

DESIGNING GENETIC ENGINEERING TECHNOLOGIES *FOR* HUMAN VALUES

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ABSTRACT

Genetic engineering technologies are a subclass of the biotechnology family, and are concerned with the use of laboratory-based technologies to intervene with a given organism at the genetic level, i.e., the level of its DNA. This class of technologies could feasibly be used to treat diseases and disabilities, create disease-resistant crops, or even be used to enhance humans to make them more resistant to certain environmental conditions. However, both therapeutic and enhancement applications of genetic engineering raise serious ethical concerns. This paper examines various objections to genetic engineering (as applied to humans) which have been raised in the literature, and presents a new way to frame these issues, and to look for solutions. Specifically, this paper frames genetic engineering technologies within the ‘design turn in applied ethics’ lens and thus situates these technologies as co-varying with societal forces. The value sensitive design (VSD) approach to technology design is then appropriated as the conceptual framework in which genetic engineering technologies can be considered so that they can be designed *for* important human values. By doing so, this paper brings further nuance to the scholarship on genetic engineering technologies by discussing the sociotechnicity of genetic engineering systems rather than framing them as value-neutral tools that either support or constrain values based on how they are used.

KEYWORDS

Genetic engineering, genetic modification, value sensitive design, VSD, bioethics, applied ethics, design

1. INTRODUCTION

Biotechnology is a family of technologies¹ that includes various things such as genetic engineering, biohybrids, bionics and exoskeletons, and bio-inspired materials (e.g.,

¹ A *technology family* is a collection of technologies that share (techniques that have) common goals, domains, or formal or functional features. This definition was developed by the TechEthos project team based on the definition of technology (see TechEthos, 2022; see also Umbrello et al., 2022).

smart biomaterials), among others (see Porcari et al., 2022). Due to its potential to create products of considerable market value, genetic engineering (also referred to as genetic modification) has garnered significant interest in both the scientific and industrial biotechnology communities (Loganathan et al., 2009). Genetic engineering refers to the use of laboratory-based technologies to intervene with organisms at the genetic level, i.e., the level of DNA, in order to force those organisms to either express or suppress some non-native trait(s). Genetically modified organisms (GMOs), often in the form of agricultural products (i.e., crops), are an ubiquitous example of how the application of genetic engineering can lead to highly efficacious and profitable commercial products. However, the mixed views of genetically modified crops and the growing discourse regarding their (potential) health effects, sustainability, and intellectual property concerns highlights the many issues attending potential genetic engineering efforts (Desquilbet and Bullock, 2009; De Vendômois et al., 2010; Nelson, 2001).

Genetic engineering may be most prevalent in agro-business domains, but it is not limited to these areas of research. In fact, such techniques have been applied to humans as well – generally with much debate – mostly with the goal of ameliorating diseases and other debilitating pathologies like cystic fibrosis lung disease (Oakland et al., 2012), for immunotherapy in treating various forms of cancer (Tüting et al., 1997), and for treating autoimmune and inflammatory diseases (Ewart et al., 2019). Such applications are generally taken to be less controversial.² However, there are more speculative and likewise more controversial potential applications of genetic engineering; rather than limiting the technology to purely therapeutic applications, there is the potential for genetic engineering to be used to enhance or augment humans in a variety of ways, such as by granting us greater strength (Bess, 2016), resistance to radiation³ (Gouw, 2020), or even to modify our ability to make moral decisions (i.e., moral bioenhancement) (Specker et al., 2014). The last two decades of bioethical debate have been dedicated to the many moral issues concerning the permissibility of using these technologies to not only treat, but improve the human condition, raising questions related to citizenship, naturalness, justice, genetic integrity, and other philosophical issues unique to these novel and transformative technologies (Sorgner, 2016).

This paper takes a different approach for examining the ethical issues related to genetic engineering technologies. Rather than framing the technologies as value-neutral

² There are, however, also examples of controversial applications of genetic engineering for such seemingly benign efforts, such as the work of He Jiankui, the Chinese scientist who genetically engineered babies to genetically protect them against HIV (Krimsky, 2019).

³ Balistreri and Umbrello (2022a) argue that genetic modification interventions could be used to safely and effectively modify the genetic patronage of astronauts whose mission is to colonize other planets in order to make them not only survive, but thrive in high radiation and low/zero gravity environments.

instruments that, via their use, support or constrain certain values, I contend that the way the technologies themselves are designed embodies values, values that change over time and exist in covariance with societal forces. As such, these technologies form part of a sociotechnical infrastructure with ubiquitous and pervasive effects that change over time. What open options are available to future designers and users is contingent on *design histories* which open up or close down certain available choices to future generations. In order to do this, this paper appropriates the value sensitive design (VSD) approach to technology design as a principled approach to technology design that acknowledges the interactional nature of technology and society as an inextricable characteristic of understanding technologies. By doing so, I show how the proper design of genetic engineering technologies via VSD can be oriented in such a way as to support important human values while constraining those that are unwanted, ultimately leaving open the possibility for future generations to update these technologies and retool them to the changing needs and values of those future generations.

In order to do this, the paper begins by exploring the conceptual elements of genetic engineering applications for humans, demonstrating the pervasive sociotechnical characteristics of this technology. I then explore some of the fundamental developments made in genetic engineering and the ethical issues raised by these. In particular, emphasis is given to the need to innovate these technologies in a responsible way given their pervasive and multi-generational impacts. This is followed by an explication of the VSD approach and how it functions. In discussing the VSD approach as applied to genetic engineering, special care is given to highlight how this methodology can be leveraged to meet the particular ethical challenges of genetic engineering, in order to arrive at an ultimate design that is sensitive to core human values. The final section discusses some of the outstanding issues still to be addressed as well as avenues for potentially fruitful future research.

2. GENETIC ENGINEERING

The field of genetic engineering began to see its coalescence in the 1970's as a consequence of Berg et alia's work in the creation of recombinant DNA molecules (Berg et al., 1974). These techniques were primarily geared toward medical applications and involved the splicing of a gene in order to get a useful protein that could then be cultured in production cells, ultimately in order to produce those proteins at scale (Morrow, 1979; Wright, 1986; Bloom et al., 1996). These early successes in mass-producing useful proteins were profitable since the more traditional sources of these proteins (i.e., human cadavers and animal organs) were costly and less bountiful. Today, genetic engineering techniques focus less on the production of useful

proteins and more on understanding the source causes of diseases that can be selectively and precisely targeted in order to ameliorate the resulting conditions. Rather than provide the subject with engineered proteins they may be lacking, novel techniques involve the therapeutic use of proteins to stimulate the body's own ability to produce that which it is missing (Mulligan, 1993; Verma et al., 2000; Wirth et al., 2013).

As genetic engineering has developed, it has grown rich interconnections with a variety of other biotechnologies. Moreover, each particular subdiscipline within the larger umbrella of "biotechnology" is apt to bring its own set of unique problems, technical and moral. As such, it will be useful to have a definition of genetic engineering which is wide enough such that it covers all areas of ethical investigation in question, but which is also circumscribed enough to box out questions related to other biotechnologies.

For our purposes, we can distinguish between (at least) three perspectives that can be used to rarefy our working definition of genetic engineering, and that will be useful for ensuring that we tackle the unique ethical issues associated with it in a principled fashion:

1. Genetic engineering techniques share specific properties and tools that set them apart from other technologies. In particular, genetic engineering works on the scale of cells in order to modify them or derive from them useful products (Nicholl, 2008).
2. Genetic engineering provides a process in which relatively difficult biological materials can be developed at scale and a means by which scalable new organisms can be created (Bothast et al., 1999; Collins and Young, 2018).
3. Genetic engineering is convergent and enabling in nature; it intersects and integrates existing domains like computing and human information [i.e., bioinformatics] as well as nanotechnology [i.e., nanopharmacy] (Tripathi, 2000; Timmermans et al., 2011).

3. ISSUES WITH GENETIC ENGINEERING

Genetic engineering, an important and transformative biotechnology, includes the research and development of novel and useful products at scale. This, of course, implicates the discipline in not just the manufacture and production of such products, but also their management. This more generalized conception of genetic engineering allows us to evaluate its potential repercussions across various domains. As we mentioned, genetic engineering has applications beyond its more intuitive uses in medicine, such as in industrial processes and agriculture. In this section, we explore

how more speculative applications and developments of genetic engineering techniques as applied to humans implicate a host of both social and ethical concerns that merit addressing. This is followed by a discussion of how many of the ethical issues concerning genetic engineering are unique to this domain and therefore merit specific consideration, especially when evaluating the most promising ways to design such convergent and transformative technologies so that they will support human values.

3.1 GENETIC ENGINEERING AND MEDICINE

What sets genetic engineering apart from the study of ‘genetics’ and ‘engineering’ is that it is particularly oriented at production via the use of biology at the cellular level. As mentioned above, traditional sources of the now mostly engineered spliced proteins came from sources which were not readily available, making their scalability, and thus ubiquitous adoption and application, strictly limited. Genetic engineering presented a way past this limitation. Genetic engineering, by its very nature, however, is “a process that uses laboratory-based technologies to alter the DNA makeup of an organism. This may involve changing a single base pair (A-T or C-G), deleting a region of DNA or adding a new segment of DNA.” (Smith, 2022). As such, the technology and its applications provide a novel locus for harm to emerge from, in addition to other associated unique ethical issues. Below, we explore some of the main developments and ethical issues of genetic engineering as it relates to human medicine as well as less therapeutic and more enhancement-oriented applications of genetic engineering.

3.1.2 THERAPEUTIC APPLICATIONS OF GENETIC ENGINEERING

Genetic engineering technologies have and will foreseeably continue to provide numerous boons to how medicine is practiced, presenting new ways to ameliorate various pathologies. As mentioned, there are several extant applications of such technologies towards therapeutic ends, that is, towards ameliorating illnesses in humans, such as for the regeneration and repair of tissues using mesenchymal stem cells⁴ for the treatment of cardiovascular injuries, various forms of cancer, kidney failure, and several neurological and bone disorders, as well as polyglucosan body disease (Hodgkinson et al., 2010; Raben et al., 2001).

The ability of genetic engineering technologies to target the *causes* of pathologies at the level of DNA positions these technologies as the future of medicine. This is likewise furthered by genetic engineering’s convergent character with other biotechnologies;

⁴ I.e., multipotent stem cells found in bone marrow (see Minguell et al., 2001).

genetic engineering presents new ways to approach illness while other biotechnologies like nanotechnology provide novel vehicles for delivery of treatments, genetic engineering treatments included. For example, in the transplantation of genetically engineered stem cells in order to stimulate vascularization and angiogenesis, biodegradable polymeric nanoparticles are used as the delivery mechanism in order to avoid complications arising from traditional delivery mechanisms (Yang et al., 2010). The ability of nanotechnology to enhance the delivery of therapies where traditional drugs and treatments fail is primarily due to the minute scale of nanoparticles and their ability to more precisely target illness loci by passing through cell walls and the blood-brain barrier more efficiently, thus increasing the delivered drug's bioavailability, and this couples in a clear way with the treatments made possible through genetic engineering (Bawa et al., 2008; Bennett-Woods, 2008; Ebbesen and Jensen, 2006; Iravani and Varma, 2019).

3.1.2 SAFETY RISKS CONCERNING HUMAN GENETIC ENGINEERING

There are at least two sources of safety issues concerning genetic engineering. The first is due to its convergent nature, primarily with that of nanotechnology. The ability for genetically engineered therapies to be delivered via nano-particles means that the body may be subjected to comprehensively invasive treatments down to the lowest level (i.e., intra-cellular), thus exposing patients to much greater risks of toxicity as compared to that of traditional pharmaceuticals. The resulting effects of such toxicity would be exacerbated by this increased bioavailability (Bennet-Woods, 2008; Jain et al., 2015). This is not only true of obviously toxic materials, but studies have shown how relatively non-toxic materials, like silver (Ag), when delivered at the nanoscale, display high levels of toxicity (Hadrup and Lam, 2014). Iravani and Varna (2019), however, argue that despite the therapeutic advantages of nanoparticle engineering for medicine, genetic engineering poses a potential solution to the toxicity issues, given that the biosynthesis of nanomaterials and nanoparticles, even on the industrial scale, provides overall greater resistance to metal toxicity.

Still, there are potential safety issues with the products of genetic engineering, independent of nanomedicine, and that is the potential to stimulate graft-versus-host disease [GVHD] (Ferrara et al., 2009), which is a potentially fatal condition that can be spurred by allogeneic stem cell transplantation, a genetic engineering procedure often used in therapeutic applications for treatments of certain lymphomas (Hirayama et al., 2019; Maude et al., 2018). There have been approaches to gene-engineered adoptive T cell therapies that minimize the risk of GVHD (see O'Leary et al., 2019; Bouchkouj et al., 2019), but these are time-consuming, thereby risking further aggravation of a patient's condition (Schuster et al., 2019), and such therapies are also subject to

production errors themselves (Locke et al., 2019). Ellis et alia (2021) argue that the source of the problem may also contain the seeds of a solution, maintaining that a balance has to be struck between further genetically modifying third-party T cells to avoid GVHD while ensuring that such T cells are procured from a safe source such as matching donors (Kochenderfer et al., 2013) or umbilical cord blood (Eapen et al., 2010; Kwoczek et al., 2017).

Overall, a cautious conclusion is that further research needs to be conducted to look at how genetically engineered therapies like those of modified T cells may be put to use without engendering new risks at the same time. Although promising techniques for doing this are being looked into (i.e., Anzalone et al., 2019), what is required is an explicit safe-by-design orientation in order to balance the tension between efficacy and safety (Ellis et al., 2021).

3.1.3 INFORMED CONSENT

Due to the novel and convergent aspects of genetic engineering, informed consent presents a particularly thorny issue, even for purely therapeutic technologies (and obviously for enhancement-oriented technologies as well). The principle of informed consent refers to:

the process by which a patient and medical provider discuss a proposed medical treatment, its anticipated consequences, potential risks and benefits, and alternatives. This process allows for open discussion between the provider and the patient and may theoretically help reduce medical errors, improve patient outcomes, and increase patient empowerment (Cordasco, 2013).

However, given the complexities of genetic engineering, its aptness to be utilized in convergence with other novel (and sometimes risky) biotechnologies, and the uncertainties attending many new treatments, there are epistemic gaps (or at least hurdles) that may preclude patients from fully grasping what is being proposed, meaning they cannot be sufficiently informed of the risks, particularly given the unforeseen risks that might emerge or the risks that are completely unforeseeable given the convergence of genetic engineering technologies with other risky technologies. Such practical limitations to informed consent are only exacerbated when discussing genetic testing (Poste, 1999).

3.2 GENETIC ENGINEERING AND HUMAN ENHANCEMENT

Though much of the work in genetic engineering has been oriented toward treating and possibly even eliminating illnesses or diseases, recent developments have demonstrated the potentiality for the technology to be put to use for human

enhancement as well. For example, in 2018, Chinese researcher He Jiankui and fellow collaborators deceived doctors, leading them to implant gene-edited embryos into two women, a clear violation of medical ethics (Normile, 2019). Jiankui's goal was to create children born with an inherent resistance to HIV.

Although such instances of human genetic engineering for enhancement purposes are rare, they betray the feasibility of using such techniques to enhance humans, rather than just treat them for existing conditions. In fact, there is a host of philosophical literature that explores the ethical issues which emerge as a consequence of such technologies geared towards enhancement purposes, with some scholars arguing against their ethical permissibility (Lin and Allhoff, 2008; Giubilini and Sanyal, 2016) and others arguing that such technologies, when safe and available, are not only permissible, but even obligatory (Agar, 2008; Harris, 2009; de Melo-Martín, 2010). The debate on the feasibility, permissibility, and even obligation to employ genetic engineering towards human enhancement ends forms a rich and vast literature, and exploring this debate falls beyond the scope of this paper. However, we will discuss some of the issues which relate to values unique to genetic engineering (rather than values that are common to most technologies; i.e., safety, efficacy, usability, etc.). In particular, we will explore some of the more and less feasible/plausible values as they emerge, although perhaps not explicitly so, within the literature. Those that will be discussed are summed up in Table 1.

Less Acceptable/Plausible	More Acceptable/Plausible
Right to unmodified genetic code	Right to an 'open future'
Right to a unique genetic code	Right to a life worth living / reasonable probability to have a good life
Respect for disability as a mere difference	Principle of justice

Table 1. Less and more acceptable/plausible values concerning genetic engineering

3.2.1 LESS ACCEPTABLE/PLAUSIBLE VALUES

We can identify at least three less acceptable or less plausible values that are implicated by genetic engineering technologies (see Table 1):

- Right to unmodified genetic code;

- Right to a unique genetic code;
- Respect for disability as a mere difference

Some have argued that the preservation of the human genome is a common good rather than something which may permissibly be dictated at the will of individuals (c.f., Ossorio, 2017). In fact, the UNESCO International Bioethics Committee's resolution on the ethics of cloning demands the preservation of the human genome, given that it is the "common heritage of humanity" (UNESCO, 1997, Art. 1). However, those who maintain positions like the 'right to an unmodified genetic code' or the 'right to a unique genetic code' leave themselves open to serious philosophical scrutiny (see de Andrade, 2010; Buttigieg, 2012; Princ, 2020). For example, as Balistreri and Umbrello (2022a) put it:

every time we have a child, we modify the genetic heritage of humanity, given that through sexual reproduction (or assisted reproduction interventions), we bring into the world individuals who have a genealogy different from that of their parents, or, in any case, of the people who contributed to the birth via their germ cells. (Balistreri and Umbrello, 2022a, p. 2)

This means that each birth, whether as a result of sexual reproduction or assisted reproductive techniques, *de facto* modifies this so-called "common heritage".⁵ Not only this, but it is this changing genome *as a consequence of each birth* which provides the unique genetic material necessary for variation and thus general human fecundity, thereby enabling the sustainability of the human species (Harris, 2014, p. 57). This is not only the case with current means of reproduction (sexual or assisted) but even with less-than-efficacious technologies like cloning. One would think that it is always the case that cloned individuals will be identical genetic copies of their genetic donor. However, this is only the case if they are the recipients of the mitochondrial and nuclear DNA from the same individual (Devolder and Gyngell, 2017; Levy and Lotz, 2005; Harris, 2004). If the cloned individual does not receive the mitochondrial and nuclear DNA from the same individual, then their genetic heritage will consequentially be different from both donors. However, if we did indeed aim to preserve the human genome as genetic, then this would mean that we could produce cloned females. Why? Only females can receive the genetic heritage, i.e., both mitochondrial and nuclear DNA, from an identical person. This would mean that in order to truly preserve the common genetic heritage of humanity, we would necessarily condemn the male sex to extinction, something that is arguably not ideal. Hence, these arguments against the use of genetic

⁵There also appears to be this tension within the UNESCO (1997) document itself, where Article 1 expresses this common heritage and its preservation, whereas Article 3 expresses the mutation and changing nature of said genome as a consequence of various factors.

engineering technologies presuppose that unmodified or unique genetic codes have some special status that is worth preserving, even at such costs. However, the former is *ipso facto* a consequence of any form of reproduction, whereas the latter is *de facto* the natural consequence of any genetic modification.

But what about ‘respect for disability as a mere difference’? A more radical argument proposed by scholars such as Elizabeth Barnes and Rosemarie Garland-Thomson is that disability is *just* a difference, it is not a disadvantage. As such, like the many other differences that distinguish one person from the next, there does not nor *should not* be a need to modify the genetic patrimony of the offspring in order to “correct” some condition thought to constitute a disability because, under this view, that condition is not a pathology (Barnes, 2009; 2016a). The position is radical given that it fundamentally argues that whatever the condition a child is born with is not only acceptable but good (c.f., Garland-Thompson, 2012; 2020). They thus defend the conservation of difference and disability, arguing against genetic engineering technologies that could potentially be ameliorative, basing this position on their premise that disability is not something to ameliorate. In fact, their argument rests on the notion that it would be a form of discrimination to consider disability as a form of pathology. However, as Kahane and Savulescu (2016) correctly point out, if such disabilities are mere differences and not only acceptable but good, then it would be likewise good and perhaps obligatory to preserve those differences, despite genetic engineering methodologies to change such differences (or remove them entirely) in further offspring, i.e., genetically propagating those biomarkers (c.f., Barnes, 2016b). The preservation of such ‘mere’ differences such as disabilities when there are means (i.e., genetic engineering) to avoid or ameliorate such conditions is hardly a sustainable position, particularly so when such a line of argumentation also leads to conclusions where such ‘mere’ differences must be conserved, i.e., propagated.

3.2.2 MORE ACCEPTABLE/PLAUSIBLE VALUES

There are at least three more plausible values that can be sustained concerning genetic engineering, and those are:

- Right to an 'open future'
- Right to a life worth living/ reasonable probability to have a good life
- Principle of justice

Arguments sustaining these three values are more thoroughly explored in Balistreri (2022) and Balistreri and Umbrello (2022a; 2022b). However, we will briefly outline them here.

3.2.2.1 RIGHT TO AN 'OPEN FUTURE' & RIGHT TO A LIFE WORTH LIVING

Balistreri and Umbrello (2022a; 2022b) use the context of future space travel and colonization as a narrative instrument to argue for the moral acceptability of genetic engineering interventions. These arguments, however, can be more broadly generalized.

Genetic engineering interventions in humans can be targeted toward either the somatic line or germline. The difference between the two is that somatic line interventions can be practiced on a healthy and consenting adult; however, these types of somatic line interventions cannot be transmitted to offspring. This is because the somatic line modifications impact the individual's cells and not the oocytes and/or spermatozoa. For this reason, and to not risk exposing potential offspring to harsh conditions in the case of extra-terrestrial spaceflight and colonization, it makes more sense to engage in germline interventions on embryos or gametes prior to fertilization so that the offspring are born with the enhancements already. This can be practiced prior to take-off (i.e., on Earth) and would naturally take place prior to birth and, therefore, without the consent of those whom such interventions will affect. Still, such does not entail that such decisions are not morally justifiable (Harris, 2017).

In fact, it is exactly because such offspring are not capable of making autonomous choices that progenitors have the right as well as the moral responsibility to make choices in their place (c.f., Scanlon, 2000). What is of moral relevance is that the choices promote, as much as possible, not only the well-being but the potential for future flourishing of said offspring.⁶ In the case of space travel and colonization, adult astronauts are free to make sacrifices and choose to undertake genetic engineering interventions to make them capable of surviving space (i.e., functionally therapeutic interventions). However, a minimally sufficient life worth living, vis-a-vis genetic engineering of offspring, is hardly a sacrifice that should be imposed on future offspring that would be required for long-term mission sustainability. To this end, it would be morally obligatory, when safe and efficacious, to employ genetic engineering technologies, as well as other converging technologies, to ensure that offspring not only meet the minimum threshold for wellbeing but that they will have a good potential for having a good and flourishing life (i.e., functional enhancement applications of genetic engineering). What this entails is a moral obligation to employ genetic engineering technologies in a context where a therapeutic application is only a minimally necessary

⁶ More simply put, the important point here is that there exists a presumed consent; that is, if progenitors could have obtained the consent of said offspring to undertake such interventions that they would have done so.

condition but not a sufficient one in order to qualify for moral acceptability. Rather, a value placed on using such technologies on future generations to amplify and empower their potential available choices is necessary, and, as a consequence, making *a priori* genetic engineering choices oriented towards providing future generations with good lives, not only those that meet the minimum threshold for survival, is likewise necessary.⁷

3.2.2.2 PRINCIPLE OF JUSTICE

Concerning justice, the clearest way of interpreting justice (which is different across the literature regarding the specific technology in question, c.f., see Floridi et al., 2018; Umbrello, 2020a; Friedman and Hendry, 2019), is to view justice as fairness (à la Rawls). However, as conceptualized within the domain of genetic engineering, it could more properly be understood as freedom from genetic inequality (Simmons, 2008). This can be understood in a number of ways. Given the efficacy of genetic engineering techniques for anticipatory diagnoses, particularly for genetic conditions, there are ethical issues that emerge in the use of genetic testing to uncover untreatable illnesses, particularly those that may emerge in late adult life. This can lead to undue anxiety and stress in potential positive diagnoses despite a lack of treatment (Marteau et al., 1992; Woolridge and Murray, 1988). However, beyond the therapeutic domain, there is the issue of gene doping, or enhancement applications of genetic engineering, often in sporting domains where genetically driven increases in muscle mass and density presents a clear advantage (Cantelmo et al., 2020). Although research is being undertaken in order to test for such genetic interventions, it remains difficult to identify such genetic enhancements in athletes (Baoutina et al., 2008). Such enhancements would confer to their hosts unfair and potentially undetectable advantages that would otherwise be prohibited if identifiable. Beyond these two issues of inequality are also the discussions surrounding designer babies (Balistreri, 2022). This is often construed as a function of trait selection by their progenitors in an attempt to confer to their offspring potentially desirable traits (height, skin/eye colour, increased learning memory, etc). Functionally, the fear surrounds a certain form of eugenics that could arise if preimplantation genetic diagnosis techniques are perfected and able to be geared toward non-disease traits (King, 1999; Robertson, 2005; Appel, 2012). This latter application could be used to promote a certain vision of ideal race, propagating certain notions of beauty, all the while exacerbating existing inequality in access to the

⁷ For a more in-depth critique against the principle of the minimum threshold of well-being concerning genetic engineering, see Balistreri and Umbrello (2022a).

techniques conferring such traits, given their relative costs and elective nature (Veit, 2018).

4. DESIGNING GENETIC ENGINEERING *FOR* HUMAN VALUES

So far we have examined how genetic engineering, both for therapeutic and enhancement purposes, raises a variety of ethical issues. In the philosophical debates on this, it is generally the practice to focus primarily on the consequences of using genetic engineering technologies and the ethical issues that emerge. However, this approach fails to grapple with all that goes into a particular technology, in particular the design histories, design architectures, and series of choices made by all those who are involved in the design process that leads to some technology. In many ways, this approach to technology is mostly instrumental, in that it understands technology as value-neutral and, instead, sees value come in only as a function of how a technology is used [i.e., *instrumentalism*] (Feenberg, 2009). However, this is only one way in which we might consider technology. Aside from *instrumentalism*, there is also *technological determinism*, which defends the notion that society is determined by the inextricable advance of technology (Dafoe, 2015; Wyatt, 2008). On the other end, there is *social constructivism*, which argues that technology is best understood as socially constructed and thus determined by social forces (Pinch and Bijker, 1984; Klein and Kleinman, 2002). Following the influence of the work of Langdon Winner (1980) and the subsequent ‘design turn in applied ethics’ (van den Hoven, 2017), the philosophy of technology has since acknowledged that technology is best understood as interactional (*interactional stance*). This position holds that technology and society co-construct and co-vary with one another, exerting pressures and forces in a dynamic way (Friedman et al., 2017). This way of understanding technology therefore requires an approach to technology design which keeps this interconnection in mind to ensure that responsible innovation can take place.

The value sensitive design (VSD) approach, a principled approach to technology design, takes as its philosophical starting point the notion that technologies are not value-neutral (unlike *instrumentalism*) and instead are *interactional* (i.e., a symbiosis between *technological determinism* and *social constructivism*) (Friedman and Hendry, 2019). The remainder of this work will be dedicated to showing how VSD may be used to address some of the prominent ethical challenges of genetic engineering canvassed above.

4.1 VALUE SENSITIVE DESIGN

VSD, sometimes referred to as ‘Values at Play’ or ‘Design for Values’ (Flanagan and Nissenbaum, 2014; van den Hoven et al., 2015), is at core a tripartite methodology of empirical, conceptual, and technical investigations. Whether carried out consecutively, in parallel, or iteratively, these investigations involve: (1) empirical enquiries into relevant stakeholders, their values, and their value understandings and priorities; (2) conceptual enquiries into these values and their possible trade-offs; and (3) technical enquiries into value issues raised by current technology and the possibilities for value implementation into new designs.

VSD is characterized by at least seven structural features that make it comparatively unique:

1. VSD is explicit in its anticipatory orientation. It affirms the long-term impacts that technologies have on society and aims to be proactive by centralizing human values early on and throughout the design process.
2. VSD expands the domain of relevant values to loci outside of the design domain. This includes the home, cyberspace, schools, and other areas of public life.
3. Beyond solely economic values, or the democratic values central to approaches like participatory design, VSD expands the domain of relevant values to focus on all values of moral importance.
4. VSD proposes an iterative and reflexive methodology of conceptual, empirical, and technical investigations that allows it to arrive at greater equifinality⁸ over time.
5. VSD is predicated on the *interactional* stance toward technology, and thus affirms that both technology and social forces exist in a dynamic interplay. Design then must be carried out with this covariance of technology and society in mind.
6. VSD draws from moral epistemology and affirms that specific moral values are independent of individuals’ beliefs in those values.
7. VSD rejects moral values’ social or cultural relativism and instead affirms the independence of certain moral values regardless of sociocultural differences. Values like justice, wellbeing, and dignity are framed as independent, universal moral values in design (Friedman and Hendry, 2019). How those

⁸ Equifinality is the principle that a given end state can be reached from many potential means.

values are *actually* manifested can be different due to the various socio-cultural understandings of those values.

As its name suggests, VSD focuses on human values, bridging the gap between design and ethics. Values are expressed and embedded in technology; they have real and often non-obvious impacts on users and society. Values are understood in VSD as “what a person or group of people consider important in life,” particularly those of moral importance (Friedman et al., 2013, p.56). The integration of VSD into the design practices of biotechnology more broadly, and genetic engineering technologies more specifically, requires a fine-grained understanding of the various approaches toward genetic engineering design.

4.1.1 TRIPARTITE METHODOLOGY

As mentioned, one of the distinguishing features of VSD is its tripartite structure, its three iterative and interdependent phases or ‘investigations’: conceptual, empirical, and technical investigations (See Figure 1). These investigations can be carried out consecutively, in parallel, or iteratively, and are meant to be in constant feedback with one another to aid designers in arriving at a design that meets whatever requirements are currently deemed relevant. Often, many VSD projects begin with conceptual investigations which aim to construct working definitions and answers to questions like “What are the ethical issues?”, “What values are associated with those ethical issues?”, and “Who are the people (or groups of people) that would feasibly be impacted on by various design choices?”. Because of this, conceptual investigations are often understood to be the most philosophically oriented of the three investigations, and here design teams can take up the philosophical literature itself as a starting point in drafting thorough working understandings of those questions, which can then be referred to and honed based on the other two investigations.

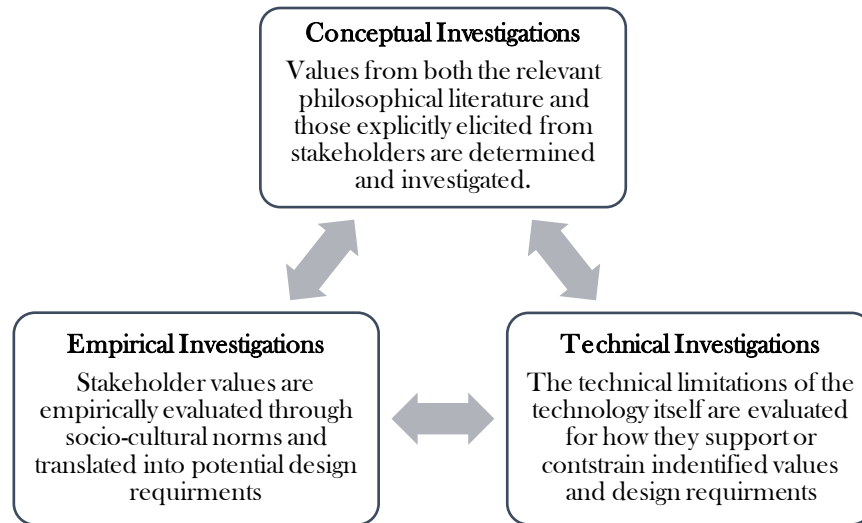


Figure 1. Tripartite VSD approach. Source: Umbrello (2020b).

Given genetic engineering's natural convergence with biology and medicine, a good starting point for conceptual investigations would be evaluating the principles central to biomedical ethics: *justice*⁹, *non-maleficence*, *beneficence*, and *autonomy* (Beauchamp & Childress, 2019). These principles function well as starting points for VSD in the domain of genetic engineering, given its emphasis on medical treatment and bodily enhancement, and they moreover serve as a basis to help address more technology-specific values and issues.¹⁰ In particular, for medical (i.e., therapeutic) applications of genetic engineering, these values can help to address many of the issues concerning the safety, efficacy, and informed consent issues outlined in Section 3.1. An example in genetic engineering which illustrates the value-sensitive design orientation is the development of gene-engineered adoptive T cell therapies for the treatment of various cancers. During the development of such therapies, concerns may arise relating to the efficacy and safety of these treatments. Safety, in this case, would be a function of not causing any unwanted genetic changes in the patient, not appropriating the necessary cells from potentially dangerous sources (even if they can thereby be produced at greater scale), and not exposing the production of such cells to manufacturing errors. The VSD approach would therefore direct designers to seek to promote (or at least not hinder) the value of safety when designing gene-engineered adoptive T cell

⁹ One can already imagine that the value of *justice* might be that the type of change you make should be a change that can be corrected/revised to allow for improvements and to make sure that technological development does not penalize older generations (i.e., avoiding obsolescence of genetic modifications), see Sparrow (2019) concerning genetic obsolescence.

¹⁰ These principles are also common starting points for other investigations utilizing the VSD approach. See, for example, Umbrello et al. (2021); Pirmi et al. (2021); Capasso and Umbrello (2022).

therapies, guiding them to bear in mind the preceding concerns. Efficacy, on the other hand, would be the ability to induce remission or the senescence of cancer cells. To a degree, efficacy is also predicated on the amount of acceptable damage that the therapy is permitted to cause at the expense of its effectiveness. The VSD approach, with regards to efficacy, would then guide designers to work toward the most effective designs, while also working within the confines set by the value of safety. These are just two of the values that can be framed using the philosophical medical literature, an operationalization that is crucial to how the VSD approach works, particularly during conceptual investigations. The ability to manage these tensions, find creative solutions, and augment, rather than abdicate, designers' ability to be responsible for the responsibility of others is a hallmark of the approach (see Simon, 2017; Jenkins et al., 2020; van Wynsberghe, 2020).

4.1.2 *STAKEHOLDER-CENTRIC*

The VSD framework is fundamentally stakeholder-focused. How values are understood, elicited, and defined, as well as how those values are then designed *for*, is contingent on stakeholders (see the list in §4.1) In particular, VSD includes several methods and tools for stakeholder identification, elicitation, analysis, and legitimation. These tools help to determine who the stakeholders are, which stakeholder groups would be best represented in order to elicit their values, tools for such elicitations, and tools for analysis of those elicitations (Cummings, 2006; Friedman et al., 2017).¹¹

Stakeholder is a central concept for VSD. When discussing values, the natural question which emerges is “*the values of whom?*”. VSD is unique in its distinction between two major types of stakeholders: *direct stakeholders* and *indirect stakeholders*. Direct stakeholders are the individuals and/or groups that directly interact with the system or its output. A prominent example of direct stakeholders would be the designers themselves who daily work with the system and the system's end users (once the system is deployed). In the case of genetic engineering technology, biotechnologists designing and using these systems would be such an example, as would recipients of genetically-engineered therapies (either ameliorative or enhancement-oriented).

¹¹ This focus on stakeholders also makes the VSD approach well-suited to guide biotechnology researchers and designers toward genetic engineering technologies which are in compliance with existing guidelines and codes of conduct concerning biotechnology and engineering biology. For example, the European Commission's *User's Guide to European Regulation in Biotechnology* (European Commission, 2014), the USA's *FDA Biotechnology Guidelines* (FDA, 2019), the UK's *Industrial Biotechnology (IB) Strategy* (Rosemann and Molyneaux-Hodgson, 2019), or, more broadly, the British Standards Institution's *Responsible Innovation Guide* (BSI, 2020) all present guidelines for research, and each include at least some relation between technological developments and stakeholder interests.

Indirect stakeholders are all the other entities affected by the use of the system, but who do not directly interact with it. Indirect stakeholders are often the class of stakeholders who are overlooked in the design of systems. We also need to keep in mind that VSD is also temporally sensitive, because stakeholder groups can change over time, and so designs which are sensitive to stakeholders' values must also be able to change. This means that future generations can, and perhaps should, be identified as an important stakeholder group when designing technologies that have such multi-generational impacts.

In the case of genetic engineering, there are strong consent-based arguments that we shouldn't impose our current values on future generations; i.e., only those capable of informed consent should be able to make the sacrifices that are part and parcel of such genetic engineering (i.e., *right to an 'open' future*), and future generations categorically cannot give informed consent. However, perhaps the type of genetic modification (i.e., the particular gene/intervention) that the genome editing technologies are geared to work on should be those that are closely linked to the possibility of practicing interventions which ensures an open future and a good quality of life for those who are born. As we described in the previous section, there is a philosophical argument to be made that astronauts aiming at extraterrestrial colonization should not procreate, given the need for subsequent generations to be subjected to such genetic engineering for the purposes of mere survival (see Balistreri and Umbrello, 2022a). What is then required is, as Lin (2006) aptly argues, an economic model that is sensitive to future generations and that permits new ways of living and innovating (see also Umbrello, 2022). VSD provides the principled theory and method(s) to do exactly just that. The approach, particularly in employing four multi-lifespan tools, is geared towards such an enterprise that genetic engineering designers could quickly adopt:

1. **Multi-lifespan timeline** (*Purpose*: Priming longer-term and multi-generational design thinking): Priming activity for longer-term design thinking, multi-lifespan timelines prompt individuals to situate themselves in a longer timeframe relative to the present, with attention to both societal and technological change which is apt to occur across that extended timeframe. (i.e., Yoo et al., 2016)
2. **Multi-lifespan co-design** (*Purpose*: Longer-term design thinking and envisioning): Co-design activities and processes that emphasize longer-term anticipatory futures with implications for multiple and future generations. These activities are geared to stimulating participants' envisioning of future [information] systems by: (1) enhancing participants' understanding of longer timeframes (e.g., 100 years), and (2) guiding participants to effectively project themselves long into the future in their design thinking. (i.e., Yoo et al., 2016, p. 4423).

3. **Envisioning Cards** (*Purpose*: Value sensitive design toolkit for industry, research, and educational practice): A set of 32 cards, the so-called Envisioning Cards build on four criteria: stakeholders, time, values, and pervasiveness. Each card contains on one side a title and an evocative image related to the card theme, and on the flip side, the envisioning criterion, card theme, and a focused design activity. Envisioning Cards can be used for ideation, co-design, heuristic critique, and evaluation. (Friedman and Hendry, 2012; Yoo et al., 2013; Umbrello, 2022).
4. **Agile Toolkit** (*Purpose*: Value sensitive design toolkit for longer-term design thinking in industry): This is a quick starter guide to employing the VSD in Agile Project Management. The toolkit aims to offer practitioners a means of integrating VSD envisioning tools into Agile workflows, thus resisting and ameliorating the short-termism implicit in Agile workflows while gaining its iterative benefits. (Umbrello and Gambelin, 2021; 2022).

Multi-generation envisioning, as promoted by VSD, provides biotechnologists with the means to design genetic engineering technologies, even for human enhancement purposes, for changing values, promoting values such as that of an *open future*, a *life worth living*, *justice*, *genetic integrity*, etc. Currently, lacunae in legislation concerning the bounds by which genetic engineering (i.e., therapeutic vs. enhancement) can be clearly delineated. VSD's ability to integrate various sources of values – i.e., the values of care and those unique to genetic engineering [Table 1] – permit it to begin closing these gaps.

5. CONCLUSIONS

The introduction of biotechnologies like genetic engineering into society poses novel and unforeseen (and possibly unforeseeable) issues for healthcare, and medicine more broadly. Genetic engineering is not only a transformative technology but also a convergent one, converging with other emerging technologies to blur the lines between sectors and disciplines. This not only sparks new social and ethical issues, among others, but also complicates how those issues can and should be confronted. In this paper, we explored what we mean when we use the term genetic engineering, its application in both humans and in other sectors, as well as how the technology is multipurpose, meaning that it can be used not only in a curative fashion, i.e., therapeutically, but also to enhance humans. Rather than frame genetic engineering technologies as static and look only at the ethical issues of their consequences, we examined the values being invoked during ethical debates and interpreted them and genetic engineering developments through the frame of design. More specifically, we

explored how we can design genetic engineering technologies *for* important human values in order to proactively confront ethical complexities, rather than addressing issues only after they are manifested.

The value sensitive design (VSD) approach presented provides both a principled theory and method that is explicitly geared towards identifying and eliciting stakeholders and their values, as well as designing not only for the present or near future, but for multiple generations. VSD thus opens up design choice architectures to permit future stakeholders and designers more choices over how they engage in design. Value sensitive design was not developed with the specific application of biotechnologies in mind, nor the more specific application to genetic engineering here being discussed, but this paper shows that the *design turn in applied ethics* may be fruitfully employed to help biomedical and genetic engineers to begin thinking about design choices in a broader way, as determined and determinate of future choice architectures. Likewise, it also shows how there is a starting point – i.e., biomedical ethical principles – that can serve as a way of framing these more specific values and principles relevant to genetic engineering within a language that is more approachable for those familiar with it. This paper, however, is far from being definitive for these debates. Rather, it aims to spark a new debate focused on the instrumentalization of genetic engineering technologies, rather than seeing them as being part and parcel of design histories and choices. VSD can also help in this latter regard. Philosophical exploration of the issues falls under the purview of conceptual investigations, which needs further work in looking at the specifics of various genetic engineering technologies and applications. Likewise, empirical and technical investigations should explore the potential people involved, how values and stakeholders change over time, as well as how the architectures of the systems themselves support or constrain values across multiple geographies, domains of application, and across time.

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REFERENCES

Agar, N. (2008). *Liberal eugenics: In defence of human enhancement*. Hoboken, NJ: John Wiley & Sons.

Appel, J. M. (2012). Toward an ethical eugenics: The case for mandatory preimplantation genetic selection. *JONA's Healthcare Law, Ethics and Regulation*, 14(1), 7-13. <https://doi.org/10.1097/NHL.0b013e318244c69b>

Anzalone, A. V., Randolph, P. B., Davis, J. R., Sousa, A. A., Koblan, L. W., Levy, J. M., ... & Liu, D. R. (2019). Search-and-replace genome editing without double-strand breaks or donor DNA. *Nature*, 576(7785), 149-157. <https://doi.org/10.1038/s41586-019-1711-4>

Balistreri, M. (2022). *Il bambino migliore?*. Rome: Fandango.

Balistreri, M., & Umbrello, S. (2022a). Should the colonisation of space be based on reproduction? Critical considerations on the choice of having a child in space. *Journal of Responsible Technology*, 11, 100040. <https://doi.org/10.1016/j.jrt.2022.100040>

Balistreri, M., & Umbrello, S. (2022b). Modifying the environment or human nature? What is the right choice for space travel and Mars colonisation? *Working paper*.

Baoutina, A., Alexander, I. E., Rasko, J. E., & Emslie, K. R. (2008). Developing strategies for detection of gene doping. *The Journal of Gene Medicine*, 10(1), 3-20. <https://doi.org/10.1002/jgm.1114>

Barnes, E. (2009). Disability, minority, and difference. *Journal of Applied Philosophy*, 26(4), 337-355. <https://doi.org/10.1111/j.1468-5930.2009.00443.x>

Barnes, E. (2016a). *The minority body: A theory of disability*. Oxford: Oxford University Press.

Barnes, E. (2016b). Reply to Guy Kahane and Julian Savulescu. *Res Philosophica*, 93(1), 295-309. <https://doi.org/10.11612/resphil.2016.93.1.15>

Bawa, R., Melethil, S., Simmons, W. J., & Harris, D. (2008). Nanopharmaceuticals: patenting issues and FDA regulatory challenges. *The SciTech Lawyer*, 5(2), 10-15.

Beauchamp, T., & Childress, J. (2019). *Principles of biomedical ethics* (8th ed.). Oxford: Oxford University Press.

Bennett-Woods, D. (2008). *Nanotechnology: Ethics and society*. Boca Raton: CRC Press.

Berg, P., Baltimore, D., Boyer, H. W., Cohen, S. N., Davis, R. W., Hogness, D. S., ... & Zinder, N. D. (1974). Potential biohazards of recombinant DNA molecules. *Science*, 185(4148), 303-303. <https://doi.org/10.1126/science.185.4148.303>

Bess, M. (2016). *Make Way for the Superhumans: How the science of bio enhancement is transforming our world, and how we need to deal with it*. London: Icon Books.

Bloom, M. V., Freyer, G. A., & Micklos, D. A. (1996). *Laboratory DNA science: an introduction to recombinant DNA techniques and methods of genome analysis*. San Francisco, CA: Benjamin Cummings Publishing Company, Inc.

Bothast, R. J., Nichols, N. N., & Dien, B. S. (1999). Fermentations with new recombinant organisms. *Biotechnology Progress*, 15(5), 867-875. <https://doi.org/10.1021/bp990087w>

Bouchkouj, N., Kasamon, Y. L., de Claro, R. A., George, B., Lin, X., Lee, S., ... & Pazdur, R. (2019). FDA approval summary: axicabtagene ciloleucel for relapsed or refractory large B-cell lymphoma. *Clinical Cancer Research*, 25(6), 1702-1708. <https://doi.org/10.1158/1078-0432.CCR-18-2743>

BSI. (2020). *PAS 440:2020 Responsible Innovation Guide*. London: The British Standards Institution. Retrieved from https://www.adamson-jones.co.uk/app/uploads/2020/04/PAS440_pdf.pdf

Buttigieg, J. (2012). The common heritage of mankind: from the law of the sea to the human genome and cyberspace. *Symposia Melitensia*, 8, 81-92. <https://www.um.edu.mt/library/oar//handle/123456789/6883>

Cantelmo, R. A., Da Silva, A. P., Mendes-Junior, C. T., & Dorta, D. J. (2020). Gene doping: Present and future. *European Journal of Sport Science*, 20(8), 1093-1101. <https://doi.org/10.1080/17461391.2019.1695952>

Capasso, M., & Umbrello, S. (2022). Responsible nudging for social good: new healthcare skills for AI-driven digital personal assistants. *Medicine, Health Care and Philosophy*, 25(1), 11-22. <https://doi.org/10.1007/s11019-021-10062-z>

Collins, J. H., & Young, E. M. (2018). Genetic engineering of host organisms for pharmaceutical synthesis. *Current opinion in biotechnology*, 53, 191-200. <https://doi.org/10.1016/j.copbio.2018.02.001>

Cordasco, K. M. (2013). Obtaining informed consent from patients: brief update review. *Making health care safer II: An updated critical analysis of the evidence for patient safety practices, 2013*, 461-470.

Cummings, M. L. (2006). Integrating ethics in design through the value-sensitive design approach. *Science and engineering ethics*, 12(4), 701-715. <https://doi.org/10.1007/s11948-006-0065-0>

Dafoe, A. (2015). On technological determinism: A typology, scope conditions, and a mechanism. *Science, Technology, & Human Values*, 40(6), 1047-1076. <https://doi.org/10.1177/0162243915579283>

de Andrade, N. N. (2010). Human Genetic Manipulation and the Right to Identity: The Contradictions of Human Rights Law in Regulating the Human Genome. *SCRIPTed*, 7, 429. <https://doi.org/10.2966/scrip.070310.429>

de Melo-Martín, I. (2010). Defending human enhancement technologies: Unveiling normativity. *Journal of Medical Ethics*, 36(8), 483-487. <https://dx.doi.org/10.1136/jme.2010.036095>

Desquilbet, M., & Bullock, D. S. (2009). Who pays the costs of non-GMO segregation and identity preservation?. *American Journal of Agricultural Economics*, 91(3), 656-672. <https://doi.org/10.1111/j.1467-8276.2009.01262.x>

De Vendômois, J. S., Cellier, D., Vélot, C., Clair, E., Mesnage, R., & Séralini, G. E. (2010). Debate on GMOs health risks after statistical findings in regulatory tests. *International Journal of Biological Sciences*, 6(6), 590. <https://doi.org/10.7150%2Fijbs.6.590>

Devolder, K., Gyngell, C. (2017). Human Cloning: Arguments for. In: *Encyclopedia of Life Sciences*. Hoboken, NJ: John Wiley & Sons Ltd, Chichester. <https://doi.org/10.1002/9780470015902.a0005224.pub2>

Eapen, M., Rocha, V., Sanz, G., Scaradavou, A., Zhang, M. J., Arcese, W., ... & Wagner, J. E. (2010). Effect of graft source on unrelated donor haemopoietic stem-cell transplantation in adults with acute leukaemia: a retrospective analysis. *The lancet oncology*, 11(7), 653-660. [https://doi.org/10.1016/S1470-2045\(10\)70127-3](https://doi.org/10.1016/S1470-2045(10)70127-3)

Ebbesen, M., Jensen, T. G. (2006). Nanomedicine: techniques, potentials, and ethical implications. In: *Journal of Biomedicine and Biotechnology*. Volume 2006, Article ID51516, Pages 1-11. <https://doi.org/10.1155/JBB/2006/51516>

Ellis, G. I., Sheppard, N. C., & Riley, J. L. (2021). Genetic engineering of T cells for immunotherapy. *Nature Reviews Genetics*, 22(7), 427-447. <https://doi.org/10.1038/s41576-021-00329-9>

European Commission. (2014). *Users Guide to European Regulation in Biotechnology*. European Commission. Retrieved from <https://ec.europa.eu/docsroom/documents/1652/attachments/1/translations>

Ewart, D., Peterson, E. J., & Steer, C. J. (2019, August). A new era of genetic engineering for autoimmune and inflammatory diseases. In *Seminars in Arthritis and Rheumatism* (Vol. 49, No. 1, pp. e1-e7). <https://doi.org/10.1016/j.semarthrit.2019.05.004>

FDA. (2019). *Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Derived from Genetically Engineered Plants*. Rockville, MD: Food and Drug Administration.

Feenberg, A. (2009). What is Philosophy of Technology?. In A. Jones & M. de Vries, *International Handbook of Research and Development in Technology Education* (pp. 159-166). Rotterdam: Sense Publishers. https://doi.org/10.1163/9789087908799_016

Ferrara, J. L., Levine, J. E., Reddy, P., & Holler, E. (2009). Graft-versus-host disease. *The Lancet*, 373(9674), 1550-1561. [https://doi.org/10.1016/S0140-6736\(09\)60237-3](https://doi.org/10.1016/S0140-6736(09)60237-3)

Flanagan, M., & Nissenbaum, H. (2014). *Values at play in digital games*. Cambridge, MA: MIT Press.

Floridi, L., Cowls, J., Beltrametti, M., Chatila, R., Chazerand, P., Dignum, V., ... & Vayena, E. (2018). AI4People—An ethical framework for a good AI society: Opportunities, risks, principles, and recommendations. *Minds and machines*, 28(4), 689-707. <https://doi.org/10.1007/s11023-018-9482-5>

Friedman, B., & Hendry, D. (2012, May). The envisioning cards: a toolkit for catalyzing humanistic and technical imaginations. In *Proceedings of the SIGCHI conference on human factors in computing systems* (pp. 1145-1148). <https://doi.org/10.1145/2207676.2208562>

Friedman, B., Hendry, D. G., & Borning, A. (2017). A survey of value sensitive design methods. *Foundations and Trends® in Human-Computer Interaction*, 11(2), 63-125. <http://dx.doi.org/10.1561/11000000015>

Friedman, B., & Hendry, D. G. (2019). *Value sensitive design: Shaping technology with moral imagination*. Cambridge, MA: MIT Press.

Friedman, B., Kahn, P.H., Borning, A., Hultgren, A. (2013). Value Sensitive Design and Information Systems. In: Doorn, N., Schuurbiens, D., van de Poel, I., Gorman, M. (eds) *Early engagement and new technologies: Opening up the laboratory*. Philosophy of Engineering and Technology, vol 16. Dordrecht: Springer. https://doi.org/10.1007/978-94-007-7844-3_4

Garland-Thomson, R. (2012). The case for conserving disability. *Journal of bioethical inquiry*, 9(3), 339-355. <https://doi.org/10.1007/s11673-012-9380-0>

Garland-Thomson, R. (2020). How we got to CRISPR: The dilemma of being human. *Perspectives in biology and medicine*, 63(1), 28-43. <https://doi.org/10.1353/pbm.2020.0002>

Giubilini, A., & Sanyal, S. (2016). Challenging Human Enhancement. In S. Clark, J. Savulescu, T. Coady, A. Giubilini & S. Sanyal, *The Ethics of Human Enhancement: Understanding the Debate*. Oxford University Press. Retrieved 15 July 2022, from <https://doi.org/10.1093/acprof:oso/9780198754855.003.0001>.

Gouw, A.M. (2020). CRISPR Challenges and Opportunities for Space Travel. In: Szocik, K. (eds) *Human Enhancements for Space Missions*. Space and Society. Springer, Cham. https://doi.org/10.1007/978-3-030-42036-9_2

Hadrup, N., & Lam, H. R. (2014). Oral toxicity of silver ions, silver nanoparticles and colloidal silver—a review. *Regulatory Toxicology and Pharmacology*, 68(1), 1-7. <https://doi.org/10.1016/j.yrtph.2013.11.002>

Harris, J. (2004). *On cloning*. London: Routledge.

Harris, J. (2009). Enhancements Are a Moral Obligation. In J. Savulescu & N. Bostrom, *Human Enhancement* (pp. 131-154). Oxford: Oxford University Press.

Harris, J. (2014). Time to Exorcise the Cloning Demo. *Cambridge Quarterly of Healthcare Ethics*, 23, 53 - 62. <https://doi.org/10.1017/S0963180113000443>

Harris, J. (2017). How to welcome new technologies: some comments on the article by Inmaculada de Melo-Martin, *Cambridge Quarterly of Healthcare Ethics*, 26(1): 166-72. <https://doi.org/10.1017/S0963180116000736>

Hirayama, A. V., Gauthier, J., Hay, K. A., Voutsinas, J. M., Wu, Q., Pender, B. S., ... & Turtle, C. J. (2019). High rate of durable complete remission in follicular lymphoma after CD19 CAR-T cell immunotherapy. *Blood, The Journal of the American Society of Hematology*, 134(7), 636-640. <https://doi.org/10.1182/blood.2019000905>

Hodgkinson, C. P., Gomez, J. A., Mirotsoy, M., & Dzau, V. J. (2010). Genetic engineering of mesenchymal stem cells and its application in human disease therapy. *Human gene therapy*, 21(11), 1513-1526. <https://doi.org/10.1089/hum.2010.165>

Iravani, S., & Varma, R. S. (2019). Biofactories: engineered nanoparticles via genetically engineered organisms. *Green Chemistry*, 21(17), 4583-4603. <https://doi.org/10.1039/C9GC01759C>

Jain, K., Kumar Mehra, N., & K.Jain, N. (2015). Nanotechnology in drug delivery: safety and toxicity issues. *Current pharmaceutical design*, 21(29), 4252-4261. <https://doi.org/10.2174/1381612821666150901103208>

Jenkins, K. E., Spruit, S., Milchram, C., Höffken, J., & Taebi, B. (2020). Synthesizing value sensitive design, responsible research and innovation, and energy justice: A conceptual review. *Energy Research & Social Science*, 69, 101727. <https://doi.org/10.1016/j.erss.2020.101727>

Kahane, G., & Savulescu, J. (2016). Disability and mere difference. *Ethics*, 126(3), 774-788. <https://doi.org/10.1086/684709>

King, D. S. (1999). Preimplantation genetic diagnosis and the 'new' eugenics. *Journal of Medical Ethics*, 25(2), 176. <https://doi.org/10.1136%2Fjme.25.2.176>

Klein, H. K., & Kleinman, D. L. (2002). The social construction of technology: Structural considerations. *Science, Technology, & Human Values*, 27(1), 28-52. <https://doi.org/10.1177%2F016224390202700102>

Kochenderfer, J. N., Dudley, M. E., Carpenter, R. O., Kassim, S. H., Rose, J. J., Telford, W. G., ... & Rosenberg, S. A. (2013). Donor-derived CD19-targeted T cells cause regression of malignancy persisting after allogeneic hematopoietic stem cell transplantation. *Blood, The Journal of the American Society of Hematology*, 122(25), 4129-4139. <https://doi.org/10.1182/blood-2013-08-519413>

Krimsky, S. (2019). Ten ways in which He Jiankui violated ethics. *Nature Biotechnology*, 37(1), 19-20. <https://doi.org/10.1038/nbt.4337>

Kwoczek, J., Riese, S. B., Tischer, S., Bak, S., Lahrberg, J., Oelke, M., ... & Eiz-Vesper, B. (2018). Cord blood-derived T cells allow the generation of a more naïve tumor-reactive cytotoxic T-cell phenotype. *Transfusion*, 58(1), 88-99. <https://doi.org/10.1111/trf.14365>

Levy, N., & Lotz, M. (2005). Reproductive cloning and a (kind of) genetic fallacy. *Bioethics*, 19(3), 232-250. <https://doi.org/10.1111/j.1467-8519.2005.00439.x>

Lin, P. (2006). Look before taking another leap for mankind—Ethical and social considerations in rebuilding society in space. *Astropolitics*, 4(3), 281-294. <https://doi.org/10.1080/14777620601039701>

Lin, P., & Allhoff, F. (2008). Against unrestricted human enhancement. *Journal of Evolution & Technology*, 18(1), 35.

Locke, F. L., Ghobadi, A., Jacobson, C. A., Miklos, D. B., Lekakis, L. J., Oluwole, O. O., ... & Neelapu, S. S. (2019). Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1-2 trial. *The lancet oncology*, 20(1), 31-42. [https://doi.org/10.1016/S1470-2045\(18\)30864-7](https://doi.org/10.1016/S1470-2045(18)30864-7)

Loganathan, R., Balasubramanian, R., Mani, K., & Gurnathan, S. (2009). Productivity and profitability impact of genetically modified crops—an economic analysis of Bt cotton cultivation in Tamil Nadu. *Agricultural Economics research review*, 22(347-2016-16870), 331-340. <http://dx.doi.org/10.22004/ag.econ.57472>

Marteau, T. M., van Duijn, M., & Ellis, I. (1992). Effects of genetic screening on perceptions of health: a pilot study. *Journal of Medical Genetics*, 29(1), 24-26. <http://dx.doi.org/10.1136/jmg.29.1.24>

Maude, S. L., Laetsch, T. W., Buechner, J., Rives, S., Boyer, M., Bittencourt, H., ... & Grupp, S. A. (2018). Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. *New England Journal of Medicine*, 378(5), 439-448. <https://doi.org/10.1056/NEJMoal709866>

Minguell, J. J., Erices, A., & Conget, P. (2001). Mesenchymal stem cells. *Experimental biology and medicine*, 226(6), 507-520. <https://doi.org/10.1177%2F153537020122600603>

Morrow, J. F. (1979). [1] Recombinant DNA techniques. *Methods in enzymology*, 68, 3-24. [https://doi.org/10.1016/0076-6879\(79\)68003-5](https://doi.org/10.1016/0076-6879(79)68003-5)

Mulligan, R. C. (1993). The basic science of gene therapy. *Science*, 260(5110), 926-932. <https://doi.org/10.1126/science.8493530>

Nelson, G. C. (2001). *Genetically modified organisms in agriculture: economics and politics*. Amsterdam: Elsevier.

Nicholl, D. S. (2008). *An introduction to genetic engineering*. Cambridge: Cambridge University Press.

Normile, D. (2019). *Chinese scientist who produced genetically altered babies sentenced to 3 years in jail*. Science. <https://doi.org/10.1126/science.aba7347>

Oakland, M., Simm, P. L., & McCray Jr, P. B. (2012). Advances in cell and gene-based therapies for cystic fibrosis lung disease. *Molecular Therapy*, 20(6), 1108-1115. <https://doi.org/10.1038/mt.2012.32>

O'Leary, M. C., Lu, X., Huang, Y., Lin, X., Mahmood, I., Przepiorka, D., ... & Pazdur, R. (2019). FDA Approval Summary: Tisagenlecleucel for Treatment of Patients with Relapsed or Refractory B-cell Precursor Acute Lymphoblastic LeukemiaFDA Approval Summary: Tisagenlecleucel for R/R BCP ALL. *Clinical Cancer Research*, 25(4), 1142-1146. <https://doi.org/10.1158/1078-0432.CCR-18-2035>

Ossorio, P. N. (2007). The human genome as common heritage: common sense or legal nonsense?. *The Journal of Law, Medicine & Ethics*, 35(3), 425-439. <https://doi.org/10.1111/j.1748-720X.2007.00165.x>

Pinch, T. J., & Bijker, W. E. (1984). The social construction of facts and artefacts: Or how the sociology of science and the sociology of technology might benefit each other. *Social studies of science*, 14(3), 399-441. <https://doi.org/10.1177%2F030631284014003004>

Pirni, A., Balistreri, M., Capasso, M., Umbrello, S., & Merenda, F. (2021). Robot Care Ethics Between Autonomy and Vulnerability: Coupling Principles and Practices in Autonomous Systems for Care. *Frontiers in Robotics and AI*, 8, 184. <https://doi.org/10.3389/frobt.2021.654298>

Porcari A., Buceti G., Pimponi D., Gonzalez G., Buchinger E., Kienegger M., Zahradnik G., Bernstein MJ, (2022), Ethical and social impacts-driven horizon scanning of new and emerging technologies. *Deliverable 1.3 to the European Commission*. TechEthos Project Deliverable. Available at: www.techethos.eu.

Poste, G. (1999). Privacy and confidentiality in the age of genetic engineering. *Tex. Rev. L. & Pol.*, 4, 25.

Primc, N. (2020). Do we have a right to an unmanipulated genome? The human genome as the common heritage of mankind. *Bioethics*, 34(1), 41-48. <https://doi.org/10.1111/bioe.12608>

Raben, N., Danon, M., Lu, N., Lee, E., Shliselfeld, L., Skurat, A. V., ... & Plotz, P. (2001). Surprises of genetic engineering: a possible model of polyglucosan body disease. *Neurology*, 56(12), 1739-1745. <https://doi.org/10.1212/WNL.56.12.1739>

Robertson, J. A. (2005). Ethics and the future of preimplantation genetic diagnosis. *Reproductive BioMedicine Online*, 10, 97-101. [https://doi.org/10.1016/S1472-6483\(10\)62214-6](https://doi.org/10.1016/S1472-6483(10)62214-6)

Rosemann, A., & Molyneux-Hodgson, S. (2020). Industrial biotechnology: to what extent is responsible innovation on the agenda?. *Trends in biotechnology*, 38(1), 5-7. <https://doi.org/10.1016/j.tibtech.2019.07.006>

Scanlon, T. (2000). *What we owe to each other*. Cambridge, MA: Belknap Press.

Schuster, S. J., Bishop, M. R., Tam, C. S., Waller, E. K., Borchmann, P., McGuirk, J. P., ... & Maziarz, R. T. (2019). Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. *New England Journal of Medicine*, 380(1), 45-56. <https://doi.org/10.1056/nejmoa1804980>

Simon, J. (2017). Value-sensitive design and responsible research and innovation. In S. Hansson, *The Ethics of Technology: Methods and Approaches* (pp. 219-235). Lanham, MD: Rowman & Littlefield.

Simmons, D. (2008). Genetic inequality: Human genetic engineering. *Nature Education*, 1(1), 173.

Sorgner, S. L. (2016). The Stoic Sage 3.0: A Realistic Goal of Moral (Bio)Enhancement Supporters?. *Journal of Ethics and Emerging Technologies*, 26(1), 83-93. <https://doi.org/10.55613/j eet.v26i1.53>

Smith, M. (2022). *Genetic Engineering*. Genome.gov. Retrieved 12 July 2022, from [https://www.genome.gov/genetics-glossary/Genetic-Engineering#:~:text=Genetic%20engineering%20\(also%20called%20genetic,a%20new%20segment%20of%20DNA.](https://www.genome.gov/genetics-glossary/Genetic-Engineering#:~:text=Genetic%20engineering%20(also%20called%20genetic,a%20new%20segment%20of%20DNA.)

Sparrow, R. (2019). Yesterday's child: How gene editing for enhancement will produce obsolescence—and why it matters. *The American Journal of Bioethics*, 19(7), 6-15. <https://doi.org/10.1080/15265161.2019.1618943>

Specker, J., Focquaert, F., Raus, K., Sterckx, S., & Schermer, M. (2014). The ethical desirability of moral bioenhancement: a review of reasons. *BMC Medical Ethics*, 15(1), 1-17. <https://doi.org/10.1186/1472-6939-15-67>

TechEthos. (2022). *Technology family*. TechEthos. Retrieved 8 July 2022, from <https://www.techethos.eu/glossary/technology-family/>.

Timmermans, J., Zhao, Y., & van den Hoven, J. (2011). Ethics and nanopharmacy: Value sensitive design of new drugs. *Nanoethics*, 5(3), 269-283. <https://doi.org/10.1007/s11569-011-0135-x>

Tripathi, K. K. (2000). Bioinformatics: The foundation of present and future biotechnology. *Current Science*, 79(5), 570-575. <https://www.jstor.org/stable/24105072>

Tüting, T., Storkus, W. J., & Lotze, M. T. (1997). Gene-based strategies for the immunotherapy of cancer. *Journal of molecular medicine*, 75(7), 478-491. <https://doi.org/10.1007/s001090050133>

Umbrello, S. (2020a). Combinatory and Complementary Practices of Values and Virtues in Design: A Reply to Reijers and Gordijn. *Filosofia*, (65), 107-121. <https://doi.org/10.13135/2704-8195/5236>

Umbrello, S. (2020b). Meaningful Human Control Over Smart Home Systems. *HUMANA.MENTE Journal of Philosophical Studies*, 13(37), 40-65. Retrieved from <https://www.humanamente.eu/index.php/HM/article/view/315>

Umbrello, S. (2022). The Role of Engineers in Harmonising Human Values for AI Systems Design. *Journal of Responsible Technology*, 10, 100031. <https://doi.org/10.1016/j.jrt.2022.100031>

Umbrello, S., Capasso, M., Balistreri, M., Pirmi, A., & Merenda, F. (2021). Value sensitive design to achieve the UN SDGs with AI: A case of elderly care robots. *Minds and Machines*, 31(3), 395-419. <https://doi.org/10.1007/s11023-021-09561-y>

Umbrello, S., Bernstein, M. J., Vermaas, P. E., Resseguier, A., Gonzalez, G., Porcari, A., Grinbaum, A., & Adomaitis, L. (2022). From speculation to reality: extending anticipatory ethics for emerging technologies (ATE) for practice, *PrePrint*.

Umbrello, S., & Gambelin, O. (2021). *Value Sensitive Design: An Agile Toolkit*. <http://dx.doi.org/10.13140/RG.2.2.18543.36006>

Umbrello, S., & Gambelin, O. (2022). Agile as a Vehicle for Values: A Value Sensitive Design Toolkit, In Albrecht Fritzsche and Andres Santa-Maria (eds.), *Rethinking Technology and Engineering: Dialogues across disciplines and geographies*, Cham: Springer. *Forthcoming*. <http://dx.doi.org/10.13140/RG.2.2.17064.08965/1>

UNESCO. (1997). Universal declaration on the human genome and human rights. *The General Assembly of the United Nations endorsed the UNESCO Declaration in Dec. 1998*. *United Nations Press Release GA/9532*.

van den Hoven, MJ., Vermaas, PE., & van de Poel, IR. (2015). Design for values: An introduction. In J. van den Hoven, PE. Vermaas, & I. van de Poel (Eds.), *Handbook of ethics, values, and technological design: sources, theory, values and application domains* (pp. 1-7). Springer. https://doi.org/10.1007/978-94-007-6970-0_1

van den Hoven, J. (2017). The Design Turn in Applied Ethics. In J. Van den Hoven, S. Miller, & T. Pogge (Eds.), *Designing in Ethics* (pp. 11-31). Cambridge: Cambridge University Press. <https://doi.org/10.1017/9780511844317.002>

van Wynsberghe, A. (2020). Designing Robots for Care: Care Centered Value-Sensitive Design. In W. Wallach & P. Asaro, *Machine Ethics and Robot Ethics* (pp. 185-211). Routledge. <https://doi.org/10.4324/9781003074991-17>

Veit, W. (2018). Cognitive enhancement and the threat of inequality. *Journal of Cognitive Enhancement*, 2(4), 404-410. <https://doi.org/10.1007/s41465-018-0108-x>

Verma, I. M., Naldini, L., Kafri, T., Miyoshi, H., Takahashi, M., Blömer, U., ... & Gage, F. H. (2000). Gene therapy: promises, problems and prospects. In *Genes and resistance to disease* (pp. 147-157). Berlin, Heidelberg: Springer. https://doi.org/10.1007/978-3-642-56947-0_13

Winner, L. (1980). Do artifacts have politics?. *Daedalus*, 109(1), 121-36. <https://www.jstor.org/stable/20024652>

Wirth, T., Parker, N., & Ylä-Herttuala, S. (2013). History of gene therapy. *Gene*, 525(2), 162-169. <https://doi.org/10.1016/j.gene.2013.03.137>

Wooldridge, E. Q., & Murray Jr, R. F. (1988). The Health Orientation Scale: a measure of feelings about sickle cell trait. *Social biology*, 35(1-2), 123-136. <https://doi.org/10.1080/19485565.1988.9988694>

Wright, S. (1986). Recombinant DNA technology and its social transformation, 1972-1982. *Osiris*, 2, 303-360. <https://doi.org/10.1086/368659>

Wyatt, S. (2008). Technological determinism is dead; Long live technological determinism. In E. Hackett, O. Amsterdamska, M. Lynch & J. Wajcman, *Handbook of Science and Technology Studies* (pp. 165-180). Cambridge, MA: MIT Press.

Yang, F., Cho, S. W., Son, S. M., Bogatyrev, S. R., Singh, D., Green, J. J., ... & Anderson, D. G. (2010). Genetic engineering of human stem cells for enhanced angiogenesis using biodegradable polymeric nanoparticles. *Proceedings of the National Academy of Sciences*, 107(8), 3317-3322. <https://doi.org/10.1073/pnas.0905432106>

Yoo, D., Derthick, K., Ghassemian, S., Hakizimana, J., Gill, B., & Friedman, B. (2016, May). Multi-lifespan design thinking: two methods and a case study with the Rwandan diaspora. In *Proceedings of the 2016 CHI conference on human factors in computing systems* (pp. 4423-4434). <https://doi.org/10.1145/2858036.2858366>

Yoo, D., Hultgren, A., Woelfer, J. P., Hendry, D. G., & Friedman, B. (2013, April). A value sensitive action-reflection model: evolving a co-design space with stakeholder and designer prompts. In *Proceedings of the SIGCHI conference on human factors in computing systems* (pp. 419-428). <https://doi.org/10.1145/2470654.2470715>