the production of SSA will undermine the agricultural production of wormwood, thereby undermining the livelihoods of farmers growing the wormwood. Sanofi can keep their prices low because of the Gates Foundation support and thereby undercut the competition. Moreover, this technology allows for the concentration of economic power in the hands of one company at the expense of many small producers. Their criticism is supported by the Dutch Royal Tropical Institute who state in a 2006 report:

The advantage of synthetic artemisinin is the combination of its predictability and, eventually, cheap production. Pharmaceutical companies will be able to enhance their control over the production process and will not have to depend on numerous supply chain actors, such as thousands of individual producers and local extractors. Long transportation distances across multiple borders will be replaced by on-the-spot production and manufacturing. However, there are also disadvantages: pharmaceutical companies will accumulate control and power over the production process; artemisia producers will lose a source of income; and local production, extraction and (possibly) manufacturing of ACT (Artemisinin based Combination Therapy, LA) in regions where malaria is prevalent will shift to the main production sites of Western pharmaceutical companies. (Heemskerk et al. [4], p. 51)

Proponents of SSA such as Amyris and Sanofi state that SSA is not intended to replace agricultural production of artemisinin, but as a supplement to reduce volatility of supply and prices (*ibid*). The worries as expressed by ETC Group and the Dutch Royal Tropical Institute are therefore unnecessary.

As it turned out, the supply of artemisinin has indeed been volatile over the years; however, the availability of SSA does not seem to have had a big impact on that, although it does appear to have helped stabilise the prices [5]. Sanofi has in any case not increased its production of SSA, because prices of naturally derived artemisinin are too low for them to compete with and because the demand has plateaued due to better diagnostics (*ibid*).

This case shows that where industrial biotechnology offers an alternative to agriculturally produced substances, questions arise about who benefits from the new production method and who is in disadvantage. It also shows that the consequences as well as the uptake of an innovation can be unpredictable. We will come back to this point later when we discuss strategies to deal with societal concerns in Sect. 4.

2.2 *The Case of Vanillin Production*

In 2011 the Swiss-based company Evolva³ developed a synthetic version of vanillin, produced by yeast whose metabolic pathways had been reprogrammed, comparable to the Amyris platform. Vanillin is the most prominent ingredient of vanilla. Most of the vanillin on the market is produced through petrochemical or chemical processes. This synthetic vanillin is much cheaper than the natural vanilla derived from the vanilla orchid, which makes up less than 1% of the vanillin used today [6].

Evolva believes that the vanillin they produce through the yeast platform is natural and more sustainable and offers a higher quality than the other artificial vanillin. It is more sustainable because it does not rely on fossil resources or paper pulp, such as other artificial vanillin. The quality is better because it comes closer chemically to natural vanilla. It is natural because it is produced through fermentation, which under EU and US law is considered a traditional or natural food production process (ibid).

However, again the ETC Group, along with other environmental organisations such as Friends of the Earth USA,⁴ opposed this innovation and the associated claims [7]. They do not dispute the quality of this product, but they state that this form of vanillin is not sustainable or natural because it has been produced with the use of highly engineered organisms. Furthermore, they fear this vanillin will undermine the livelihoods of vanilla farmers, who do produce in a sustainable manner, with respect for their direct natural environment. These two environmental organisations claim that industrial biotechnological processes are far from respecting local ecology since they could turn any crop into a feedstock for their processing facilities, while the ‘natural’ value chain needs to be attuned to the local ecology and support it in order to ensure ongoing production. Hence, according to the environmental organisations, this traditional value chain is better for the conservation of fragile rain forests.

2.3 *The Case of Algae-Based Oil Production*

When Ecover,⁵ a Belgian company producing sustainable cleaning products, announced a change to one of the ingredients in its basic cleaning formula, it suddenly found itself under attack from a coalition of environmental organisations whose members used to be among Ecover’s most loyal customers, with the international ETC Group prominent among them. The new ingredient which invoked all these criticisms was vegetable oil produced from genetically engineered algae [8], a procedure developed by the US-based company Solazyme.⁶

³www.evolva.com.

⁴<https://foe.org>.

⁵<https://www.ecover.com/nl/>.

⁶<http://solazymeindustrials.com/>.

As far as Ecover was concerned, this ingredient did not fundamentally differ from anything it had used before. In their detergents Ecover had used enzymes produced by genetically modified bacteria for years, as most companies in this area do and had hardly received any criticism for it. In the eyes of its critics, however, the oil produced by engineered algae does represent something fundamentally different. To these critics, the engineered algae symbolise a socio-technological system that is inherently unsustainable because it reinforces existing economic inequalities. The controversy led Ecover to stop using the algae-produced oil and to reflect on its strategy as a company seeking to be a front-runner in the field of sustainable innovations as Ecover describes itself [9].

In an open letter in *The Ecologist*, Jim Thomas, ETC Group's spokesperson on this matter, condemned Ecover for using what he considered to be synthetic biology which he refers to as 'extreme genetic engineering'. In his letter that was signed by 17 other NGOs, Thomas voiced concerns about the safety risks associated with this technology as well as possible socio-economic effects such the displacement of income for small farmers that depend on coconut oil [8]. Coconut oil could also provide a sustainable alternative to palm oil, one that is far less disruptive, in the eyes of Thomas and the wider environmental coalition.

This response took Ecover and Solazyme completely by surprise, as Tom Domen, long-term innovation manager at Ecover, described in an interview [9]. Both companies considered the algae technology to be in line with the technologies that were already widely used, such as enzymes derived from genetically engineered bacteria, the so-called white or industrial biotechnology. Ecover has been using such enzymes in their detergents for a long time. There is hardly any opposition against this white biotechnology because they are kept in containment in industrial plants, which minimises the risk of escape and contamination of the environment. To Ecover and Solazyme, the algae-based oil production was just another variation on an existing theme, one that is supposed to solve a pressing sustainability issue, namely, the problematic production of palm oil, the demand for which continues to grow.

3 Five Social and Ethical Issues in Industrial Biotechnology

These cases indicate some common societal themes that are brought forwards by innovations in industrial biotechnology. As stated above these are:

- (a) Sustainability
- (b) Naturalness
- (c) Risk management
- (d) Innovation trajectories
- (e) Economic justice

These themes are interesting and relevant to the advancement of industrial biotechnology because different perspectives exist on how we should deal with them. These perspectives can be related to different values, assumptions and beliefs among different actors as described below.

3.1 *Sustainability*

Whether an application of industrial biotechnology can be considered sustainable can be determined by measuring the quantifiable impact of that application, such as contribution to CO₂ reduction, use of resources such as water, release of toxic substances and so forth [10, 11]. However, as emerges from the cases discussed above, other nonquantifiable factors may also play a role in assessing sustainability. These factors may be difficult to quantify because they are very complex and surrounded by many uncertainties and/or difference in perspectives, for instance, the effect on the social well-being of people working in a bio-based value chain such as for biofuels. Although efforts are ongoing to measure this, well-being is notoriously hard to define because of the many different ways to operationalise it [12]. Nevertheless, literature on assessment of social sustainability for bioeconomy is becoming more frequent, and several social issues like employment, working condition, labour right, gender equality, social development and food security have been discussed [13–15].

Some other aspects of sustainability may be hard to quantify because their assessment is very ideological and relates to preferred societal structures and possible future effects of a specific technology. This may be the case when a biotechnological application competes with other applications that may be considered more natural or the production thereof requires more attention for preserving local ecosystems. This is, for instance, one of the issues that emerges in the vanillin case, where the production of natural vanilla is tied up closely with local ecosystems and local traditional farming practices. Proponents of the synbio vanillin will say that it does not compete with traditional vanilla but with chemical production of artificial vanillin, compared to which it can be considered more sustainable because it needs less land. However, many actors oppose genetic engineering in any form because they deem it inherently unsustainable, while more ecologically sound technologies, in their view, are available. They perceive genetic engineering as enabling economic monopolies and as introducing unnecessary risks [16].

The advancement of industrial biotechnology and many of its products depends on a reliable and widely supported system for sustainability assessment. Sustainability is not something that can be directly witnessed. Potential consumers and society at large need reliable indicators to show them which products are sustainable and which aren't. Such indicators will only be considered reliable when people feel that they reflect the concerns they have about sustainability and hence serve the wider public good and not a particular interest. When designing indicators for the sustainability assessment of products from industrial biotechnology, it is important to acknowledge the different views on sustainability [17, 18]. These different views will be further explicated in the following subthemes which all relate to the overarching theme of sustainability.

3.2 *Naturalness*

The issue of sustainability is closely linked to that of naturalness. The concept of naturalness raises two distinct issues. Firstly, there is the question of what natural is exactly and which products can be termed natural and which cannot. Secondly, there is the issue of what nature is and how we should relate to nature.

The first question pops up around the labelling of products derived from industrial biotechnology. If a fragrance or flavour is made through microbial or enzymatic processes, it can be labelled natural under both US and European laws. However, if this production relies on engineered organisms under industrial conditions, it might not fit with commonly held conceptions of natural which mostly refer to something existing in or produced by nature, as it is described in a dictionary [19]. To the vanillin produced with the help of engineered organisms, natural might suggest that it is actually derived from the vanilla orchid [20]. Environmental organisations are calling to make the distinction between these two types of products clearer [21].

The second issue, to which the first is connected, is a more fundamental one that originates from differences in values, beliefs and convictions. For some people (such as environmental activists), nature is something fragile that should be treated with the utmost care, so as not to upset vulnerable ecological balances. For other people (such as some working in industrial biotechnology or in high-risk investment), nature is essentially a resource, which has many wonderful things to offer and can provide viable solutions to pressing problems [22].

Different worldviews in which nature plays a pivotal part are depicted below. These are adapted from cultural theory (cf. [16, 23]). The little ball represents nature and the position in which nature is supposed to be, i.e. it sits in a precarious balance (vulnerable nature) or it is safely contained and can take a hit (nature as resource). These two positions are usually the most outspoken ones in discussions on genetic technologies (Fig. 1).

The perspective described as ‘controllable nature’ can be considered a midway position between vulnerable nature and nature as a resource, i.e. nature is considered to be relatively robust, but risks to the ‘natural balance’ are also acknowledged. Within this perspective, (global) regulation is considered essential to avoid any disastrous effects. Policymakers are typically put in this perspective, but also some environmental NGOs fit here, like FoE EWNI.

The capricious nature perspective is mostly associated with groups that have little political power and little influence on the economic conditions of their lives. Nature is considered to be something capricious and uncontrollable, comparable to many other aspects of life. Smallholders in developing countries may, for instance, be placed in this quadrant.

From the perspective that nature is essentially something vulnerable, approaching living organisms as entities that can be controlled and designed is a seriously flawed misconception about how we should deal with living organisms. In this perspective, living organisms are inherently unpredictable and should be treated as such. Pursuing a strategy in which living organisms are treated as predictable and controllable is

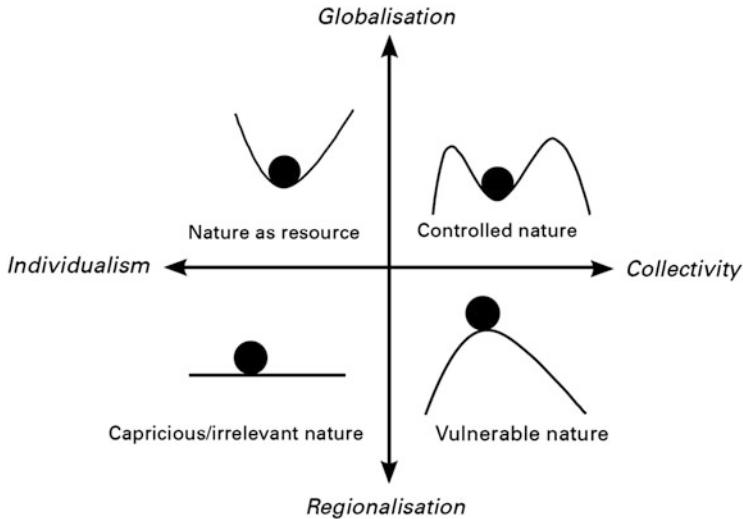


Fig. 1 Worldviews

therefore basically a mistake which diverts money and other resources away for more viable and truly sustainable solutions such as community based, organic farming practices [7, 9, 24].

From the perspective that nature is a resource that is essentially robust, industrial biotechnology is an excellent opportunity to find optimal solutions to pressing problems such as climate change and scarce resources. What's more, we cannot afford to forego the many possibilities that nature has to offer via industrial biotechnology if we want to achieve a sustainable world. This position is diametrically opposed to that of the perspective of nature as ultimately fragile [9].

The above-described perspectives are two extreme positions. There are many other positions possible that may be somewhere in between these two, or totally different altogether, such as a position that is more or less indifferent about nature and does not see any way humans could control nature. However, the positions explicated above very clearly represent a source of conflict about the acceptability of biotechnology and are therefore relevant. In considering how to assess industrial biotechnology, it can help to keep these two positions in mind to assure a complete picture of possible societal and ethical issues.

3.3 Risk Management

These differing perspectives on naturalness give rise to differing perspectives on the management of risk. Risk management refers to the identification (e.g. is there a risk?), estimation (e.g. how big is the risk?) and evaluation of the risk (e.g. how acceptable is the risk?) [25]. For many people, the risks of industrial biotechnology

are small, because the organisms are kept in closed vats. The chances of any of them escaping are low, and even if they would escape, they probably would not survive outside of the industrial conditions.

However, for other actors such as Friends of the Earth, USA, and the ETC Group, the risks of applications such as synbio are both undeniable and considerable:

While other types of pollution such as synthetic chemicals break down over time and do not breed, synthetic biological creations are designed to self-replicate and once released into the environment they would be impossible to stop and could wipe out entire species. This type of pollution, known as genetic pollution, can be devastating since it cannot be cleaned up. (FoE [26], p. 9)

These environmental NGOs think that those working in industrial biotechnology should be very careful with engineered organisms because basically they cannot be controlled. Since they are living organisms, they might escape from any setting, adapt to their environment and disturb it.

Experts in the field agree that there is no way to contain synthetic or genetically engineered organisms – particularly algae. According to Lissa Morganthaler-Jones, CEO and co-founder of Liverfuels Inc., a small number of genetically engineered algae have already leaked from the lab into the environment. ‘They have been carried out on skin, on hair and all sorts of other ways, like being blown on a breeze out the air conditioning system’, she said. (FoE [26], p. 9)

To other actors, the increased sophistication in biotechnology, the advancement to synthetic biology, indicates higher levels of safety. Because it is possible to control living organisms to an ever-increasing extent, the risks become smaller and smaller. Safety switches can be built in, for instance [9]. Safety switches are traits that ensure that living organisms can only survive within a specific, controlled environment. They might need a specific substance, for instance, that is only available in a laboratory. If the organisms leave the controlled environment, they will not be able to survive [27].

From the above we can conclude that there is a difference in the way the risks of industrial biotechnology may be identified and estimated. Moreover, there is also a difference in the way the risks are assessed. To critics of industrial biotechnology, even if the risks are small, which they do not think is the case anyhow, they would not evaluate these risks as acceptable because they think there are other, better alternatives to achieve a sustainable society or to create high-quality products, mostly through sustainable eco-agricultural practices, such as natural vanilla in the vanillin case or sustainably sourced coconut oil in the Ecover case.

3.4 Innovation Trajectories

Another important societal and ethical question is what kind of innovation trajectory industrial biotechnology is supporting. In the Ecover case, for instance, some of the critics thought that the engineered algae would lead to a technological lock-in. They

saw the algae as a platform that enables an optimally rationalised management of biomass, which serves the interest of large industry, but which does not stimulate sustainable agriculture. Additionally, these critics state that there are more viable opportunities to achieve a sustainable agriculture which are being foregone by concentrating on engineered algae. In this case, sustainably sourced coconut oil was proposed as an alternative.

However, other actors have a different view on the future innovative potential of the algae. The sustainability manager of Ecover, for instance, considered the use of engineered algae as a first stepping stone towards even more sustainable applications, such as algae that do not have a large need for sugar as a feedstock, but instead rely on sunlight and water. Additionally the plants for these algae can be distributed in a decentralised manner thereby avoiding concentration of knowledge and power [9]. This actor envisioned a totally different innovation trajectory connected to the algae.

Such clashes in expectations about innovation trajectories also emerge in the vanillin case and the artemisinin case, where the developers of the product claim that their application will not compete with the plant-derived alternative, but instead will serve to stabilise the market (artemisinin) and/or compete with the less sustainable petrochemical version. Opponents instead think that the innovation will compete with their natural counterparts and will only serve the interests of specific companies.

A similar conflict in expectations can be seen around biofuels. When the first-generation biofuels were being put to use, many supporters of this technology claimed that these first-generation biofuels would provide a stepping stone for more sustainable second- and third-generation biofuels. However, many critics feared that the first-generation biofuels would turn out to be a technological lock-in, implying that once all the investments in first-generation biofuels had been made, there was no incentive for the industry to switch to more sustainable next-generation biofuels [2].

The first-generation biofuels did indeed prove to be somewhat of a lock-in [28]. It turned out to be difficult for the EU to lower the cap for first-generation biofuels in the directive for sustainable transport due to resistance from the first-generation biofuels industries [29]. However, while more sustainable second- and third-generation biofuels haven't become available in large quantities yet, first-generation biofuels have become more sophisticated, and there is evidence suggesting that the first generation is as sustainable as the second generation, thereby questioning the need to look to second- and third-generation biofuels as sustainable solutions [30].

The articulation of a future innovation trajectory can serve as a legitimisation for a specific application. Even if the direct benefit of a specific application is not immediately clear, it can still seem desirable because of the future innovations the application enables [31]. The environmental life cycle assessment (LCA) of the engineered algae in the Ecover case, for instance, did not show a huge improvement in comparison to alternatives such as palm oil [16]. However, because Ecover perceived the algae as a contribution to a potentially more sustainable technology, they embraced the algae nonetheless. The same thing can be said to apply to first-

generation biofuels, which received governmental support, at least partly, because of their potential contribution to more sophisticated second- and third-generation biofuels [2].

Because these expectations about the future of innovation trajectories can have a considerable impact on the shaping of technology and society alike, it is important that they are open for input by a wide range of actors to ensure a democratic development of technology [32]. For example, some relevant questions are: What purpose do we expect an innovation to serve? Do we pursue an innovation simply because it is technologically possible? What are possible alternatives to the innovation trajectory? Wide-ranging input to such questions is not only desirable for democratic purposes but also for instrumental ones. If the envisioned innovation trajectory has wide societal support, the technology can be expected to disseminate more successfully and to reach societally desirable goals such as sustainability more easily.

3.5 *Economic Justice*

Another important issue for industrial biotechnology is that of economic justice, or put differently, who benefits from this technology? Many critics state that applications of industrial biotechnology lead to a concentration of knowledge and power in the hands of a few companies. This has been said for biofuels [24, 26, 33, 34] as well as for more speciality chemicals ([4, 24]; ETC Group 2016):

What is being sold as a benign and beneficial switch from black carbon to green carbon is in fact a red hot resource grab (from South to North) to capture a new source of wealth. If the grab succeeds, then plundering the biomass of the South to cheaply run the industrial economies of the North will be an act of 21st century imperialism that deepens injustice and worsens poverty and hunger. Moreover, pillaging fragile ecosystems for their carbon and sugar stocks is a murderous move on an already overstressed planet. (ETC Group [24])

Each of the cases described above features a prominent concern for the fate of small-scale farmers producing the natural substance for which a synthetic alternative is produced. Such concerns also extend to farmers producing biomass for biofuels, or farmers who might be forced to abandon their land in favour of large biofuel producers.

In contrast with this concern, many authors point out that if the production of biomass for bio-based products is managed under the right conditions, biofuels can have beneficial, sustainable effects for both small-scale farmers and society as a whole [35]. Such conditions encompass good governance [36], an appropriate division of responsibilities [33], investments in agricultural innovations and stable price regime [37] and the inclusion of a wide range of stakeholders in the design of a sustainable bioeconomy (ibid; [33, 38, 39]).

Overall the value of economic justice is widely shared. The main challenge here is how to bring it about effectively in relation to industrial biotechnology. Some actors claim that industrial biotechnology should be largely abandoned because they see it

as inherently tied up with unjust economic systems. Others see many promising opportunities offered by industrial biotechnology [17]. The call for wide-ranging participation is one we will pick up on here as a means of dealing with the many societal and ethical issues surrounding industrial biotechnology.

4 Responsible Research and Innovation for Industrial Biotechnology

As we have shown, there are many societally intricate issues related to industrial biotechnology. To support societally intricate technological trajectories, the approach of Responsible Research and Innovation (RRI) has been proposed. RRI has been defined as:

A transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the ethical acceptability, sustainability and societal desirability of the innovation process and its marketable products (in order to allow a proper embedding of scientific and technological advances in our society). (Von Schomberg [40], p. 9)

The approach of Responsible Research and Innovation (RRI) can be understood as an attempt to align new technologies with societal concerns and needs. RRI is intended to help designers and manufacturers of new technologies identify and accommodate public concerns when developing a new technology by engaging with a wide range of relevant actors [41]. As such RRI can be considered as a tool to answer questions about the direction in which we would want to use available scientific and technical knowledge (cf. [32]).

RRI has four dimensions, namely, anticipation, reflexivity, inclusion and responsiveness [42]. We will consider in turn how these might play out a role in industrial biotechnology.

4.1 Anticipation

Anticipation involves systematic thinking aimed at increasing resilience, while revealing new opportunities for innovation and the shaping of agendas for socially-robust risk research. (Stilgoe et al. [42])

Aside from promising visions on sustainability, new industrial biotechnologies also bring about new uncertainties. Questions arise about the exact environmental impacts of new technologies and about how to control new potential risks. And questions arise about what sustainability amounts to and what innovation trajectories should be instigated to achieve sustainability. Well-informed anticipation that includes a variety of perspectives may potentially substantially reduce uncertainty

and thereby prevent the occurrence of unwanted consequences. RRI asks innovators to consider the possible effects of their innovation in an integral and structured way.

However, anticipation is always necessarily limited. Unexpected consequences may emerge even after the most thorough and inclusive anticipation efforts. As van de Poel [43] shows, this is due to the complex epistemological uncertainties that surrounds a new technology, i.e. technologies can have impacts on so many different levels that it is often impossible to predict all of them correctly, also because many of these effects depend on how individuals will eventually apply a new technology and what (moral) meanings they associate with a technology.

Still it is important to try and foresee the possible effects an innovation might have and to try and accommodate this, as much as possible. When an alternative for a naturally occurring substance is produced by means of industrial biotechnology, it makes sense to think about the effects the new product may have on the existing value chain. Moreover, it is also possible to anticipate uncertainty and try to design an innovation in such a way that it can be adapted if unforeseen, unwanted effects occur (ibid). With the production of biofuels, for instance, it can be advisable, for example, to set up production systems that are flexible in terms of feedstock [44]. If new insights emerge that indicate that a particular feedstock might not be so sustainable after all, a flexible production system allows to switch to another, more sustainable feedstock.

4.2 Reflexivity

RRI asks for reflexivity in actors implying that they critically assess their own preconceptions. When different actors have different perceptions about the desirability of a technology, it can be possible for actors to construct a compromise or even a shared perspective on that technology. However, such a shared perspective or compromise requires a willingness to reconsider one's own position and the associated preconceptions [16, 45]. If environmental activists are unwilling to reconsider their preconception that *all* genetic engineering is unsustainable, it will be hard to achieve a common vision with other people who are convinced that genetic engineering is essential to achieve a sustainable society. However, possibly these groups can find a common ground, such as agreeing that instead of genetic engineering, directed evolution as a means to achieve sustainable applications, is considered acceptable by all groups involved. To achieve such a common ground, each of the actors involved will need to carefully consider their values, beliefs and convictions to see what kind of innovations are compatible with it or what kind of compromises might be acceptable.

4.3 Inclusion

Inclusion implies that a wide range of people and perspectives is taken into account when developing a new technology [42]. In the bio-based economy, inclusion already takes place in many shapes, such as for the certification and monitoring of sustainable biomass [46]. There is an ongoing international debate on the norms for sustainable biomass as well as on the quality of the labels monitoring these norms [17]. A wide variety of actors takes part in these debates, such as NGOs, companies and governmental organisations. Their views are incorporated in schemes for the certification and monitoring of the sustainability. The criteria by which sustainability is determined are hence done in an inclusive, participatory manner.

According to RRI such inclusion should go beyond the formulation of criteria and extend to the actual design choices that are being made when developing a new technology. There are of course many practical and institutional barriers to actually implement a wide variety of perspectives into the R&D phase of innovation, such as confidentiality issues, a balanced division of responsibility [47] and stakeholders who might not be willing to get involved [48] or are unable to get involved due to geographical or time-management reasons [49].

Even if these barriers occur, there are still actions that companies and other innovators can undertake to assure a representation of a wide variety of perspectives. One option is to learn from other related cases what are relevant concerns from stakeholders. The cases described above can, for instance, serve as guide for the kind of societal concerns that might affect comparable industrial biotechnology products [16]. Also, stakeholders that are at a given time unavailable might be represented by other parties that are available such as academic experts or NGOs [49].

Once a wide variety of perspectives has been identified, either indirectly as described above or directly through interviews or workshops, they can be used to inform the design choices made in an innovation trajectory. Such choices can, for instance, concern the choice for a particular feedstock, for a particular kind of technology or for centralised or decentralised production facilities [44].

4.4 Responsiveness

The last dimension of RRI is that of responsiveness and this might be seen as an overarching attitude for which the other three strategies are essential conditions. Responsiveness is the action that is taken after innovators have anticipated possible effects of their innovation, have been reflective and have included a wide variety of perspectives [32, 49].

Stilgoe et al. [42] define responsiveness as a willingness to change an innovation when it becomes clear that it conflicts on crucial issues with values of other stakeholders: 'Responsible innovation requires a capacity to change shape or direction in response to stakeholder and public values and changing circumstances'.

Especially in a setting that is continuously evolving and where the learning curve on social values is steep such as in the bio-based economy, a responsive attitude is crucial to achieve societally robust innovations. The public outcry over using food crops for fuel has, for instance, intensified the policy support for fuels from nonedible parts of crops and algae. This can be considered a responsive attitude towards societal concerns of biotechnological innovations.

It can be difficult to be responsive because innovations are sometimes locked into their own trajectory. It is possible to change the policy surrounding biofuels, but it may also be difficult to change the production platforms of the biofuels. Responsiveness is hence not always technologically possible without abandoning existing production facilities. Therefore responsiveness can be a costly affair if not managed properly. According to RRI philosophy, companies should always be aware of the need for responsiveness and try to incorporate it in their innovation strategies by ensuring some form of flexibility. For the biotech companies described in the beginning, such responsiveness seems available to different degrees because they can switch to different end products if needed without changing the core of their business, namely, the production platform (engineered micro-organisms).

Responsiveness does not necessarily always imply a change in course of those developing an innovation. Although they had the option to change to other end products, all three biotech companies that faced societal criticism (e.g. Amyris, Evolva and Solazyme) are actually still producing as they were before. They have considered the societal criticism, and they did not deem it necessary to change their innovations. The management of Solazyme started a new company focussing on health foods based on non-engineered algae, named TerraVia, thereby expanding their portfolio. They are also still producing oil from engineered algae. However, the end-user of the algae-based oil that Solazyme produced, Ecover, has stopped using the oil as ingredient for their detergents, even though they still deem it a desirable innovation. The innovation manager, Tom Domen, thought the company needed to reconsider its communication and engagement strategies before continuing with a controversial innovation such as the algae-based oil [9].

These different responses to societal criticism show that responsiveness does not necessarily imply the same course of actions for each company. Ultimately, the response to other stakeholders' values and concerns needs to be in line with the innovators' own values and concerns; otherwise it becomes a hollow public relations exercise in which the company or the innovators lose track of their own moral compass and motivation. Responsiveness does not imply a blind catering to societal concerns; it does, however, imply a reflection on one's own motives and values in light of such societal concerns. This might lead to an adaptation of the technology, but it should, at minimum, lead to a better articulation and explication of the reasons and values behind choices made in a particular innovation process.

5 Reflecting Social Issues in Sustainability Assessment for Industrial Biotechnology

Sustainability was already introduced in Sect. 3.1 as one of the five social ethical issues in relation to potential social, environmental and economic impacts that may derive from the application of novel biotechnologies. Such impacts should in principle be qualitatively or quantitatively assessed to determine whether a process, product or service should be realised or not. In other words, knowing the potential positive or negative consequences (in terms of social, environmental and economic impacts) of a novel biotechnology-related project – throughout the entire value chain – is a valuable instrument to motivate and support debates among the five social ethical issues (see Sect. 3) and allows a structured reflection on the four dimensions of RRI (see Sect. 4).

In the case of economic and environmental impacts assessment, multiple methodologies are already available and have extensively been described in literature [50]. However, in the case of social sustainability assessment, literature is scarce since methodologies are still under development, being social impact assessment (SIA) and social life cycle assessment (SLCA) the most commonly used approaches [13, 51]. The former considers on-site specific impacts, while the latter accounts for the entire life cycle. In the case of the SLCA methodology, a twofold classification of social impacts is considered, i.e. stakeholder categories and impact categories, and such social impacts are subdivided into social, socio-economic and geographical subcategories. These subcategories deal with 31 aspects of the entire value chain, such as working conditions and employment, health and safety (H&S) aspects (at different levels), access to resources (material and immaterial), contribution to economic and technology development and corporate responsibility, among others [52].

In the particular case of industrial biotechnology for biofuels and biochemicals production, some of the most critical social issues are related to food security, land use, water availability, energy security, rural and social development, employment, working conditions and health and safety impacts [50]. For instance, land expansion for industrial biotechnology applications had raised concerns in the last decade on food security and land competition for food production, especially in view of the increasing food demand of a constantly growing population. Although this connection has been in public scrutiny as the food-vs-fuel debate, there is evidence that the effect of biofuels production on food prices is limited as compared to the effects from the oil prices [35]. Another concern from biomass production and expansion for industrial biotechnology applications is that such projects may significantly affect water availability and quality for other basic uses like sanitation or food production. Although this concern highly depends on contextual features (e.g. geographical location, crop type, cultivation practice and agricultural practices, among others), it has also been demonstrated that water consumption per ton of bio-based feedstock can significantly be decreased due to technological improvements in water recovery and recycling by using closed-loop water cycles and municipal wastewaters.

However, it is also acknowledged that further water stress would raise from growing biomass production demands [50]. On the other hand, industrial biotechnology-related projects, like biofuels and biochemicals production, have shown positive social effects, at local and global scales, in terms of employment creation (e.g. over 3.5 million (direct and indirect) jobs globally in the bioenergy transportation sector by 2010 [53]), value generation (e.g. increase in the municipal GDP per capita, regional tax income and poverty reduction [54]), infrastructure investments and social services contributions.

6 Conclusion

Industrial biotechnology carries the promise of sustainable solutions based on natural resources. However, some issues invoke societal criticism, showing that different actors have different perspectives on salient issues. These issues include sustainability, naturalness, risk management, innovation trajectories and economic justice. To achieve societally robust innovations, innovators can learn from actors who have a different view on a specific application. The framework of Responsible Research and Innovations offers guidelines to organise such learning. These guidelines are based on the principles of anticipation, inclusion, reflexivity and responsiveness. The outcome of such a learning process might be that an innovation trajectory is adapted, or at minimum that the innovators are aware of possible objections to their innovation and can widen their understanding of their own motivation for pursuing that innovation. Currently efforts are on the way to integrate social and economic aspects into LCA, but these are still in their infancy.

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