Special Section: Synthetic Biology: Ethical and Philosophical Challenges

Synthetic Biology and Ethics

Past, Present, and Future

MATTI HÄYRY

Abstract: This article explores the ethical issues that have been identified in emerging technologies, from early genetic engineering to synthetic biology. The scientific advances in the field form a continuum, and some ethical considerations can be raised time and again when new developments occur. An underlying concern is the cumulative effect of scientific advances and ensuing technological innovation that can change our understanding of life and humanity.

Keywords: synthetic biology; genetics; ethics; morality; humanity; life; cloning; stem cells; genetically modified organisms; genetically modified food; precaution; hope; Pascal's wager; gene therapies

What Are We Talking About?

Synthetic biology as a branch of science *studies* the possibility of producing organisms or their parts by using animate and inanimate materials. Synthetic biology as a branch of engineering *produces* organisms and their parts by using animate and inanimate materials.

Apart from these simple characterizations, synthetic biology can be defined in a variety of ways, depending on the specific disciplines and approaches involved, and on the interests of those formulating the definitions. Here are a few descriptions that have been presented in current ethical discussions on the matter. Synthetic biology:

> seeks to apply the principles of engineering to the practice of biology and make possible the development of biological systems, including entire organisms, that have never been found in nature and serve precisely specified human purposes[1]
>
> [is] the application of engineering principles to (re)design and construct novel biological systems and devices[2]
>
> [is] the use of a mixture of physical engineering and genetic engineering to create new (and, therefore, synthetic) life forms[3]
>
> [is] an emerging field of research that aims to combine the knowledge and methods of biology, engineering and related disciplines in the design of chemically synthesized DNA to create organisms with novel or enhanced characteristics—and traits[4]

This article was produced as a part of the Academy of Finland project *Synthetic Biology and Ethics* (SA 272467, 2013-2017) The author gratefully acknowledges the Academy's support.

Cambridge Quarterly of Healthcare Ethics (2017), **26**, 186–205.

doi:10.1017/S0963180116000803

> [is] a multifarious field that comprises a range of research programs such as bioengineering, synthetic genomics, protocell research, and unnatural molecular biology[5]
>
> [comprises] the design and construction of new biological parts, devices, and systems, and … the re-design of existing, natural biological systems for useful purposes[6]
>
> [can be seen] as the fully fledged successor of genetic engineering, since both disciplines aim at rearranging sub-cellular molecular structures. In doing so, genetic engineering was concentrating on the genome of existing organisms, and was limited to replacing single genes. Synthetic biology now takes hold on, firstly, long DNA-sequences (up to whole genomes), secondly, elaborated metabolic and signalling pathways design, and, thirdly, novel, not naturally occurring parts to expand or replace natural DNA chemistry.[7]

It seems, at first glance, that the unique feature here is the study and creation of new types of entities: "organisms that have never been found in nature;" "novel biological systems and devices;" "new synthetic life forms;" and "organisms with novel or enhanced characteristics and traits." This, however, is not particularly accurate. Because new types of biological entities can also be produced by traditional breeding and gene technologies that mix the genomes of different species, this is not the distinctive feature of synthetic biology (if there is any).[8]

More promising sources of originality can be found in the artificial or human-made flavor of the enterprise; in calculation and planning that replace spontaneous natural processes; and in the aspect of precise and repeatable production. Sound bites for these in the sample definitions include "design of chemically synthesized DNA;" "synthetic genomics and unnatural molecular biology;" and "re-design of existing, natural biological systems for useful purposes." How these elements of "synthetic rational engineering" could demand us to redirect our ethical thinking needs to be considered. The background of these considerations is twofold. As pointed out in the last and longest characterization in the preceding list, scientific advances from early genetics to synthetic biology form a continuum, and ethical norms and values have already been applied to the earlier kinds of inquiry and production. The questions are, accordingly: what remains the same and what changes when we move on to synthetic biology?

The ethics of synthetic biology as an academic discipline *studies* the value- and norm-related questions raised by synthetic biology as a branch of science and as a branch of engineering. The ethics of synthetic biology as a political practice *regulate* research and production in synthetic biology to prevent damage, mitigate risks, and control conflicts of interest. Possible conflicts of interest range from economic, political, and social, to cultural, ideological, moral, and religious.

In the subsequent sections, I will first outline the ethical reactions that have followed advances in molecular biology, genetics, and related emerging disciplines and technologies during the last few decades; and then take a closer look at some philosophical questions that underlie the ethics of synthetic biology. These philosophical questions are: the permissibility of creating life, the role of hope and fear in technology assessments, and the need for openness and public acceptance for engineering life.

Background in Research

Because the following may look like a rather impressionistic sketch of advances in science and ethics, let me begin by listing the investigations that have led to the views expressed here.

I started my research in bioethics in 1984, exploring the then usual suspects of abortion, euthanasia, quality of life, justice in resource allocation, paternalism in health care, AIDS, assisted reproduction, the rights of nonhuman animals, and the nature and methodology of applied philosophical ethics.[9] My first published study in the ethics of genetics was an exploration of the main "categorical" arguments against genetic engineering: the arguments from "playing God" and "unnaturalness."[10] During the 1990s, I participated in many nationally and regionally funded research projects, and the work in them produced further publications on the ethics of genetic engineering,[11] agricultural genetics,[12] biotechnology and the environment,[13] human reproductive cloning,[14] and the methodology of genetic ethics and professional ethics.[15] Since 1997, I have been constantly in charge, alone or with others, of major research projects on the ethics of genetics, genetic information, systems biology and bioinformatics, human enhancements, and synthetic biology. My publications from the last two decades present the results of these projects,[16] as well as the results of my more conceptual work on the theories, principles, values, norms, approaches, and philosophy of emerging science and technologies.[17] It is against this more detailed research background that I offer the following overarching comments.

The Early Story and Its Lessons

In the Beginning, There Was "Genetic Engineering"

As recombinant DNA techniques began to advance during the 1970s, three practical applications emerged from the development: the agricultural use of genetically modified organisms (GMOs), the production and marketing of genetically modified (GM) food, and the promise of gene therapies for otherwise incurable diseases. They all attracted slightly different reactions.

Engineered Bacteria in Our Fields

The first reported release of GMOs in the natural environment occurred when ice-minus *Pseudomonas syringae* bacteria were sprayed on strawberry and potato fields in California in 1987.[18] Crops are commonly infected by the natural, ice-plus variant of *P. syringae*, which promotes ice-nucleation in the host plants and causes frost damage. The GM ice-minus strain of *P. syringae* does not produce the ice-nucleation protein and does not allow ice formation; therefore, the theory was that its introduction in the crops would improve the situation. The first tests on strawberries were only partially successful, because environmental activists destroyed some of the plants. The tests on potato fields, however, were a scientific success.

The ethical objections of the protesters were later on summarized by Andy Caffrey of the Earth First group that organized the field trash: "When I first heard that a company in Berkeley was planning to release these bacteria Frostban in my community, I literally felt a knife go into me. Here once again, for a buck, science, technology and corporations were going to invade my body with new bacteria

that hadn't existed on the planet before. It had already been invaded by smog, by radiation, by toxic chemicals in my food, and I just wasn't going to take it anymore."[19]

And as anti-GM activist Jeremy Rifkin has added, comparing the new threat to already existing ones: "What differentiates genetically engineered products from petrochemical products is these products are alive. So they are inherently more unpredictable when you place them in the environment. These products reproduce. Chemical products don't do that. These products mutate. Chemical products don't do that."[20]

GMOs were, then, seen as a new and dangerous kind of pollution: an impurity that should not be introduced into the natural environment.

Frostban was never used in professional farming, but the 1987 protest had very little lasting effect, as GMO crops of corn, soy, rice, cotton, canola, zucchini, alfalfa, sugar beet, and many others are now grown all over the world.[21] Only the European Union has been holding back on this expansion, but even this is probably based on trade interests rather than on scientific risk assessments.[22] Elsewhere, GMOs flourish, and the interesting question here is: what should be deduced from the situation? Should one say that Caffrey, Rifkin, and other anti-GMO activists were wrong and that their alarmism was unfounded? It has been 30 years, and the planet is still alive and relatively well. Or is the issue that the time span is too short, and that if we keep adding these cumulative elements to the system, the limits will eventually be reached and unrepairable damage will be done? Thirty years is a short period in the accumulation of environmental harm, so it may be too early to tell. If the latter line is taken, we have our first historical argument against synthetic biology. We must not, so the argument goes, add new foreign elements into the natural environment, lest we mess up the spontaneously evolved order and give way to unpredictable and uncontrollable developments.

Tomato Stories

It only took a few years after the first field tests for GM food products to reach the market. The herald of the new age was biotech company Calgene's Flavr Savr's tomato, introduced in 1994.[23] Because of its modification, the Flavr Savr tomato could be picked when it was ripe but still have a shelf life comparable to the shelf life of unmodified tomatoes that had to be picked green at the cost of losing flavor. Flavr Savr was never economically viable because of high production and distribution costs, but by passing the United States Food and Drug Administration's (FDA) evaluation,[24] it paved way for other GM food crops. The FDA identified no risks in the GM product that would have exceeded the risks of natural products, and saw no reason for special permits in normally safety-tested cases such as this. The political background of the decision was the United States government's conviction (still supported today, judging by a recent endorsement by more than 100 Nobel Laureates)[25] that GM crops would start a new technologically advanced and economically prosperous era in the country's and the world's food production.[26]

While Calgene was incrementally taken over by Monsanto (an American-based multinational biotech company that looms large in the GMO story)[27] between 1995 and 1997, and the Flavr Savr project folded, the United Kingdom experienced

a novel development that marked a transition from an "American" to a more "European" approach.[28] The newly formed company Zeneca engineered a pectin-enriched tomato that was canned, labeled, and sold successfully in the popular Sainsbury's chain of supermarkets during the latter half of the 1990s.[29] Just as the industry began to hail the dawning of a GM food revolution, however, resistance against the "Frankenstein food" began to increase. Other chains, among them (the also widely popular) Tesco, took a public stand against GM food products, and Sainsbury's was forced to withdraw the tomato paste from the market.[30]

Opposition to genetic modification was strong in Britain at the turn of the millennium, with Prince Charles coming out as a strong champion of the anti-GM cause,[31] crops trampled,[32] and the public opinion shifting from "These really *are* tastier!" to "Who knows what's *in* them?"

Without going any deeper into the scientific facts of the matter, which are still contested for some crops, the tomato story provides another useful insight into the ethics of synthetic biology; namely, the question of labeling.[33] In a world of consumer choice and market freedom that broadcasts the value of honesty and transparency, the original openness practiced by Sainsbury's sounds respectable. They had GM tomato in their cans, and anyone purchasing the can could read about it in the label. The matter is not, however, as straightforward as that. In the United States, the view channeled through the FDA was, and is, that ostensible labeling is misleading and counterproductive. The premise is that there is no scientific proof of any considerable risks. Therefore, if popular opinion has it that GM food is dangerous, popular opinion has it wrong. Even allowing labeling, let alone making it mandatory, would give non-GM food producers an ungrounded (non-fact-based) and unfair (bias-based) advantage. And because genetic modification is the future of food production, this would be detrimental to the well-being of nations and humanity as a whole.

The official United States attitude is reflected in federal legislation. The state legislature of Vermont decreed in June 2016 that GM food must be labeled so that it is clear to the customer at the counter that GM products have been used.[34] In July 2016, however, this was overridden by a law signed by President Barack Obama. The latter law is, somewhat confusingly, called the "labeling law." It does indeed make GM labeling formally obligatory; therefore, the use of the title is not entirely unjustified. But at the insistence of the industries (Monsanto has been named), the labeling need *not* be visible to the consumer at the counter, as the Vermont law had required. Electronic labeling accessible by a smartphone is sufficient, and this, critics say, puts people in unequal positions.[35] Be that as it may, it is clear that the United States federal law does not do what its critics would expect a labeling law to do.

In Europe, this thinking was, and is, turned on its head both factually and attitudinally. The premise is that there are, in some areas of genetic modification, some scientific indications of harm. And because this is the case, precaution is needed. At the very least, consumers should be notified if GM components are in use.[36]

Because synthetic biology is about introducing new entities to the natural environment, the questions of progress, precaution, and openness need to be addressed also in its context. Should manufacturers simply be honest about it and tell people every time they are in contact with a new material? Or should the official United States view be taken, in which manufacturers do not tell, at least not very explicitly, because there is nothing to be afraid of and they need

not bow to popular ignorance and reactionary ideology? Or should we be cautious in the way recommended by the European Union? I will return to these questions subsequently.

Gene Therapies, Tomorrow

Attempts to introduce genetic material from other organisms directly into an ailing human genome have been made since 1980.[37] This had been preceded by bone marrow and organ transplantations, also known to cause genetic alterations; however, these are more inexact methods of mixing genetic materials for therapeutic purposes. In gene therapies, a carrier or "vector" (often a virus) is harnessed to transport a specifically modified DNA molecule to the cells of the patient's body in the hope that the foreign molecule has a positive, useful, and clearly defined effect on the functioning of the target organism.

The development of gene therapies has been slow, laborious, and at times scandal ridden. Since the 1980s, the promise has been that these cures will be available in the next 20 years. A plethora of trials are ongoing, but the majority of them are in the early stages, still trying to find methods that have some effect but do not seriously harm their intended subjects.[38] A handful of gene treatments have been experimentally extended to humans, but this is where the scandals have cropped up. The most notorious of these are the Jesse Gelsinger case and trials with X-linked severe combined immunodeficiency (X-SCID), popularly known as the "bubble boy syndrome."[39] In both instances, the main trouble may have been with subject selection (Gelsinger should probably not have been allowed to participate) or the vector (in the X-SCID cases, a leukemia virus with its inescapable risks), not in the actual gene manipulation; however, any publicity like this (deaths involved in both cases) sets research back and makes investors warier.

There are even fewer commercially available gene therapies. In 2003, China was the first to approve the use of a gene therapy, Gendicine, for certain cancers.[40] In 2011, Russia permitted the use of another gene therapy drug, Neovasculgen, for treating peripheral artery disease.[41] And in 2012, the European Commission approved Glybera, a genetic treatment for a rare inherited disorder, for clinical use.[42] With the introduction of a new genome editing method, clustered regularly interspaced short palindromic repeats (CRIPSR)-associated protein-9 nuclease–(Cas9), more and speedier applications in human gene therapy, synthetic biology, and other related fields are, however, once again predicted and expected.[43] Time will tell.

Because gene therapies and synthetic biology share features, and now CRISPR-Cas9 and similar methods will serve them both, what lessons could be learned from the historical development of genetic cures? One observation is that because human lives are not immediately threatened, as they are in the case of gene therapy for lethal and otherwise incurable conditions, synthetic biologists are possibly less prone to use techniques that are known to be dangerous, such as infecting people with cancer viruses as in the X-SCID experimental treatment. There is, presumably, no emergency that would drive them to such action. Similar risks need to be constantly thought of, however. Another observation is that the creation of "synthetic gametes," albeit that they are "just" genetically manipulated and not really that "synthetic," raises questions about germ-line modifications.[44] If modifications occur in any other somatic cells of the body, the theory is that the

alteration affects only the patient being treated.[45] If they are targeted to gametes, however, the changes are potentially hereditary, which means that either a flaw is eradicated once and for all from a family line, or a new heritable disease introduced to it. Insofar as synthetic biology partakes in the development of artificial gametes, this is something that has to be taken into consideration.

On a wider socioeconomic scale, the promise of gene therapies and the promise of synthetic biology are, at least on the surface, similar. Gene therapy was thought to be the solution to all problems, and objections stating that high-tech developments only benefit a limited number of people and leave the world's real issues unsolved were brushed aside as reactionary scaremongering. Synthetic biology also promises, among other things, to be the forerunner of a bio-based economy that will, in the next 50 years, replace our current fossil-based system, end pollution, and lead to unprecedented prosperity.[46] The issues of hype, hope, fear, and precaution are alive and well with these new developments and the anticipation of them.

The Turn of the Millennium and Beyond

Science Catching the Media's Interest

The turn of the millennium saw two developments that caught the public eye; namely, human reproductive cloning and human embryonic stem cell research, also known as therapeutic cloning. These were followed by a relative calm during which scientists refined their systemic approaches to molecular biology and genetic engineering. The headlines were grabbed again briefly by synthetic biology, and by yet another cloning-related technology that was used for the creation of a "synthetic" organism, a bacterium named Synthia.

Cloning, Anyone?

The technique of cloning by nuclear transfer method came to its fruition in 1997, when Ian Wilmut and his colleagues at the Roslin Institute in Scotland reported that they had produced the first mammalian clone.[47] They had removed the nuclei from 277 sheep's ova and then fused the "empty" ova with mammary gland cells from other sheep. This resulted in 29 growing embryos, and the implantation of these in surrogate mother sheep in 13 pregnancies. On July 5, 1996, a healthy lamb, Dolly, was born.

What happened next was remarkable, and has repercussions for all discussions on biotechnology, or on technologies related to producing or manipulating life. It is fair to say that the existence of Dolly (and later on cloned cats, cattle, rats, mules, horses, dogs, wolves, camels, and others) in and by itself raised no major worries. The thought that the same nuclear transfer method could be employed to produce human beings, however, did. In a regulative and legislative frenzy, human reproductive cloning was immediately condemned by the United Nations Educational, Scientific and Cultural Organization (UNESCO);[48] by the following year it was prohibited by the national legislatures of Argentina, Austria, Brazil, Denmark, Georgia, Germany, Iceland, Mexico, Norway, Peru, Slovakia, Spain, South Africa, and the United Kingdom; and a few years later at least 30 countries had banned the technique's use in human reproduction.[49]

What is remarkable about this tidal wave of bans (not moratoria, as one would expect with new and unsafe technologies) is its focus on one particular method and one particular use of it. Human cloning, or the replication of early human beings for reproductive purposes, is fully condoned in many legislatures[50] (although not all) if it is done by "embryo splitting:" by dividing six to eight cell embryos manually to produce more items for implantation in assisted reproduction. Therefore, it seems that it is permissible to create human lives that would not have been possible without human scientific intervention. With this observation, the blame seems to be located squarely with the nuclear transfer method; however, the use of the method, even with human materials, does not raise objections in all contexts. Personalized therapies involving human embryonic stem cells could require the use of the Dolly technique; however, this is not seen as a problem in all the countries that have banned reproductive cloning. This means that the perception of wrong or evil in human reproductive cloning—and likewise in synthetic biology in the "creation of life from scratch"—must stem from something less tangible: something more symbolic, metaphorical, or even metaphysical.

One dimension of the matter is the Frankenstein effect. If one puts together human parts (or in synthetic biology inanimate components) and then shock the result into life by some magical technique, horrible things are bound to happen. Never mind that Frankenstein's creation in Mary Shelley's original story was good-natured, and only turned against Frankenstein and his family after the scientist had abandoned his creation and tried to get rid of it.[51] The plot supported by popular imagination seems to be that the "monster" was born inadequate and potentially bad, because that is what happens when people take on the role of God. The "God" of this line of thinking can be a recognized deity in one of the world's religions, such as in an early Vatican reaction: "Human cloning would not result in identical souls because only God can create a soul, a panel set up by Pope John Paul II has concluded. The Pontifical Academy of Life said the spiritual soul, 'the constitutive kernel' of every human created by God, cannot be produced through cloning."[52]

This describes it, or at least one formulation of it: If you are manufactured by humans, you will not be a complete human being yourself. Alternatively, the legitimate creating force can be nature, or in the case of synthetic biology, natural evolution. Although humankind has interfered with the "natural" world in numerous ways before, accusations of overstepping *the* fatal boundary crop up regularly, most recently in the case of Synthia, the synthetically produced bacterium.

What About Therapeutic Cloning, Then?

Following in the footsteps of cloning by nuclear transfer method, stem cell research took a leap forward when researchers at the University of Madison Wisconsin reported in 1998 that they had managed to produce a stable line of human embryonic stem cells.[53] They had let a fertilized human egg develop into a blastocyst, then extracted the inner pluripotent cells from it and succeeded in making them continue dividing in vitro in their pluripotent state, without differentiation to more particular cells of the human body.

Because stem cells, and particularly embryonic stem cells, can perform the functions of many parts of the human body, they were, and are, seen as a

potential foundation of many kinds of research and therapies.[54] Personalized medical solutions could be based on producing matching pluripotent cells either by cloning by nuclear transfer of the patient's own genome or by reversing the development of the patient's somatic cells and inducing them to return to their pluripotent state.[55] In either case, any material used in therapies would be compatible with the patient's genetic makeup and provoke fewer immune reactions.

The ethical issues raised by human embryonic stem cell research and the promise of future therapies are partly similar to the issues of human reproductive cloning and partly different from them, in a way that augurs criticisms to synthetic biology. The similarity is based on the fact that both tinker with human beings at a very early stage of their development. People who think that human reproduction should be a natural event and that human life has significant moral value as soon as an embryo is formed shun practices that are perceived as artificial or that prevent the development of embryos into adult human beings. Cloning is rejected because of its artificial character, and stem cell cultivation is rejected because it stops the biological progress of embryos, leaving them in the undifferentiated, pluripotent state. The difference is that whereas cloning does not necessarily involve industrial proportions, work on stem cells usually does. Although it is true that some dystopias feature mad dictators producing clone armies, cloning can also be thought of as a way of having children when it would be otherwise impossible: one partner's somatic cell combined with the other partner's egg could produce a child that would be more "theirs" than offspring created by other methods. Embryonic stem cell research, however, operates on cell cultures of countless embryos whose development has been arrested. This practice of turning humans, or parts of humans, into a material resource has elicited objections that are likely to crop up in discussions on certain types of synthetic biology as well.[56] The question of reifying or instrumentalizing humanity or life is passed on from earlier discussions to the new stage.

A Technical Calm Before the Storm?

In 2003, the widely publicized sequencing of the human genome was declared completed.[57] Fueled by this, three science (and partly science fiction) scenarios thrived. The idea of genetic testing for dormant diseases in individuals and populations became popular, and benefits were predicted in somatic medicine, reproductive medicine, forensics, insurance, employment, genealogy, and business.[58] Beyond testing individuals, large-scale DNA-and-data collections—human genetic databases or "biobanks"—became to be seen as a major way forward in research, medicine, forensics, and medical industry.[59] And the possibility of prenatal and preimplantation testing and screening of fetuses and embryos raised hopes—and fears—about producing healthier and better individuals and thereby "improving" the human race.[60]

By this time, genetics had completed the tacit project of "saving the life of ethics" that had been started a few decades earlier by medicine.[61] Moral philosophy and ethics had been declared dead by analytic philosophers who could not find a solid basis for universally binding norms, and by social scientists who believed in the relativity of manners and values. Difficult medical choices, and then issues in genetics, made these considerations look like academic frivolity, and forced

the discipline of bioethics into existence. The new discipline, after a period of resistance, turned out to be a perpetual motion machine: critical ethicists raise issues and others either argue with the ethicists about the merits of the case or devise regulations that make the issues nonexistent or invisible. The three developments mentioned have been debated at length following this logic. Critics have argued that many kinds of genetic information are futile and even harmful to individuals, databases lead to the emergence of a police state, and selecting children adds to parental pressures and allows a new rise of dubious eugenics. Their commentators, in turn, have responded to these claims, and legislators and administrators have tried to regulate practices that raise the worst concerns (cloning bans are an example of this) and make other developments more palatable by promoting the "public understanding of science," or less frightening by the engagement of experts and laypersons in committees and review boards who monitor new advances.

In the meantime, scientific work continued during the first decade of the millennium and reached a plateau where ethical problems were farther removed from day-to-day work in the laboratory. The academic buzzwords were "systems biology," "bioinformatics," and various other synonyms, and because work in these fields is technical and mostly unintelligible to nonscientists, the ethical attention that it has drawn has been small, compared with the big debates on cloning, stem cells, and genetic testing. These are, however, exactly the areas that will contribute to the large-scale arrival of synthetic biology in the coming years. Systems biology broadens the perspective from very specific and isolated alterations in the genome to interrelations between molecular changes and, beyond them, to genetic–environmental interactions in and between organisms. And developments in bioinformatics make the direction and control of multifactorial changes in organisms more understandable and ordered.

This is a point in the development of any emerging technology at which it is understandable to say, as one commentator said about developments in the life sciences 30 years ago: "It's very hard to sustain a great deal of worry about these things when, after ten years of pretty constant interest and attention, there have been no untoward events."[62]

This 1987 comment by Daniel Callahan was promptly followed by heated debates on the safety and justice of marketing GMOs, the immorality of cloning and stem cell research, and the Gelsinger and bubble-boy scandals in gene therapy trials. A similar development could be in store for synthetic biology. The key to understanding this is to think about the nature of technological development. In the terms presented by Joseph Schumpeter (and there are others, but these are sufficient here), advances come in three stages: invention, innovation, and diffusion.[63] Ethical considerations follow these stages in a rather predictable way. A new technological invention such as gene-splicing is made, the media is full of hype about its benefits, and critical ethicists paint dark pictures of the possible dangers and the unfair distribution of the benefits among populations. After a while, this discussion calms down, and several years of innovation work go into the development of the invention into marketable products behind the scenes. By the time the innovation is ready to be diffused, be it in the form of research instruments or medical tests or therapies, the worries are long forgotten and resurface only if or when something goes horribly wrong or someone introduces a new complaint.

Synthia, or "Creating Life from Scratch"

Synthetic biology has been said to represent the second ethical quantum leap in biology.[64] The first occurred when scientists started to genetically modify life by recombining the DNA of different species 30 years ago. In synthetic biology, scientists can now introduce into the building blocks of organisms elements that would not have been there by any combination of existing animate materials.

The creation of the first organism—a bacterial cell—controlled by a chemically synthesized genome was reported by the J. Graig Venter Institute in 2010.[65] Researchers at the Venter Institute synthesized the genome of *Mycoplasma mycoides* by constructing computer records of its structure and then building a replica of the genome from inanimate elements. Once the genome had been completed, it was transplanted into a *Mycoplasma capricolum* cell that had its DNA removed. The bacterium produced, Synthia, was capable of replicating itself over and over again; therefore, it was by definition viable and alive. The obvious headlines screamed: "Scientists create life out of nothing" and "Synthetic biologists play God."[66]

Synthia caught the attention of the media, and the attention of the United States Presidential Commission for the Study of Bioethical Issues. The Presidential Commission made Venter's enterprise an example of one of the three main dimensions of the ethics of synthetic biology, the creation of life, alongside security and safety.[67] Like other commentators and indeed Venter himself,[68] however, the Commission was quick to note that the fear of generating life is not really applicable to the case presented by the Venter Institute, as the human-made genome was a copy of an existing one, and it was inserted into an already living cell. Therefore, the serious discussion on the permissibility of creating life can perhaps be postponed until scientists can build an organism by using only inorganic chemicals. That could then be the third ethical quantum leap in biology.

Apart from the question of creating life, Synthia brings back the issue of cloning by nuclear transfer. Implanting an artificial genome into an "empty" cell—and make that cell an ovum for more complex organisms—is cloning by this method, which is perceived as dubious at least when human beings are concerned, and they may well be concerned at some point in the future. Questions were raised after closed-door meetings by scientists and others in New York and Harvard to discuss the synthesizing of the human genome.[69] Although the secrecy was consequently explained to have stemmed from the need to protect an unpublished scientific paper and the scientists and industrialists in question came out with a proposal to proceed cautiously and only for the best purposes, critical ethicists did not take kindly to the procedure.[70] Although proponents talk about therapeutic uses, synthetic human genomes could mean the production of artificial human beings, and that would not be greeted with enthusiasm in all corners.[71] And apart from this, openness, transparency, and popular acceptance cannot be bypassed in contemporary ethical discussions and decisionmaking.

The Philosophical Concerns That Will Not Go Away

The Problem

What, then, are the philosophical questions that have been raised during the history of molecular biology and genetics, and are still alive in the ethics of

synthetic biology? Three concerns seem to stand out. The first is that creating new life forms is either intrinsically bad or leads to bad consequences. The second is that either unwarranted fear or unfounded optimism guides work or regulations in the field. And the third is that engineering life, like all emerging technologies, needs public approval to proceed smoothly.

In the aftermath of Venter's Synthia, the United States Presidential Commission chose to approach all three matters with a combination of pragmatism and optimism. Referring directly to the Institute's result, they stated in the Executive Summary of their report: "The [Venter] feat therefore does not constitute the creation of life, the likelihood of which still remains remote for the foreseeable future. What remains realistic is the expectation that over time research in synthetic biology may lead to new products for clean energy, pollution control, and more affordable agricultural products, vaccines, and other medicines. The Commission therefore focused on the measures needed to assure the public that these efforts proceed with appropriate attention to social, environmental, and ethical risks."[72]

These three sentences neatly encapsulate the Commission's science-friendly stand. The first sentence says that the Venter Institute did not create life (which is true); that no one else is likely to create life in the near future (which can be questioned); and that what happens later is nothing to be concerned about (which begs the question). The second sentence says that synthetic biology *may* lead to many good things (which is true, but is only a part of the whole truth). And the third sentence says that scientists have to assure the public that synthetic biology is ethical (not necessarily to make it ethical, just to assure the public that it is).

In all fairness to the Commission, their report goes on to give structure and foundations for these views; therefore, their professionalism is not in question, any more than are their good intentions. The language of their recommendations is good textbook language for regulative ethics:

> The Commission calls on the government to make its efforts transparent, to monitor risks, to support (through a peer-review process) the most publicly beneficial research, and to educate and engage with the public as this field progresses. The government must regularly review risk assessment and other issues as the science of synthetic biology progresses. Only through openness and active engagement with all the relevant communities will the government ensure ongoing public support and appropriate oversight. The Commission emphasizes the need to engage the public over time through improved science education, a publicly accessible fact-checking mechanism for prominent advances in biotechnology, and other efforts promoting clearer communication on the state of science.[73]

And their concluding ethical principles continue on the same lines:

> To reach its recommendations, the Commission identified five ethical principles relevant to considering the social implications of emerging technologies: (1) public beneficence, (2) responsible stewardship, (3) intellectual freedom and responsibility, (4) democratic deliberation, and (5) justice and fairness. The principles are intended to illuminate and guide public policy choices to ensure that new technologies, including synthetic biology, can be developed in an ethically responsible manner.[74]

This is all reasonable; however, the message is still undermined by what precedes these passages in the first citation. I will explain why I think that the report leaves the real questions unanswered.

The first citation, and especially its second sentence, "synthetic biology may lead," with the conclusions drawn, reveals a positive and hopeful attitude toward progress. With a different attitude to scientific advances, the conclusions could equally well have been quite the opposite, perhaps something along the following lines:

- The Venter Institute came so close to creating life from scratch that we should be worried (assuming the there is something wrong in creating life from scratch).
- Because the promises of synthetic biology are vague, and because we do not know who would reap the benefits and who would bear the burdens, we should not, as scientists and citizens, commit ourselves to this endeavor before we know more about its nature and consequences.
- Instead of convincing the general public about something that we do not even ourselves know to be true, we should, for the time being, put on the brakes and work to ensure the ethicalness of synthetic biology before committing ourselves to its development.

I will elaborate briefly on these points.

Creating New Life Forms

Creating new life forms can *go* wrong in two main ways. It can produce something physically dangerous, and its applications can be socially harmful. In addition, creating new life forms can *be* wrong for more symbolic reasons. It is, therefore, slightly odd that the United States Presidential Commission simply brushed the objection aside by noting that Synthia is not, strictly speaking, a new life form, and that there is no need to discuss the matter yet. This is especially odd because the Commission starts its report by hailing the opportunity to investigate the ethics of a new technology from a forward-looking perspective, before it is too far advanced.[75]

The traditional symbolic arguments against emerging technologies, which have been rehearsed and criticized in great detail in the media and in the literature, are the arguments from the perspectives of "unnaturalness" and "playing God." Nothing particularly fresh has been said about them for some time, and they have obvious shortcomings if they are meant to be categorical objections to new practices; however, they seem to contain a grain of truth, which had already been pointed out by Ruth Chadwick 1989.[76] Human beings are neither omniscient nor omnipotent. We do not know all the consequences of our actions the way an ideal god-like agent would; and we cannot fix things if they go wrong the way an ideal god-like agent could. Although this does not mean that we should be paralyzed in our decisionmaking and never do anything, it does mean that we should think carefully before we do things that can change the natural (not-human-made) order of things. If nature has given us a raw deal, we can try to improve our situation, but only when we are reasonably confident that we will not make things worse by our interventions.

Other symbolic objections to introducing new life forms into the natural environment concern purity (in some undefined sense) and the polluting effect of human-made entities. This is a consideration that synthetic biology shares with the use of GMOs in food and agriculture. The objection has not been thoroughly examined in the context of synthetic biology; however, comparisons can be made to the mentality of "clean food" cooperatives. As a rule, materials and entities that have come into being "naturally," without technological manipulation, are preferred to those produced by science and its applications. The difficulty here, before a complete analysis has been prepared, is that the symbolic, abstract, or intrinsic harmfulness of "impurities" is regularly mixed with an anticipation of concrete harm and technology's instrumental role in causing it.

GM food has been greeted by many Western governments and corporations as the solution to world's hunger problem. GM crops will be resistant to pests and pesticides, produce better yields, and make consumers healthier and farmers richer. These are bold claims in the face of opposition pointing out that pest resistance wears out quickly, pesticide resistance pollutes the environment, harvests have not improved globally by the introduction of GMOs, consumers might be better off with indigenous plant species, and farmers are caught in the jaws of the multinational corporations (again, Monsanto among the first). Before the introduction of the new products, farmers could decide what seed varieties they wanted to use, cross them, and produce and store their own seeds. In the current situation, they have to use GM seeds, are in some cases legally forbidden to cross varieties, and have to buy their GM seeds again every year, because in fear of environmental contamination, GM crops have been manipulated not to reproduce in nature.[77] Similar concerns can easily be raised about the use of synthetic biology in the production of new fuels and raw materials. The impact on the natural environment is unclear, the change from other energy sources and building ingredients to synthetic-biology products shifts the distribution of wealth and not necessarily for the better, and traditional good practices are eradicated, with unknown consequences.

Hope, Fear, and Precaution

Why, therefore, did the United States Presidential Commission choose to ignore the potential wider dangers of synthetic biology and conclude that keeping an eye on its development was sufficient? The answer lies in attitudes toward technology. All ethicists agree that we should not make decisions that put people in harm's way in the pursuit of trivial benefits. What they do not agree about is what should be considered realistic harms and trifling benefits.

The standard called the *precautionary principle* has been popular in environmental policy and technology assessments during the last decades. The idea has many formulations,[78] but the core message is clear. If the consequences of a decision could be catastrophic, the decision should not be made before its safety has been adequately scientifically secured.[79] This reverses the logic of those who think that as a society we should proceed with new advances unless they can be shown to be hazardous. The burden of proof is shifted from the opponents of novel technologies to their proponents, and the default value is that possibly dangerous decisions should be postponed until meticulous investigations show that they do not have the detrimental implications suspected.[80]

The critics of the precautionary principle have noted that its logic requires society to ban most useful practices; all that is needed is that someone question their safety, on whatever grounds. Almost all genuinely original advances in science and technology, synthetic biology included, are by definition unpredictable, because they have not been tried before, but this, the critics continue, is not a good policy. If nothing is done, serious diseases remain uncured, useful and harmless innovations remain unimplemented, and preventable human suffering is allowed to continue. The precautionary principle does not guide one to be reasonably cautious, but rather to be directed by irrational fear.

Science-friendly ethicists such as the Presidential Commission's members rely on a different idea that has been named in the discussion the *hopeful principle*.[81] This proceeds from the conviction that technological progress is essential for the future well-being of humanity, and that hindrances based on fears and anxieties cause more suffering than even the most dangerous inventions would. The ensuing prescription is that because synthetic biology may lead to beneficial developments, it should be allowed to continue, under ethical scrutiny, but otherwise unimpeded, unless it can be reliably shown to be unsafe.

The underlying logic of both principles is similar, and can be traced back to the "wager argument" introduced by Blaise Pascal to prove whether or not God exists: we have rational grounds for believing that this is the case, and for behaving accordingly.[82] If God exists and we concede it, our reward will be eternal bliss. If God exists and we deny it, our punishment will be eternal torment. The stakes are, in other words, very high. Not so in the opposite case, however. Even if God did not exist, we would not gain much by professing a godless universe: only a few transitory pleasures that we could experience by not bowing to biblical rules. As rational gamblers, we should understand that whatever the probabilities, infinite profits and losses outweigh finite ones. Infinity divided by any finite number is still infinity. Under uncertainty we should, according to Pascal, choose the commitment with finite costs and infinite gains, or conversely, not choose a commitment with finite gains (permission to commit a few sins) and potentially infinite costs (eternal suffering in the afterlife).

Comparisons between Pascal's wager and the precautionary and hopeful principles reveal where the actual weight of the arguments is situated. For Pascal, the promise or threat of the afterlife was real enough to warrant his conclusion. More secularly minded people might object by noting that the "few transitory pleasures" alluded to by him constitute human life, the only existence that we know, which is too precious to be thrown away in the hope or fear of the logical possibility of another kind of existence. Likewise, the threat of disaster caused by genetic engineering or synthetic biology is real enough and important enough for the proponents of the precautionary principle to stall scientific and technological progress, whereas the hope of bliss moves the champions of the hopeful principle to argue for minimal restrictions on emerging advances.

Letting the Customers Decide, Informedly?

Bearing in mind that disagreement is rife concerning both deeply held values and perceived facts, it would seem inadvisable to try to sell synthetic biology in all its forms to the general public as some of the language of the United States Presidential Commission's report seems to suggest. The primary issue cannot simply be how

to assure people about the acceptability of something that is as contested as scientific and technological progress in molecular biology, genetics, and synthetic biology.

To present the matter in its proper everyday context, it should be observed that most basic and applied research in synthetic biology is not as headline grabbing as the Venter Institute's "creation of life from scratch." In an ongoing Academy of Finland research program,[83] my philosophical team surveyed the themes and topics explored by the scientific teams. Their questions include: "How to use viruses to introduce changes in bacteria?" "How to engineer biological systems rationally?" "How to make synthetic hybrid photo-electro organisms?" "How to make cell factories functional in production?" and "How to get artificial biofilms from simple building blocks?" None of these represents the kind of research that would draw the attention of science critics, and problems can, by and large, be avoided by keeping the research useful, preventing harm in the laboratory, seeking permissions, and abiding by the rules of ethical committees and institutional review boards.

This can be a part of the challenge here, however. Scientists are working on innocuous-looking projects, which in and of themselves stir little controversy, but which in combination revolutionize technology, production, economy, and probably also our notions of life and humanity. This is exactly why bodies such as the United States Presidential Commission fall short in their work if they do not address the bigger issues. At the very least, they give ammunition to their opponents, whatever their cause of contention is. In a similar vein, science critics can turn off any interest that official commissions have in the wider issues by making scientific research, in synthetic biology or in other fields, the sole or main culprit for world's evils. It has been said many times before, but it bears saying once more, that whatever is wrong with societies and the global community is a function of our political systems and economies and their inability to distribute the benefits of technology, old and new, more evenly. Science plays only a supporting role in this.

Ideally, if we commit ourselves to the values of autonomy, democracy, and equality, we should all be well informed about what happens in the field of emerging technologies, we should all have a say in how they are developed, and we should all benefit from their advances. Ethics committees, commissions, and task forces are insufficiently equipped to realize these goals; therefore, something else is needed. Unfortunately, the question "Who or what is?" has as yet not been answered in a satisfactory manner.

Notes

1. Kaebnick G, Murray TH, Parens E. *Ethical Issues in Synthetic Biology*, 2009; available at http://www.thehastingscenter.org/who-we-are/our-research/selected-past-projects/ethical-issues-in-synthetic-biology-2/ (last accessed 31 July 2016).
2. Biller-Andorno N, Ter Meulen R, Newson A. Synthetic biology for human health: Issues for ethical discussion and policy-making. *Bioethics* 2013;27:ii–iii, at ii.
3. Hunter D. How to object to radically new technologies on the basis of justice: the case of synthetic biology. *Bioethics* 2013;27:426–34, at 428.
4. Gutmann A. The ethics of synthetic biology: guiding principles for emerging technologies. *Hastings Center Report* 2011;41(4):17–22, at 17.
5. Holm S. The scientific aspirations of synthetic biology and the need for analytic ethics. *Ethics, Policy & Environment* 2012;15:25–8, at 25.

6. See note 5, Holm 2012, at 25. The original source for this is a popular synthetic biology community website; available at http://syntheticbiology.org/ (last accessed 31 July 2016).
7. Boldt J. Do we have a moral obligation to synthesize organisms to increase biodiversity? On kinship, awe, and the value of life's diversity. *Bioethics* 2013;27:411–8, at 412.
8. The view that there is no distinctive element here, just a continuum, is supported by the definition referred to in note 6, which could be applied to genetic engineering in many forms that predate synthetic biology.
9. Häyry H, Häyry M. AIDS now. *Bioethics* 1987;1:339–56; Häyry H, Häyry M, Karjalainen S. Paternalism and Finnish anti-smoking policy. *Social Science and Medicine* 1989;28:293–7; Häyry H, Häyry M. Utilitarianism, human rights and the redistribution of health through preventive medical measures. *Journal of Applied Philosophy* 1989;6:43–51; Häyry M, Häyry H. Health care as a right, fairness and medical resources. *Bioethics* 1990;4:1–21; Häyry H, Häyry M. Euthanasia, ethics and economics. *Bioethics* 1990;4:154–61; Häyry M. Measuring the quality of life: Why, how and what? *Theoretical Medicine* 1991;12:97–116; Häyry H, Häyry M. Who's like us? In: Cavalieri P, Singer P, eds. *The Great Ape Project: Equality Beyond Humanity*. London: Fourth Estate; 1993:173–82; and Häyry M. *Liberal Utilitarianism and Applied Ethics*. London: Routledge; 1994.
10. Häyry M. Categorical objections to genetic engineering: a critique. In: Dyson A, Harris J, eds. *Ethics and Biotechnolo-gy*. London: Routledge; 1994:202–15.
11. Chadwick R, Levitt M, Whitelegg M, Häyry H, Häyry M, Lunshof J. *Cultural and Social Attitudes to Biotechnology: Analysis of the Arguments with Special Reference to the Views of Young People*. Brussels: Directorate General, Science Research and Development, 1995; and Häyry M, Takala T. Genetic engineering and the risk of harm. *Medicine, Health Care and Philosophy* 1998;1:61–4.
12. Häyry M. How to apply ethical principles to the biotechnological production of food: the case of bovine growth hormone. *Journal of Agricultural and Environmental Ethics* 2000;12:177–84.
13. Häyry M, Takala T. Biotechnology and the environment: from moral objections to ethical analyses. In: Brinkmann K, ed. *Ethics: The Proceedings of the Twentieth World Congress of Philosophy, Vol. 1*. Bowling Green, OH: Philosophy Documentation Center; 1999:169–78.
14. Häyry M. But what if we *feel* that cloning is wrong? *Cambridge Quarterly of Healthcare Ethics* 2001;10:205–8; and Häyry M. Philosophical arguments for and against human reproductive cloning. *Bioethics* 2003;17:447–59.
15. Häyry M. *Playing God: Essays on Bioethics*. Helsinki: Helsinki University Press; 2001; and Häyry M. Utilitarian approaches to justice in health care. In: Rhodes R, Battin MP, Silvers A, eds. *Medicine and Social Justice: Essays on the Distribution of Health Care*. New York: Oxford University Press; 2002:53–64.
16. Häyry M, Takala T. Genetic ignorance, moral obligations and social duties. *Journal of Medicine and Philosophy* 2000;25:107–13; Häyry M, Takala T. Genetic information, rights, and autonomy. *Theoretical Medicine and Bioethics* 2001;22:403–14; Häyry M, Chadwick R, Árnason V, Árnason G, eds. *The Ethics and Governance of Human Genetic Databases: European Perspectives*. Cambridge: Cambridge University Press; 2007; and Häyry M. Genetic engineering of human beings. In: Chadwick R, ed. *Encyclopedia of Applied Ethics,Vol. 4*, 2nd ed. San Diego: Academic Press; 2012:436–44.
17. Häyry M. European values in bioethics: why, what, and how to be used? *Theoretical Medicine and Bioethics* 2003;24:199–214; Häyry M. Another look at dignity. *Cambridge Quarterly of Healthcare Ethics* 2004;13:7–14; Häyry M. Precaution and solidarity. *Cambridge Quarterly of Healthcare Ethics* 2005;14:199–206; Häyry M, Takala T. Human dignity, bioethics, and human rights. *Developing World Bioethics* 2005;5:225–33; Häyry M. *Rationality and the Genetic Challenge: Making People Better?* Cambridge: Cambridge University Press; 2010; and Häyry M. Protecting humanity: Habermas and his critics on the ethics of emerging technologies. *Cambridge Quarterly of Healthcare Ethics* 2012;21:211–22.
18. Sugavan LK. Ice-minus bacteria (P. syringae) – Frost fighting Superman. *Biotech Articles* 2011; available at http://www.biotecharticles.com/Applications-Article/Ice-minus-Bacteria-P-Syringae-Frost-fighting-Superman-819.html (last accessed 31 July 2016).
19. BBC News. GM crops: A bitter harvest. June 14, 2002; available at http://news.bbc.co.uk/2/hi/science/nature/2045286.stm (last accessed 31 July 2016).
20. See note 19, BBC News 2002.
21. International Service for the Acquisition of Agri-Biotech Applications. Global Status of Commercialized Biotech/GM Crops. ISAAA Brief 46-2013: Executive Summary, 2013; available at http://www.isaaa.org/resources/publications/briefs/46/executivesummary/ (last accessed 31 July 2016).

22. Falkner R. International Cooperation against the Hegemon: The Cartagena Protocol on Biosafety. In: Falkner R, ed. *The International Politics of Genetically Modified Food Diplomacy, Trade and Law*. New York: Palgrave Macmillan; 2006:15–33, at 18–20.
23. Bruenig G, Lyons JM. The case of the Flavr Savr tomato. *California Agriculture* 2000;54(4):6–7.
24. Leary WE. F.D.A. approves altered tomato that will remain fresh longer. *The New York Times,* May 19, 1994; available at http://www.nytimes.com/1994/05/19/us/fda-approves-altered-tomato-that-will-remain-fresh-longer.html (last accessed 31 July 2016).
25. Chokshi N. Stop bashing G.M.O foods, more than 100 Nobel Laureates say. *The New York Times,* June 30, 2016; available at http://www.nytimes.com/2016/07/01/us/stop-bashing-gmo-foods-more-than-100-nobel-laureates-say.html?_r=0 (last accessed 31 July 2016).
26. Thompson PB. How we got to now: Why the US and Europe went different ways with GMOs? *The Conversation,* November 6, 2015; available at http://theconversation.com/how-we-got-to-now-why-the-us-and-europe-went-different-ways-on-gmos-48709 (last accessed 31 July 2016).
27. Pringle P. *Food, Inc.: Mendel to Monsanto – The Promises and Perils of the Biotech Harvest*; New York: Simon & Schuster; 2005.
28. What happened to the Flavr Savr? *Chemical & Engineering News,* April 19, 1999; available at http://pubs.acs.org/cen/hotarticles/cenear/990419/7716bus1box3.html (last accessed 31 July 2016).
29. See note 26, Thompson 2015.
30. BBC News. 1996: First GMO food goes on sale in the UK; available at http://news.bbc.co.uk/onthisday/hi/dates/stories/february/5/newsid_4647000/4647390.stm (last accessed 31 July 2016).
31. BBC News. Prince warns of GM crop "threat." June 11, 2002; available at http://news.bbc.co.uk/2/hi/uk_news/2038976.stm; BBC News. Prince's GM fears are "hysteria". 12 June 2002; available at: http://news.bbc.co.uk/2/hi/uk_news/2039959.stm (last accessed 31 July 2016).
32. BBC News. Campaigners "trampled GM crops." June 8, 2002; available at http://news.bbc.co.uk/2/hi/uk_news/scotland/2033298.stm (last accessed 31 July 2016).
33. Wohlers AE. Labeling of genetically modified food: closer to reality in the United States? *Politics and the Life Sciences* 2013;32(1):73–84.
34. Strom S. G.M.O.s in food? Vermonters will know. *The New York Times,* June 30, 2016; available at http://www.nytimes.com/2016/07/01/business/gmo-labels-vermont-law.html?action=click&contentCollection=U.S.&module=RelatedCoverage&region=Marginalia&pgtype=article (last accessed July 31, 2016).
35. Houck B. President Obama signs controversial bill requiring GMO labels. *Eater,* July 31, 2016; available at http://www.eater.com/2016/7/31/12337356/us-passes-law-gmo-labels (last accessed 31 July 2016).
36. European Commission. *Genetically Modified Organisms*, July 8, 2016; available at http://ec.europa.eu/food/plant/gmo/index_en.htm (last accessed 31 July 2016).
37. Sun M. Martin Cline loses appeal on NIH grant. *Science* 1982;218:37.
38. *Gene Therapy Clinical Trials Worldwide,* February 2016; available at http://www.abedia.com/wiley/phases.php (last accessed 31 July 2016).
39. Cavazzana-Calvo M, Thrasher A, Mavilio F. The future of gene therapy. *Nature* 2004;427(6977):779–81.
40. Pearson S, Jia H, Kandachi K. China approves first gene therapy. *Nature Biotechnology* 2004;22:3–4.
41. Gene therapy for PAD approved. *Human Stem Cell Institute* December 7, 2011; available at http://www.dddmag.com/news/2011/12/gene-therapy-pad-approved (last accessed 31 July 2016).
42. Ylä-Herttuala S. Endgame: Glybera finally recommended for approval as the first gene therapy drug in the European Union. *Molecular Therapy* 2012;20:1831–2.
43. Ledford H. CRISPR: gene editing is just the beginning. *Nature* 2016;531:156–9.
44. Smajdor A, Cutas D. Artificial gametes. Nuffield Council of Bioethics, December 2015; available at http://nuffieldbioethics.org/wp-content/uploads/Background-paper-2016-Artificial-gametes.pdf (last accessed 31 July 2016).
45. See, however, Boyce N. Trial halted after gene shows up in semen. *Nature* 2001;414;677.
46. Philp JC, Richie RJ, Allan JEM. Synthetic biology, the bioeconomy, and a societal quandary. *Trends in Biotechnology* 2013;31:269–72.
47. Wilmut A, Schnieke E, McWhir J, Kind AJ, Campbell KHS. Viable offspring derived from fetal and adult mammalian cells. *Nature* 1997;385:810–3.
48. *Universal Declaration on the Human Genome and Human Rights*, adopted by the General Conference of UNESCO at its 29th session on November 11, 1997; available at http://portal.unesco.org/shs/

en/ev.php-URL_ID=1881&URL_DO=DO_TOPIC&URL_SECTION=201.html (last accessed 31 July 2016).
49. United Nations Educational, Scientific and Cultural Organization. *National Legislation Concerning Human Reproductive and Therapeutic Cloning*. Paris: Division of Ethics of Science and Technology; 2004; available at http://unesdoc.unesco.org/images/0013/001342/134277e.pdf (last accessed 31 July 2016).
50. American Medical Association endorses "pre-embryo splitting" [human cloning] as ethical. *Irving News Comments*, September 11, 2004; available at http://lifeissues.net/writers/irvi/irvi_42pre_embryosplitting.html (last accessed 31 July 2016).
51. Shelley M. *Frankenstein or the Modern Prometheus* [orig. 1818, revised edition 1831]. Cologne: Könemann Verlagsgesell-schaft mbH; 1995.
52. Vatican: Human clones wouldn't have same souls. *The Augusta Chronicle*, June 25, 1997; available at http://chronicle.augusta.com/stories/1997/06/25/tec_210414.shtml#.V7SRH0Yp3gt (last accessed 31 July 2016).
53. Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS, et al. Embryonic stem cell lines derived from human blastocysts. *Science* 1998;282:1145–7.
54. Wu DC, Boyd AS, Wood KJ. Embryonic stem cell transplantation: potential applicability in cell replacement therapy and regenerative medicine. *Frontiers in Bioscience* 2007;12:4525–35.
55. Yu J, Vodyanik MA, Smuga-Otto K, Antosiewicz-Bourget J, Frane JL, Tian S, et al. Induced pluripotent stem cell lines derived from human somatic cells. *Science* 2007;318:1017.
56. Habermas J. *The Future of Human Nature*. Cambridge: Polity; 2003, at 98–9.
57. National Human Genome Research Institute. The Human Genome Project Completion: Frequently Asked Questions, October 30, 1010; available at https://www.genome.gov/11006943/human-genome-project-completion-frequently-asked-questions/ (last accessed 31 July 2016).
58. For a critical account, see, for example, Takala T. *Genes, Sense and Sensibility: Philosophical Studies on the Ethics of Modern Biotechnologies*. Turku: Reprotalo; 2000.
59. For a critical account, see, for example, note 16, Häyry et al. (eds.) 2007.
60. For a critical account, see, for example, note 17, Häyry 2010.
61. Toulmin S. How medicine saved the life of ethics. *Perspectives in Biology and Medicine* 1982;25:736–50.
62. Daniel Callahan interviewed in: Boffey PM. Concern over genetics prompts a new coalition of critics. *The New York Times,* June 9, 1987; available at http://www.nytimes.com/1987/06/09/science/concern-over-genetics-prompts-a-new-coalition-of-critics.html?pagewanted=all (last accessed 31 July 2016).
63. Schumpeter JA. *Business Cycles: A Theoretical, Historical and Statistical Analysis of the Capitalist Process*. New York: McGraw Hill; 1939; and Schumpeter JA. *Capitalism, Socialism and Democracy*. New York: HarperCollins; 1942.
64. Savulescu J. Master the new loom before life's tapestry unravels at our hands. *Times Higher Education*, April 19, 2012; available at http://www.timeshighereducation.co.uk/story.asp?storycode=419685 (last accessed 31 July 2016).
65. Gibson DG, Glass JI, Lartigue C, Noskov VN, Chuang R-Y, Algire MA, et al. Creation of a bacterial cell controlled by a chemically synthesized genome. *Science* 2010;329(5987):52–6.
66. Alleyne R. Scientist Craig Venter creates life for first time in laboratory sparking debate about "playing god." *The Telegraph,* May 20, 2010; available at http://www.telegraph.co.uk/news/science/7745868/Scientist-Craig-Venter-creates-life-for-first-time-in-laboratory-sparking-debate-about-playing-god.html (last accessed 31 July 2016).
67. Presidential Commission for the Study of Bioethical Issues. *New Directions: The Ethics of Synthetic Biology and Emerging Technologies*. Washington, DC, December 2010; available at http://bioethics.gov/synthetic-biology-report (last accessed 31 July 2016).
68. Scientist: "We didn't create life from scratch." *CNN Reports*, May 21, 2010; available at http://edition.cnn.com/2010/HEALTH/05/21/venter.qa/ (last accessed 31 July 2016).
69. Achenbach J. Secret Harvard meeting on synthetic human genomes incites ethics debate. *The Washington Post*, May 13, 2016; available at https://www.washingtonpost.com/news/speaking-of-science/wp/2016/05/13/secret-harvard-meeting-on-synthetic-human-genomes-incites-ethics-debate/?tid=a_inl (last accessed 31 July 2016).
70. Achenbach J. After secret Harvard meeting, scientists announce plans for synthetic human genomes. *The Washington Post*, June 2, 2016; available at https://www.washingtonpost.com/news/speaking-of-science/wp/2016/06/02/after-secret-harvard-meeting-scientists-publish-proposal-to-create-synthetic-human-genomes/ (last accessed 31 July 2016).

71. Balmer A. The secretive "second world" of human synthetic biology. *The Guardian*, May 18, 2016; available at https://www.theguardian.com/science/political-science/2016/may/18/the-secretive-second-world-of-human-synthetic-biology (last accessed 31 July 2016).
72. See note 67, Presidential Commission 2010, at 3.
73. See note 67, Presidential Commission 2010, at 4–5.
74. See note 67, Presidential Commission 2010, at 5.
75. See note 67, Presidential Commission 2010, at 3.
76. Chadwick R. Playing God. *Cogito* 1989;3:186–93; see note 10, Häyry 1994; Dabrock P. Playing God? Synthetic biology as a theological and ethical challenge. *Systems and Synthetic Biology* 2009;3:47; and Illies C. New debates in old ethical skins. In: Engelhard M, ed. *Synthetic Biology Analysed: Tools for Discussion and Evaluation*. New York: Springer; 2009:89–126, at 101–5.
77. Belay M, Nyambura R. GM crops won't help African farmers. *The Guardian*, June 24, 2013; available at https://www.theguardian.com/global-development/poverty-matters/2013/jun/24/gm-crops-african-farmers (last accessed 31 July 2016).
78. United Nations Environment Programme. *Rio Declaration on Environment and Development* 1992, § 15; available at http://www.unep.org/Documents.multilingual/Default.asp?DocumentID=78&ArticleID=1163; Staff, Science and Environmental Network. *Wingspread Conference on the Precautionary Principle*, 1998; available at http://www.sehn.org/wing.html; Commission of the European Communities. *Communication from the Commission on the Precautionary Principle*, 2000; available at http://europa.eu/rapid/press-release_IP-00-96_en.htm; United Nations.2000 Cartagena Protocol on Biosafety to the Convention on Biological Diversity – treaties; available at un.org/doc/Treaties/2000/01/20000129%2008-44%20PM/Ch_XXVII_08_ap.pdf (last accessed 31 July 2016).
79. See note 17, Häyry 2005 and Häyry 2010, at 190–3.
80. Jonas H (transl. Jonas H, Herr D). *The Imperative of Responsibility: In Search of Ethics for the Technological Age* [orig. 1979]. Chicago: University of Chicago Press; 1984.
81. Holm S, Takala T. High hopes and automatic escalators: a critique of some "new" arguments in bioethics. *Journal of Medical Ethics* 2007;33;1–4.
82. Pascal B (transl. Levi H). *Pensées* [orig. 1670] *and Other Writings*. Oxford: Oxford University Press; 1995, at 153–6; Stich SP. The recombinant DNA debate: a difficulty for Pascalian-style wagering. *Philosophy & Public Affairs* 1978;7:187–205; see note 11, Häyry and Takala 1998.
83. *Synthetic Biology* (FinSynBio), 2015; available at http://www.aka.fi/en/research-and-science-policy/academy-programmes/current-programmes/FinSynBio/ (last accessed 31 July 2016).