On the nature of nature

A study on the use and meaning of nature and (un)naturalness in the literature on genetic modification

CGM 2022-01

ONDERZOEKSRAPPORT

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Preface

The concept of naturalness often plays a significant role in the debate on genetically modified organisms, especially when the debate focuses on ethical and societal issues. Many people argue against the use of such organisms because they are “not natural”. Naturalness, however, is not a very clear concept and the term is often used loosely, without clear definition, explanation or specification, resulting in miscommunication and misunderstanding. That is also logical. Also, nature in itself is a complicated and diverse concept, with many different interpretations. Our views on nature and naturalness very much depend on our attitude towards nature, on how we experience nature and on our world view; they are therefore very diverse among people with different beliefs and values, are often inconsistent and certainly also change over time.

In the reports of the COGEM, the concept of naturalness is often referred to in relation to genetic modification. These references occur in a wide variety of contexts, including a scientific (biological) context, a legal context (which – types of – organisms require legal oversight, because they are unnatural or no longer pristine and might pose a risk) and a societal context (in norms and values of acceptation of certain technologies).

To gain insight into the different views on naturalness, its use in literature, and in societal and political debates, COGEM commissioned desk research with the following research questions:

1. What are the existing views on naturalness in scientific, legal and societal contexts associated with biotechnology and genetic modification?
2. What are the similarities and differences among these views?
3. How, with what aim, and by whom is the concept of naturalness used in discussions on genetic modification?

The results of this research have now been documented in this valuable report that really goes into depth on all these research questions in an analytical and systematic away. It has become a very rich and well-structured scientific document and the steering committee is very pleased with this product of the study. The committee is convinced that this report will be useful for future reference by the COGEM and a very useful resource for readers who want to become acquainted with the diversity of opinions related to naturalness and its use in scientific, legal, societal and political debates.

I want to thank the members of the steering committee for their involvement and commitment. The debates we had during our meetings with the research team were intense, enriching and productive.
Among the members of the committee were also three COGEM staff members; I also want to thank them, not only for excellent organization and support of the activities of the steering committee but also for very active participation in the debate as committee members.

Finally, a big compliment for the research team for a very well-planned research trajectory in which deadlines were always met and drafts were always of high quality, for always responding to suggestions

and queries of the members of the steering committee, for creating a very fruitful interaction with the steering committee and for steering the steering committee. But most of all, I commend the research team for producing this valuable report which, I am sure, will be widely used in the future activities of the COGEM.

The views expressed in this report are the views of the authors, not of the steering committee or the COGEM.

Paul C. Struik

Chairman of the steering committee

Disclaimer

This report was commissioned by the Netherlands Commission Genetic Modification (COGEM). The content of this publication is the sole responsibility of the authors and does not necessarily reflect the views of the COGEM.

Chapter 1 - Introduction

"*If there was ever a time when it was important to think hard about nature and its relationship to technology, that time is now."*

- Christopher Preston (2018) (p. 162) (1).

1.1 Nature and (un)naturalness as familiar, yet elusive terms

Be it on food products, in beauty product advertisements, at philosophy conferences, in newspaper articles or in scholarly publications, discussions on and references to (un)naturalness are ubiquitous. Biotechnological developments, from in vitro fertilization to cloning, and from xenotransplantation to synthetic biology, have sparked considerable debate about their (un)naturalness, as well as about the (ir)relevance of naturalness as an ethical criterion (2–4).

References to nature and (un)naturalness have been particularly prominent in the context of genetic modification (5). In this context, discussions on (un)naturalness have amongst others concerned genetically modified (GM) crops and food, genetically modified organisms (GMOs) and their release into the environment, and germline modification in humans (3). In both scientific and legal contexts, naturalness for instance features in the definition of a GMO that is used in a European regulatory context. According to this definition, a GMO is "an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination" (2001/18/EC) (6). Similarly, there are discussions on whether and when GM foods may be labelled as 'natural' (7–10), and how the risks of (the release of) GMOs may be estimated when a 'natural' reference in the form of a wild-type organism with similar characteristics is lacking (10). Discussions on genetic modification also mention its potential effects on nature. It has for instance been argued that GM technologies "*use nature to surpass nature*" (p. 443) (11).

The perceived (un)naturalness of genetic modification has also been found to play a role in its moral evaluation. Concerns about the unnaturalness of GM food products, for instance, have been shown to influence people's acceptance of these products (12). Similarly, the perceived unnaturalness of germline modification in human embryos (13) and of gene drives in non-human organisms (14) have raised concerns about the moral permissibility of these applications and technologies. Human germline modification, moreover, has elicited debates on whether it could enhance or preserve human nature (15) or would rather threaten or change it in a problematic way (16). As these examples underline, convictions about (un)naturalness may consciously or unconsciously impact what people eat, how they live, and what their views are on whether genetic modification should be used to treat disease or to alter the environment around us (2,17).

Nonetheless, it is not always clear what is meant by 'nature' and '(un)naturalness'. In some cases, these terms are used without further specification or elaboration on what they are taken to mean. This is for instance the case when it is mentioned that opponents of genetic modification "*consider the creation of genetically modified plants to be unnatural*" (p. 41) (18). In other cases, there is more explicit elaboration regarding whether or when something can be considered (un)natural. If it is pointed out that some changes made by genetic modification technologies "*are also ones that could arise spontaneously in nature"* (p.2-3) (19) this for instance raises the question whether these changes should therefore be

considered natural. Yet others contend that "*all technological acts that make use of scientific knowledge of the physical environment are natural*" (p. 18) (5) or that "*engineering is (..) just what we do and it's natural"* (p. 114) (20). In these instances, human technological interventions more generally seem to be considered natural.

As these examples illustrate, the terms 'nature' and '(un)naturalness' are used in various ways, to refer to different things, and there are widely varying opinions on what is natural and what is not. This underlines that the terms nature and (un)naturalness are, as Kate Soper puts it, "*at once both very familiar and extremely elusive: [ideas] we employ with such ease and regularity that it seems as if we ourselves are privileged with some 'natural' access to its intelligibility; but also [ideas] which most of us know, in some sense, to be so various and comprehensive in its use as to defy our powers of definition*" (p. 1) (21). It has even been contended that 'nature' may be the most complex term in the English language (22).

While the terms 'nature' and '(un)naturalness' are evidently open to more than one interpretation, the sources of this ambiguity are less clear. To start, these terms could be *used* in different ways. It may be the case that these terms are so-called 'essentially contested concepts': concepts that are (implicitly) value-laden, causing different users to have preferences for different meanings, although no one meaning can be proven to be the right one (23–25). Indeed, a previous report on ideas about (un)naturalness in public and political debates about science, technology and medicine concluded that these terms are often used as placeholders for underlying values or concerns (2). It could also be the case that these terms are used in varying ways or with distinctive aims in different disciplines. Life scientists, legislators, courts, policymakers, and philosophers may for instance use these terms differently. Moreover, the ambiguity of these terms could arise because they are attributed different *meanings.* This could for instance be the case if the terms have more than one meaning, as is the case for homonyms – the 'bat' used to play a baseball game differs from the 'bat' that may fly around one's garden at night. If this also holds for 'nature' and 'naturalness', a clear delineation of these terms could allow us to avoid (some of) these discrepancies to avoid miscommunication.

1.2 Aim of this report

This report, commissioned by the Netherlands Commission on Genetic Modification (COGEM), aims to investigate the use and meaning of nature and (un)naturalness in the literature on genetic modification in more detail. By unraveling the conceptual and normative complexity of references to nature and (un)naturalness in the debate on genetic modification, this report aims to provide the COGEM, as well as other interested parties, orientation in understanding and interpreting references and arguments related to nature and naturalness. First, it investigates the *use* of these terms in a legal, societal, and scientific context by analyzing the positive law, grey literature, and scientific literature on genetic modification. In doing so, differences and similarities in use across these contexts are identified. Second, the *meaning* of nature and (un)naturalness is investigated in more detail by analyzing the philosophical literature on this topic.

Before we proceed with this analysis, we first shortly introduce and discuss genetic modification. Subsequently, we set out the approach and structure of the different chapters of this report.

1.3 A short history of genetic modification

The genome is the totality of the heredity material that is stored predominantly in the cell nucleus in the form of DNA (26). In the 1950s, Francis Crick, James Watson and Rosalind Franklin discovered the double helix structure of the DNA (27). Since then, it has become increasingly clear that genes are not static structures nor just "*simple, elementary units of heredity*" (p. 8) (26); the informational content of the genome is dynamic and "*dependent in multiple ways on elements that are not (..) part of the genome*" (28), including environmental and epigenetic influences. Genetic mutations, for instance, frequently occur after unrepaired DNA damage, which may for example be caused by the sun's ultraviolet radiation. Moreover, processes such as horizontal gene transfer (in which a gene is transferred from the genome of one organism to another without mating) and gene drive (genetic mechanisms that allow for a particular genetic element to be propagated throughout a population more frequently than expected based on Mendelian inheritance) also affect the informational content of organisms' genomes (29,30).

Over time, humans developed various techniques to modify the genome. Since the 1920s, genetic changes have been induced by exposing tissues or cells to radiation or chemical mutagenic compounds, thereby creating undirected and untargeted genetic changes. Such 'classic mutagenesis' has been used to create random genetic variations, for instance to develop crop varieties with novel traits of agricultural importance (31).

Subsequent techniques aimed to improve the efficiency, precision, and accuracy of the induced genetic changes (32). In 1972, the first 'recombinant DNA' experiment was conducted in which a genetic element was created by combining genetic material from different sources (33). In this experiment, scientists succeeded in combining genetic material from two different strains of bacteria. As recombinant DNA technology aimed to induce more directed and targeted changes in the genome[1], its emergence is generally considered to be the birth of modern genetic modification. The emergence of recombinant DNA technology also led to concerns about its potential risks, which were discussed by an international group of scientists at the so-called 'Asilomar Conference' in February 1972. The discussions in Asilomar led to recommendations regarding the levels of risk associated with different experiments and the levels of containment and safety measures warranted in view of these risk levels (33).

In the years and decades that followed, recombinant DNA technology has been used in different organisms. In micro-organisms, it has for instance been used to manufacture recombinant insulin, produced by inserting the human insulin gene into yeast or *E. Coli* bacteria. In plants, recombinant DNA has been used to provide herbicide or insect-resistant crops. With the prospect that genetic modification would "*move outside the safe walls of the laboratory*" (p. 23) (33) and be deployed for commercial purposes, (public) concerns about recombinant DNA increased again. Amongst others, this led to the destruction of GM plant field trial sites and, in 1998, to a temporary de facto moratorium on the cultivation and import of GM crops in the European Union (33). Recombinant DNA has also been used in non-human animals (from now on referred to as 'animals'), both to create animals for scientific study and to produce human proteins. In the early 1990s, the first transgenic bull, 'bull Herman', was born, in whose genome the gene encoding for human lactoferrin was introduced. Bull Herman and later the cloned sheep

[1] As is the case for classic mutagenesis, recombinant DNA does not direct *where* the intentionally induced changes occur; the DNA is randomly integrated into the host genome. Unlike classic mutagenesis, though, *which* genetic changes result from the use of recombinant DNA technologies is directed.

Dolly again incited discussion about the (un)desirability of genetic modification[2] – this time in relation to animals and animal welfare (33). In contrast, gene therapy – the use of recombinant DNA techniques for therapeutic purposes in humans – was more generally accepted by members of the public (33).

In more recent years, genetic modification techniques have emerged that aim to modify the genome in more specific ways, both with respect to which changes are induced and where in the genome these changes are brought about. These 'genome editing' technologies use nucleases – enzymes that can cut RNA or DNA – that are specifically engineered to bind to targeted DNA sequences. The first genome editing technologies used engineered nucleases such as zinc finger nucleases (ZFN) and transcription activator-like effector nucleases (TALENs). However, their usage was limited due to the complexity involved with engineering these nucleases to achieve the specificity required for genome editing. More recently, the emergence of CRISPR-Cas9 (an acronym for 'Clustered Regularly Interspaced Short Palindromic Repeats' together with 'CRISPR-associated protein 9') allowed genome editing technologies to become easier and cheaper to use. These technologies have been deployed in micro-organisms, plants, animals, and humans.

In parallel, new applications of these technologies have been developed, such as gene drive technologies (GDTs). GDTs promote the rapid, progressive spread of a particular genetic element across a population of sexually reproducing organisms with a short generation time, such as mosquitoes or small rodents. Whereas a given gene is usually passed on to approximately half of an organism's offspring in normal Mendelian inheritance, GDTs can promote the biased inheritance of this gene, so that it is passed on to most or even all of its offspring (34). GDTs are developed with the aim of deploying them for different purposes, such as decreasing the impact of vector-borne diseases, invasive species[3], and agricultural pests.

In the coming years, these developments are likely to continue and novel types of genome editing technologies will undoubtedly arise. Recently, for example, a gene editing tool called Retron Library Recombineering (RLR) was developed that can generate up to millions of mutations at the same time (35,36).

1.4 Different applications of genetic modification

As this short history underlines, genetic modification techniques have been used in or are developed for a wide variety of organisms and settings. This report concerns the use and meaning of 'naturalness' arguments in discussions about genetic modification in a wide sense, including its various applications in micro-organisms, plants, animals and humans. Next to differentiating between the organisms in which genetic modification is applied, one can also distinguish between different areas in which these technologies are deployed: medical (red), agricultural (green) or industrial (white) biotechnology (37). Finally, one can differentiate between cisgenesis and transgenesis, i.e. respectively the genetic modification of an organism with a gene from a crossable or sexually compatible organism versus the

[2] Although Dolly was *not* genetically modified, members of the public commonly linked cloning to genetic modification, and there was (and perhaps is) a widespread belief that Dolly was genetically modified. Consequently, (concerns about) cloning also played a prominent role in discussions on genetic modification (33).

[3] The term 'invasive species' is generally used to refer to non-native species that enter a particular ecosystem and threaten native species and/or biodiversity within that ecosystem. There has been substantive debate on what exactly constitutes an invasive species, see for example (182).

genetic modification of an organism with one or more genes from non-sexually compatible organisms (for instance from a different species) (38,39). In contrast to transgenic organisms, cisgenic organisms thus only have genes that they could also have had as a result of conventional breeding (39).

In the context of the analysis presented in this report, it is relevant to distinguish between these different applications as they have evoked discussions with different themes and dynamics (37). Members of the general public, for instance, have been found to make different ethical judgements about genetic modification depending on the type of organism and the aim of its application. Applications of genetic modifications in micro-organisms, non-food applications in plants, and medical applications in humans have generally been regarded more positively than applications in animals, in the context of food production or potential non-medical applications in humans (40–42). With regard to the different biotechnology areas, industrial (white) biotechnology similarly seems to evoke less fundamental ethical questions than agricultural (green) and medical (red) biotechnology (37). Finally, members of the public have generally been found to be more concerned about transgenesis than cisgenesis (41,43).

These differences in opinions about different applications of genetic modification may in turn also influence the use and meaning of nature and (un)naturalness in these different contexts and are thus taken along in the analyses presented in this report.

1.5 Approach and structure of this report

As was addressed previously, references to nature and (un)naturalness feature in laws, the grey literature and the scientific literature on genetic modification. While a distinction between these different contexts is helpful to identify similarities and differences between the ways in which these terms and arguments play a role in legal, societal and scientific discussions more generally, it should be noted that these discussions have many inter-linkages. Scholarly discussions about genetic modifications influence the way in which these discussions are held in policymaking and politics. Vice versa, societal discussions influence what concerns are analyzed in more depth in academic scholarship. In some ways, these interlinked discussions may thus also be considered a single discussion that is referred to as "the societal discussion" on genetic modification (44). Despite these interlinkages, there may also be differences in the way in which references to (un)naturalness feature in these different settings. To take these into account, different bodies of literature have informed this report.

The report itself is structured in the following way. In the first part (**Chapter 2)**, we analyze the **use of nature and (un)naturalness** in positive law[4], the grey literature[5], and the scientific literature on genetic modification. We identify how and with what purpose references to nature and (un)naturalness are used in legal, societal, and scientific contexts, and their similarities and differences. In doing so, we identify whether these terms are used in value neutral or value-laden ways, and whether – and if so, how – references to these terms are made in different ways in different bodies of literature or in relation to specific applications of genetic modification. We show that references to nature and (un)naturalness in a legal context are mostly value-neutral, whereas references to nature and (un)naturalness in the grey literature and scientific literature are more often value-laden. Moreover, we demonstrate that some value-laden references to nature and (un)naturalness in the grey literature and scientific literature bring

[4] I.e. law actually and specifically enacted or adopted by a competent authority.

[5] I.e. reports and policy documents of learned societies and non-governmental organizations.

up underlying concerns or values with regards to (1) safety and uncertainty, (2) the integrity or intrinsic value of the modified entities or (3) the appropriate attitude or role of humans.

In the second part of the report **(Chapters 3-5)**, we analyze the **meaning of nature and (un)naturalness**, using the philosophical and bioethical literature on nature and (un)naturalness to interpret and reflect upon the previous analyses in more detail. Different meanings of the terms nature and (un)naturalness are identified and the similarities and differences between these meanings are evaluated. In **Chapter 3**, we identify four overarching meanings of nature: (1) nature as a biophysical reality, (2) nature as the non-human, (3) entangled nature, and (4) nature as the essential characteristics of a thing. This chapter also highlights that the natural world is not merely something to be discovered, but also something that is at the same time actively constructed. In **Chapter 4** different interpretations of the previously identified concepts of nature are investigated in more detail. In doing so, the identified meanings are related to the references to nature and (un)naturalness identified in the previous analysis of the law, grey literature and scientific literature on genetic modification. In **Chapter 5**, we discuss that (some) references to nature and (un)naturalness can also be a way to voice moral intuitions that warrant in-depth discussion of the underlying concerns. In **Chapter 6**, we summarize the final conclusions of the report and reflect on its implications. Based on these reflections, we formulate a concrete set of questions to clarify, examine, and discuss the concerns that may underlie references to nature and (un)naturalness in the context of genetic modification. We hope and expect that these questions can help to investigate one's own convictions regarding nature, (un)naturalness and genetic modification, and can serve as a starting point to have a fruitful debate about these issues with others.

In different chapters of this report, so-called '**concept maps**' visually represent the outcome of our analyses. Concept maps provide a clear overview and summary of concepts and ideas and the relationships between them. At the same time, however, the reader should keep in mind that concept maps also necessarily emit ambiguity as well as nuances and overlap between different concepts and ideas.

Chapter 2 – The use of nature and (un)naturalness in the literature on genetic modification

As the previous chapter alluded to, the terms 'nature' and '(un)naturalness' are used in various ways, to refer to different things, and sometimes to make opposite claims. It was pointed out that this could be because these terms are sometimes used in value-laden ways and/or used in diverging ways in different disciplines or with regards to different applications of genetic modification.

This chapter aims to investigate this in more detail by analyzing the *use* of 'nature' and '(un)naturalness' in laws, the grey literature, and the scientific literature on genetic modification. We identify how and with what purpose references to nature and (un)naturalness are used in these different contexts and highlight similarities and differences. In the following section, we elaborate on the approach that was taken to analyze and contrast the references to nature and (un)naturalness.

2.1 Approach

References to nature and (un)naturalness in laws, reports and policy documents, and scientific publications on genetic modification were identified, analyzed, and compared.

To start, the various uses of 'nature', 'natural' and 'naturalness' in positive law – i.e. law actually and specifically enacted or adopted by competent legislative and regulatory authorities – were analyzed. Dutch positive law is partly of national and partly of international origin. With regards to the latter, we focused on binding United Nations treaties, binding treaties of the Council of Europe (CoE) as well as CoE recommendations, and European Union regulations and directives. Nationally, the focus was on legislation and legislation-based regulation. The uses of nature and (un)naturalness in legal documents were analyzed using relevant authoritative explanations (explanatory reports, general comments, and parliamentary proceedings). In addition, case law was looked at. The various uses of 'nature', 'natural' and 'naturalness' by Dutch and European courts of law in the context of genetic modification were also analyzed. More details on the methodology of the legal analysis can be found in Appendix 1.

Concurrently, the grey literature – i.e. reports and policy documents of learned societies and non-governmental organizations – was examined. An initial list of relevant organizations (see Appendix 2) was identified by the research team and the steering committee, and all reports of these organizations were screened to identify reports on genetic modification. Where relevant, reports that predominantly focused on biotechnology, synthetic biology, cloning, and organic farming were also included for analysis. Next to this, the database of the National Library of the Netherlands ('Koninklijke Bibliotheek') was searched to identify additional relevant reports (see Appendix 2 for more information). Moreover, screening of the reference lists of included articles – so-called 'cross-referencing' – also yielded several relevant reports. We focused on reports that were published in Dutch[6] and English. Subsequently, the selected reports were screened to identify references to nature and (un)naturalness.

Thereafter, references to nature and (un)naturalness in the scientific literature on genetic modification were analyzed. Given the large amount of literature on genetic modification, the analysis of the scientific literature inevitably had to be limited to a sample of this literature. A list of key moments in

[6] In this report, all quotations from Dutch reports were translated to English by the authors.

the development and application of genetic modification were taken as a starting point for our analysis (see Appendix 3), as it was hypothesized that these moments have given the societal and academic debate on genetic modification a particular impetus (44). Relevant scientific literature on these key moments was selected based on input from the research team, the steering committee, and several experts in this field (see Appendix 3 for more information). Articles were included if they met the following inclusion criteria: they had to (1) concern one of the stipulated key moments; (2) contain the term(s) nature, (un)natural and/or (un)naturalness; and (3) be written in Dutch or English. Both review articles about the key moments and original primary research articles in which the key moments were described were included. Where relevant, cross-referencing was used to include additional relevant references by screening the reference lists of included articles. Subsequently, the included articles were screened to identify references to nature and (un)naturalness. Inclusion of articles was ended when saturation was reached, i.e. when screening additional articles no longer yielded novel uses of nature and (un)naturalness.

In all three analyses, the identified references to nature and (un)naturalness were examined and contrasted in more detail. In doing so, we first identified whether nature and (un)naturalness were used in value-neutral or value-laden ways. We considered these terms to be used in value-neutral ways if these references did not imply an ethical judgement or (positive or negative) value. In the references referred to as value-neutral, in other words, no link is made between (un)naturalness and goodness or badness or particular underlying values[7]. Subsequently, we clustered references that were similar in terms of the context in which these references were brought up. This clustering was an iterative process in which the clusters or categories of different uses were re-evaluated and adjusted several times. In doing so, we analyzed whether – and if so, how – references to nature and (un)naturalness were made in different ways in relation to specific topics or contexts. It was, for instance, investigated whether these terms were used in different ways in the context of genetic modification in different organisms or different areas of biotechnology, and in relation to cisgenic versus transgenic modification.

Next to identifying similarities and differences in the use of nature and (un)naturalness *within* the law, grey literature, and scientific literature, we also identified overarching similarities and differences in the use of references to these terms between these different bodies of literature. In the analysis of the scientific literature, differences and similarities between uses in life science, social science and ethics articles were also identified.

2.2 Positive law

2.2.1 Value-neutral references to nature and (un)naturalness

In a legal context, ‘naturalness’, ‘nature’ and ‘natural(ly)’ are almost exclusively used in contrast to humans or the human made. In most of the references to nature and (un)naturalness in the positive law, these terms are used in a value-neutral way. In what follows, the results of the analysis of international,

[7] To be sure, this does not mean no such connections *could* not be made nor that (some) concept(ion)s of nature and (un)naturalness *are* in fact value neutral. Whether concepts can be value-neutral is debated and different views on this matter exist; according to some, concepts are never value-neutral (45,183). From a constructivist standpoint, for instance, any reference to or description of nature or (un)naturalness inevitably provides a particular human perspective (183). In this view, categories used to distinguish the natural from the unnatural are necessarily human impositions (see also Chapter 3, p. 36). In this chapter, we limit ourselves to observing whether references to nature and (un)naturalness explicitly link these terms to goodness or badness or to particular underlying values.

European and national legislation and regulation are followed by those of rulings by national and European courts of law.

'Nature' and 'natural(ly)' are found in large numbers in relevant national law. In these references, 'natural' is almost always used as an adjective, referring to human beings as legal subjects (as opposed to legal persons, being fictitious entities). In this context, the term 'natural' is used in a value-neutral way. National legislation and regulation did not contain any value-laden references to 'naturalness'.

In international treaties, 'nature' and 'natural(ly)' in combination with the relevant keywords appear in one source, the Cartagena Protocol to the Convention on Biological Diversity (45). Apart from the fact that 'natural' is also used as an adjective of 'person', it appears in the Convention's definition of 'modern biotechnology', as consisting, among other things, of "*the fusion of cells not belonging to the same taxonomic family, which overcomes natural physiological reproductive or recombination barriers and which is not one of the techniques used in traditional breeding and selection"*. 'Natural' refers to barriers to reproduction or recombination that could not be overcome without human intervention (old methods or new techniques); without such intervention, these cells would not fuse; such cells do not fuse on their own. Again, 'natural' refers to something unaffected by human activity, to processes that occur among organisms without human intervention. In this context, the term 'natural' is not used in a value-laden way.

In regulations, directives, and decisions of the European Union, 'naturalness', 'natural(ly)' and 'nature' often appear in combination with the appropriate keywords. The regulations found cover a wide range of topics: food safety, the release of GMOs into the environment, organic production and its labelling, veterinary medicines, animal nutrition, plant protection products, the transparency and sustainability of the food chain, the prevention and control of the introduction and spread of invasive species, the protection of animals used for scientific purposes, risk assessment of GMOs, the introduction of seeds to the market, the possibility for Member States to restrict or prohibit the cultivation of GMOs in their territory, lists of varieties, hay milk, biological diversity, maximum residue levels of harmful substances, etc., etc.. 'Natural(ly)' is also part of the definition of GMO in several directives: "*organisms, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by reproduction and/or natural recombination*" (emphasis added) (46). In this specific context, 'natural' refers to processes in which human activity is absent. Its use is not in any way value laden. The term 'unnatural' is not used in relevant international treaties, EU legislation or Council of Europe Recommendations.

The analysis of case law shows similar results. Combined with 'genetic modification' and 'genetically modified', 'naturalness' cannot be found in Dutch case law. 'Nature' and 'natural(ly)' are used by a variety of national courts (administrative as well as civil) in rulings with references to genetic modification. 'Natural' is used as an adjective of "*characteristics of protected landscapes*", of "*habitats of species*" (6), of "bacterial strains" (47), of viruses (as opposed to "*modified viruses*") (48) and of "*occurring chromosomal DNA*"(49). 'Unnatural' can be found in a recent civil ruling relating to the authorization of the use of COVID-19 vaccines. The court quoted the appellant who argued "*that the substance to be injected against COVID-19 contains mRNA (messenger RNA), which introduces a synthetic, unnatural gene into our cells*" (50). 'Unnatural' appears to be synonymous with 'synthetic' and – therefore – with 'man made'.

The European Court of Human Rights in Strasbourg has not used '(un)naturalness', 'nature', '(un)natural(ly)' in rulings with references to genetic modification. However, the Court of Justice of the European Union did, in 9 rulings to be specific (51–59), but only in quotes of and references to regulations, directives and decisions already discussed in this paragraph. Consequently, their use in these court rulings is also not value laden.

2.2.2 Value-laden references to nature and (un)naturalness

In the legal context, 'naturalness', 'nature' and 'natural(ly)' are also occasionally used in a value-laden way. In national legislation and regulation, only one value-laden reference to 'naturalness' can be found. In this governmental decree – not relevant for the present purposes since it does not pertain to genetic modification – 'naturalness' is used (together with 'quiescence' and 'openness') to refer to a scenic property or quality (of the Wadden Sea) (60). In this specific context 'naturalness' is more or less synonymous with 'pristine' or 'untouched'. In addition, 'naturalness' can be found in two international treaties to which the Netherlands is a party (61,62). Although these treaties are also not relevant for the present purposes, for 'naturalness' is not used in the context of genetic modification, it is clearly used in contrast to what is affected by human beings. Strictly speaking, these uses of 'naturalness' cannot qualify as completely value-neutral, since it is used to refer to properties or qualities that are considered worthy of preservation.

'Naturalness' also occurs in three relevant European Union regulations (on food enzymes, food additives and on the use of flavors in food) and with identical meanings (63–65). In these regulations 'naturalness' is a property of products and production processes. Naturalness is presented as a property or quality about which consumers should not be misled, as is the case with 'freshness'. Although it is very difficult to derive its meaning by providing a synonym, 'naturalness' used in this specific context cannot be said to be used in a value-neutral way in the strict sense either, since it does refer to a property or a quality valued positively.

In relevant national law, 'natural' is almost always used as a value-neutral adjective referring to human beings as legal subjects, as was discussed previously. In one relevant law, however, 'natural' is not used in combination with 'person' (66). Food processing businesses are prohibited to attribute certain properties or qualities to food products in their consumer information. It is forbidden to claim or even to suggest that food products prevent or cure illnesses. However, one exception is made for mineral water. Apart from extraction, testing, bottling and distribution, this water is not subject to processing. Nothing has been added to it and nothing has been taken out of it. According to that law, mineral water is allowed to be labelled 'natural' in consumer information. In that specific context, 'natural' not only connotes 'pristine' (or 'untouched'), but also 'wholesome', 'salubrious' or even 'healthy'.

Although 'natural(ly)' appears frequently (and 'nature' only occasionally) in relevant EU legislation, the range of meanings is fairly limited. Only once - in a directive on the manufacture, presentation and sale of tobacco and related products - does it seem to have the previously found meaning of 'wholesome', 'salubrious' or 'healthy' (67). Because, as a consequence, the adjective 'natural' may suggest that tobacco products are less harmful, its use in consumer information is prohibited. As was

previously mentioned, the word 'unnatural' cannot be found in relevant international treaties, EU legislation or Council of Europe recommendations.[8]

In relevant national law, finally, the meaning of 'natural' occasionally seems to coincide with 'traditional', i.e. when it refers to certain production techniques (extraction of sea salt, production of hay milk), and in a few cases it is more specific and more or less synonymous with 'non-chemical' (e.g. in connection with crop protection products). And when the law refers to 'natural materials' (only those that may be used in hives for beekeeping: wood, wax, propolis, etc.), something like 'non-synthetic' is meant. In these very specific contexts, their use is also probably value-laden in that those production processes and materials are valued positively.

All in all, when the words 'natural' or 'naturally' can be substituted with synonyms not merely referring to the absence of human intervention (and without loss of meaning, by words like 'pristine', 'untouched', 'wholesome', 'traditional'), their use appears to be value laden. It is not implausible that outside the realm of genetic modification the words are used in a value-laden way more frequently. Where 'naturalness' refers to a scenic property of quality, for example, that seems to be the case. In the context of genetic modification, however, their use is almost exclusively value neutral.

2.3 The grey literature

2.3.1 Value-neutral references to nature and (un)naturalness

In the grey literature on genetic modification, the terms 'nature' and 'natural' are similarly regularly used to refer to organisms, genetic constructs or processes in the 'wild', i.e. that are not constructed or modified by humans, for instance in a laboratory. In many instances in which the term 'natural' is used in this way, no value judgements are expressed. Authors for instance refer to the '*natural environment'* (39), '*natural horizontal gene transfer'* (40), '*natural mutation*s' (16), and '*natural biological system*s' (41). The term 'nature' is also sometimes contrasted to humans or the human made without value judgements, such as when it is stated that "*meiotic [gene] drives are widely present in nature*" (p. 60) (30) or pointed out that genomic rearrangements "*can occur spontaneously during conventional breeding and in nature*" (p. 12) (72).

In some instances, these references to naturalness relate to when something can be considered natural. This is for instance the case in discussions about property rights and patenting of GMOs. As a report by the Nuffield Council points out, "*naturally-occurring phenomena such as electricity or wild species of plants or animals are not regarded as inventions but as discoveries and thus are not eligible to be patented"* (p. 3) (73). This has led to discussions about whether (particular) GMOs – such as a transgenic mouse called the 'Harvard mouse' – should be considered 'naturally-occurring' (as mice are) and thus not patentable, or whether the use of genetic modification alters a mouse in such a way that they differ enough from naturally occurring mice to consider them a product of human invention that can be patented (74,75).

In contrast to the terms 'natural' and 'nature', the terms 'unnatural' and 'artificial' are much less commonly used in value-neutral ways in the grey literature on genetic modification. If they are, they are

[8] It is, however, used in a number of national ministerial decrees (relating to the deposition of nitrogen, the prosecution of child pornography, water management and technical standards for river barges). In all of these instances it is used to refer to something affected by human beings. This use of 'unnatural' is also value-laden in that it is said of something valued negatively.

commonly used within quotation marks, as is the case in a report that describes the development of an "*alternative genetic alphabet*" that consisting of bases that could produce proteins that do not exist in nature. This report states that "*several 'unnatural' bases have been developed (..)"* (p. 7) (76).

2.3.2 Value-laden references to nature and (un)naturalness

In the grey literature on genetic modification, the terms 'nature', 'natural' and 'unnatural' are most frequently used in value-laden ways. Sometimes (an application of) biotechnology or genetic modification is explicitly approved of, praised, or preferred based on its naturalness or disapproved of, criticized, or condemned based on its unnaturalness. In these cases, the natural is explicitly coupled to the good and the unnatural to the bad. It is for instance stated that "*certain groups feel uncomfortable about the unnatural character of modern biotechnology and the high degree of manufacturability of nature*" (p. 15) (77) or that consumers see GM food "*as unnatural, while naturalness is seen as intrinsically good*" (p. 20) (5).

Sometimes, these value-laden references to nature and (un)naturalness voice concerns that express fundamental disagreement with the use of these technologies. At other times, these references voice questions, worries, or concerns without an expression of fundamental disagreement. In yet other instances, it is underlined that these worries or concerns are not specific to genetic modification, and in fact lead to a reevaluation of already established practices. One report on biotechnology in plants, for instance, stated:

> *[In the discussion on biotechnology in plants,] the arguments of an intrinsic nature relate to respect for 'naturalness' (..). On the basis of this criterion, many conventional breeding techniques are subject to the same criticism [as biotechnology]. Indeed, biotechnology pushes an already established practice to the extreme, such that it becomes necessary to – even retrospectively – rethink the whole agricultural and horticultural sector* (p. 10) (78).

In many value-laden references to nature and (un)naturalness, it remains unclear what aspect or which consequence of genetic modification is considered unnatural and how, and for what reason this is considered problematic. Most of these unspecified, value-laden references to (un)naturalness are found in reports that refer to the opinions of citizens or in reports written by organizations that are critical about genetic modification. Reports for instance state that "*the unnaturalness of GMOs*" is a reason for citizens not to buy them (p. 29) (79) or that people consider GM food "*unsafe, unnatural, and unnecessary*" (p. 14) (80).

In other instances where the natural is explicitly coupled to the good and/or the unnatural to the bad, it is more clearly specified what aspect or consequence of genetic modification is considered unnatural. It is for example stated that (specific applications of) genetic modification are unnatural because they disturb natural species boundaries (81) or an organisms' natural integrity (82), because they prevent an organism from following its natural instincts (83), do not allow it to portray its natural (species-specific) behavior (83), or because they disturb the natural balance (84) or the natural order (5).

At other times, the terms 'nature', 'natural' and 'unnatural' are used in more implicitly value-laden ways: while it is not explicitly stated that nature or naturalness are considered good or

unnaturalness is considered bad, the terms appear to be used to invoke positive or negative connotations, respectively. One example that illustrates this is the discussion in the grey literature on the labeling of 'natural' products. When certain technology companies labeled GM fibers, saffron and vanilla as 'natural' (8–10), this was met with opposition from groups that are critical of genetic modification. The ETC group, for instance, states the following with regards to the fact that GM fibers were labeled as 'natural' by the company producing them:

> *(..) the payoff of syn bio fiber production is cheaper high-value fibers produced in factory-based fermentation tanks that require fewer workers – all under the green guise of "natural" sustainability. A closer look reveals that there is nothing natural or sustainable about synthetic biology's high-tech (..) approach to novel fiber production (p. 2) (9).*

According to these organizations, technology companies use the label 'natural' to suggest that the products possess certain positive characteristics, such as sustainability, and to cover up their 'true (unsustainable) character'.

More generally, this may be interpreted as an example of the rhetorical tendency to 'naturalize' biotechnology to invoke positive connotations – a tendency that is discussed in another report in the grey literature (85). As the foregoing reflections illustrate, the reverse tendency – to 'denaturalize' biotechnology, so to say – can also be observed: the rebuttal of such claims or the labeling of products or actions as unnatural are also used to invoke negative connotations.

2.3.3 Underlying values or concerns

In the grey literature, many value-laden references to nature, naturalness and unnaturalness did not imply naturalness was valuable and unnaturalness objectionable as such. These references rather related (un)naturalness to other underlying values or concerns. These values or concerns related to three different aspects: safety and uncertainty, the integrity or intrinsic value of the modified entities, and the appropriate attitude to or place of humans in the world around us. In what follows, these references are discussed in more detail. Each section is followed by a short summary which is highlighted in grey.

a) Safety and uncertainty

In many instances, (un)naturalness was considered a proxy for safety or uncertainty. In the grey literature, many reports mentioned that members of the public associated naturalness with safety and unnaturalness with uncertainty or risk. A biotechnology 'trend analysis' in 2009 for instance reported that "*genetic modification is experienced as unnatural, with potential unexpected and uncontrollable effects on, amongst others, biodiversity*" (p. 116) (86). Organizations that are critical of genetic modification also link (un)naturalness to safety or uncertainty. In a report on GM crops, Greenpeace for example contended that "*the use of so-called gene (or genome) editing techniques like CRISPR-Cas (..) could effectively turn nature (..) into a gigantic genetic engineering experiment with unknown, potentially irrevocable outcomes*" (p. 2) (87).

The connection between (un)naturalness and uncertainty was also discussed in relation to regulatory precautions that are deemed necessary for GM research and GM products. A report that re-

evaluates the safety regulations for working with GMOs, for instance, compares experimental horizontal gene transfer by genetic modification to natural horizontal gene transfer, stating:

> *When such events happen in nature all the time, the question could be asked what the increased risk is of horizontal gene transfer that occurs in the laboratory. (p. 56) (..) Since we have seen that bacteria exchange genes in nature, the risk of experimental genetic modification should be evaluated against the backdrop of events that happen in nature, resulting in similar exchange* (p. 61) (69).

Other reports point out that a similar line of thinking led to the legal definition of a GMO. As mentioned in the introduction, EU law (2001/18/EC) defines a GMO as "*an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination*" (6). The idea behind this definition, according to a report by the COGEM, is that "*altering the hereditary material in an 'unnatural way' carries inherent risks that are expressed in the resulting organism (product)*" (p. 12) (88). This, in turn, is seen as a reason to subject the use of genetic modification technologies to special regulations and to deem additional safety studies necessary. Classic mutagenesis techniques, in contrast, "*were exempted [from the GMO directive] because of their long-term safety record*" (p. 14) (79).

At the same time, this definition has also led to discussion about the connection between the naturalness and the risks of genetic modification technologies, and whether the focus should be on the naturalness of the *process* or of the resulting *product*. A report by the Rathenau institute states:

> *This definition raises the question whether a crop modified with CRISPR-Cas9, which could also have occurred naturally, is a GMO. (p. 12) (..) The answer to the question depends in part on the interpretation of the phrase 'in a way that does not occur naturally'. If 'in a way' refers to the method, then the technique is relevant and all techniques that do not take place naturally fall within the scope of the GMO Directive. In nature, CRISPR-Cas9 does not cut genetic material in plants and therefore the CRISPR crops should be regulated as GMOs. However, if you assume that 'in a way' refers to the way the genetic material is rearranged, the technique used to rearrange the DNA is irrelevant, as long as the rearrangement could have taken place in nature. This reading (..) excludes crops modified with CRISPR from the GMO legislation. However, the Court has clarified that all products of genome editing are subject to the GMO Directive (p. 12, footnote)* (79).

As this passage illustrates, an important divide can be observed between references to the naturalness of the process (the genetic modification technique) or the naturalness of the product (the characteristics of the GMO). Whereas EU law takes a process-approach in which the naturalness of the process is taken to be a proxy for safety, others do not necessarily consider this connection valid. Some for instance point out that the "*alteration of genetic material is a natural process, which is even essential for the evolution of species and their adaptation to a changing environment. The genome of every human or animal contains dozens of new mutations compared to the parents, a multitude of the number that is introduced with CRISPR-Cas*" (p. 172) (70). Similarly, a report on experimental horizontal gene transfer by genetic modification states that "*it will be hard to accept for scientists that experimental actions that can take*

place in nature unlimited and uncontrolled, need to be carried out under extra safety regulations in the laboratory" (p. 74) (69).

Others argue that the connection between naturalness and safety is more logical if naturalness is taken to concern the *product* rather than the process. According to some, risks and uncertainty are (predominantly or only) increased and/or additional risk assessment is only necessary if the induced mutations create organisms with a novel phenotype, i.e. organisms with (combinations of) characteristics that do not occur in nature. A report on the plasticity of plant genomes, for instance, states:

> *If a genetic modification or gene editing does not lead to novel phenotypes compared to possible phenotypes in nature or breeding, the biosafety risks of that modification will be most probable below the baseline of conventional breeding. However, <u>if new genetic elements are added, or if new combinations of genetic elements are made that cannot occur in nature, cultivation or breeding, or occur with an extremely low likelihood, this may trigger additional risk assessment</u>* (p. 12) (72).

It is also highlighted that there is no 'natural reference' – a wild-type organism – to which a GMO can be compared in a risk analysis if GMOs have novel characteristics that do not occur in nature (10), creating more uncertainty with regards to potential risks. Correspondingly, several non-EU countries, such as the US, have regulations that are based on a 'product-based approach' (88).

This product-based view on naturalness was also found to impact views on GMOs that cross species boundaries. Some reports mention that plants and animals that cannot be created through natural crossing are considered particularly unnatural and are "*directly associated with 'potentially dangerous, unhealthy and undesirable'*" (p. 15, quotation marks added) (89). A similar line of thinking is also reflected in some 'tiered' governance frameworks for GMOs. The Norwegian Biotechnology Advisory Board, for instance, has developed a governance framework with differentiated risk assessment that consists of different tiers, in which "*the first tier concerns genetically engineered organisms that have changes that exist or that can arise naturally. (..) The second tier concerns gene edits that are more complex, but still within the species boundaries (..). The third tier concerns conventional transgenic organisms or organisms that contain non-existing and synthetic DNA sequences*" (p. 20) (90).

Some references that connected naturalness to safety did not refer to the naturalness of the process or the resulting product, but related safety to the naturalness of the environment in which the GMOs would be released. These references implied that it would be hard to predict how technologies that are made in a laboratory would function in these 'natural' environments. A report on gene drives, for instance, mentions:

> *Gene drive technology makes it possible to radically intervene in wild/natural populations. This automatically leads to perceived loss of human control. In wild/natural populations only the moment of introduction is human controlled. Yet the fate of the individuals with the gene drive is determined by population dynamics and ecology beyond human control. Laboratory experiments testing efficacy almost inevitably use organisms which are highly uniform and different from wild populations. <u>The gene drive systems are unlikely to perform in the same way in natural conditions</u>*

that are much more variable and unpredictable; the likely effect of this is that the drives will not spread as readily as simple models suggest (p. 63) (30).

This reference suggests that if genetic modification is used in wild populations or environments, the potential risks and uncertainty are larger because the conditions are less predictable and controllable than in a laboratory.

Finally, some references to nature and naturalness underline that genetic modification could disturb a certain balance or order in nature, and thereby cause unpredictable and undesirable effects. A report on biotechnology in plants, for instance, states these technologies evoke fears of "*infringement of the natural order (Creation or that which came about through evolution) of which the consequences are incalculable because it is without precedent*" (p. 9) (78). According to the report, this concern is particularly relevant to an infringement of the natural order by transgenesis, i.e. gene transfer between unrelated species.

All in all, (un)naturalness is often considered a proxy for (un)safety and (un)certainty. Sometimes, this connection is unspecified, at other times it is specifically connected to the naturalness of the process, the resulting product, the environment in which the modified organisms would be released, or the balance that genetic modification or GMOs would disturb. The crossing of species boundaries was specifically mentioned as an example in which unnaturalness was linked to concerns about safety and uncertainty as no 'natural' reference exists to which transgenic organisms can be compared.

b) The integrity or intrinsic value of the modified entities

In other instances, references to nature and (un)naturalness expressed concerns that (applications of) genetic modification would treat organisms, species, ecosystems, or the environment in ways that harm or do not sufficiently acknowledge the integrity or intrinsic value[9] of the modified entities. These references to nature and (un)naturalness generally underline that the entities in question should be seen as ends in themselves, and not (only) as means to human ends. As is discussed in what follows, these references were related to different levels of biological organization, connecting naturalness to integrity, intrinsic value or dignity at respectively the level of the genome or cell, the individual organism, the species, the ecosystem in which GMOs are released, nature or life as a whole.

References that connected naturalness to the integrity of organisms at the level of the genome were the least common. Whereas some – such as some proponents of organic agriculture – argue that respect for the integrity of living nature warrants against direct intervention at the DNA level (39), others are more skeptical of the idea of genetic integrity since genomic changes occur regularly under 'natural'

[9] Due to space considerations, this report clusters references that link nature and (un)naturalness to integrity or intrinsic value. However, it is important to note that 'integrity' and 'intrinsic value' are not synonyms. Broadly speaking, integrity refers to the 'wholeness' or 'completeness' of the phenotype of an entity, the genotype of an entity or the species (44). Intrinsic value, in turn, refers to the idea that something possesses value in and of itself, beyond the value that it has for (other) humans (44). It is also important to point out that both these terms, like nature and (un)naturalness, are attributed different meanings by different authors. For a more elaborate reflection on the meanings of integrity and intrinsic value in the context of genetic modification in animals, see e.g. Brom (1995), De Vries (2006) and De Vries (2009) (44,121,184).

circumstances. A report by the Centre for Bioethics and Health Law, for instance, states: "*Talking about the integrity of the genome can lead to problems. In a biological or genetic context, a process-oriented approach is key. The demarcation of the genome is relative; changes take place regularly under 'natural' circumstances."* (p. 88-89) (44). Where references of this kind were made, they referred to genetic modification in 'living' non-human organisms, i.e. animals, plants and micro-organisms.

Other references connected naturalness to the integrity or intrinsic value of (individual) organisms or entities. These references almost always applied to animals. A report by the COGEM, for instance, states:

> *In discussions with stakeholders [of GM foods] – developers, farmers – naturalness is also an important ethical issue. Related to animals, the possibility to exhibit natural behavior is seen as an important factor for the (..) integrity of the animals in question* (p. 20) (5).

According to another report, "*a concept like integrity is not about the suffering of an animal, but about the moral respect for its own-ness."* (p. 26) (91). In a few instances, authors also connected the naturalness or integrity of animals to their 'telos': their "*inherent nature*" (p. 120) (82). According to some, genetic modification would modify the telos of animals in a problematic and drastic way that is aimed primarily towards human ends. Some reports on genetic modification in animals also linked naturalness to intrinsic value at the level of individual organisms (92). With regards to genetic modification in humans, nature was also connected to human dignity in a few instances. A report by the Nuffield Council, for instance, states that, according to some, genome editing in humans "*offends against the essential dignity and nature of the person as a free and independent human being"* (p. 67) (93).

Yet other references connected naturalness to integrity at the level of the population or species. These references were most often made in relation to transgenesis in plants or animals. One report, for instance, states: "*the crux in relation to biotechnology is that a specific boundary can be crossed: the natural species boundaries are no longer a barrier, and the natural integrity of the species is violated*" (p. 119) (82). Similarly, some references connected naturalness to the integrity or intrinsic value of species or ecosystems in which GMOs would be released, for instance underlining that "*even where [genetic modification] does not necessarily entail animal suffering, (..) [there may still be] concerns about the maintenance of ecological integrity and stability*", raising questions about the "*valorization of the 'natural' and the 'natural' relation of beings"* (p. 87) (68). Finally, some references connected naturalness to the integrity or intrinsic value at the level of nature or life as a whole.

References related to the integrity or intrinsic value of the modified entities also frequently voice concerns about instrumentalization. In some references, concerns about instrumentalization feature implicitly. The ETC group, for instance, stated that "*most synthetic biology companies are coming up with artificial DNA codes that [force] microbes to make industrially useful compounds*" (p. 7) (8). In this case, the word 'forcing' seems to imply that these organisms are used for human ends in a problematic way.

In other cases, concerns about instrumentalization are more explicit. A report on the use of genetic modification in organic farming, for instance, states:

> *Genetic modification technologies disturb natural reproductive boundaries and do not respect the intrinsic value and the own nature of plants and animals. (..) In organic farming, living beings are*

considered to have value beyond their usefulness for people. They should not be relegated to mere instruments. They have an intrinsic value that imposes limits on human intervention in nature (p. 7) (91).

All in all, references to nature and (un)naturalness often express concerns that (applications of) genetic modification would harm or disrespect the integrity or intrinsic value of the modified entities. These references connected naturalness to the integrity or intrinsic value at the level of the genome or cell, the individual organism, the species, the ecosystem in which GMOs are released, or nature or life as a whole. The crossing of species boundaries via transgenesis was specifically mentioned as an intervention that could have a particularly large (negative) impact on an organism's integrity. References of this kind also frequently voice concerns about instrumentalization, i.e. using particular entities as mere ends for human goals, rather than as ends in themselves. References to nature and (un)naturalness that expressed concerns about the integrity or intrinsic value of the modified entities mostly related to animals, sometimes to plants, and less frequently to humans or micro-organisms.

c) The appropriate attitude, place, or role of humans

In many other instances, references to nature and (un)naturalness expressed convictions or concerns with regards to the appropriate attitude, place or role of humans in nature.

With regards to the appropriate attitude of humans, various references to nature and (un)naturalness stressed the importance of remaining humble in our attitude towards nature, both when it comes to 'human nature' and the nature around us. A report on genome editing by the Nuffield Council, for instance, states that:

> *Bioconservatism may arise from a reasonable concern about scientific hubris (..), which is skeptical about the wisdom of human agents disrupting finely balanced systems that have reached their present state through lengthy evolutionary processes. (..) Whether this providence is thought to be divine or natural, human interference beyond a certain point may be thought to overreach the limited cognitive capacities of human agents and the limits of predictability for the systems in question* (p. 27) (68).

This attitude is also linked to safety, since it is thought to "*reduce the chance of serious accidents*" (p. 48) (94). Similarly, a report by the Rathenau institute on the debate on synthetic biology, quotes a participant in the debate who contended:

> *As a convinced evolutionist, I know all too well that nature is imperfect in many ways. But I think it would be an act of folly to believe that humankind can easily change that (..) We must beware of the idea that we always know better and make everything perfect.* (p. 61) (95).

In contrast, some other references to nature and (un)naturalness expressed the attitude that nature is something that humans can or should improve. Sometimes, this is relatively implicit, for instance when it is stressed that "*natural gene drives have their limitations"* (p. 4) (30). Other times, this attitude is more

explicit, such as when a report on transgenic mosquitoes states that "*the replacement of natural populations by transgenic mosquitoes is necessary for success [in decreasing the impact of malaria]"* (p. 4) (96).

Many other references to nature and (un)naturalness expressed convictions regarding the appropriate place or role of humans in nature. In some references, it was stressed that humans are part of nature, and argued that it is thus inevitable and not necessarily problematic if humans harm nature. In other instances, it was contended that humans have in fact "*been designed by nature to be good designers*" (p. 114) (20).

Other references to nature underlined that genetic modification technologies would distance humans from nature. A report commissioned by the COGEM on the perceptions of citizens on 'GMO free production chains' (production chains in which no use is made of genetic modification) reports that some citizens were concerned that "*genetic modification will push humans further away from nature and implies an undesirable 'industrial' and 'scientific' approach to food"* (p. 108) (84).

Finally, many references to nature referred to the different roles that humans may have in nature, which can affect their views on genetic modification. Another report commissioned by the COGEM on the views of adherents of twelve important religions and philosophies of life, for instance, reports that according to the Islam:

> *Humankind is appointed as a steward/viceroy (khalifah) of nature. On the one hand, this means that man is entitled to use natural resources and other living beings. On the other hand, he may not cause (permanent) damage to nature out of responsibility towards future generations and out of respect for the Creator* (p. 34) (97).

Many reports in the grey literature also referred to different secular attitudes towards nature: humans may be considered dominators, stewards, partners, or participants of nature. These different attitudes are explored in more detail in Chapter 4.

All in all, references to nature and (un)naturalness expressed convictions or concerns with regards to the appropriate attitude, place, or role of humans in nature. Some references of this kind stressed the importance of being humble, whereas other references expressed the attitude that nature is something humans can or should improve. Many references referred to humans as a part of nature, warned for an increased distance between humans and nature, or reflected on different roles humans may have in nature (such as dominators, stewards, partners, or participants of nature).

2.4 The scientific literature

2.4.1 Value-neutral references to nature and (un)naturalness

The terms 'nature' and 'natural' were also regularly used in value-neutral ways in the scientific literature to refer to organisms, genetic constructs or processes in the 'wild', i.e. not constructed or modified by humans, for instance in a laboratory. Value-neutral references to nature and (un)naturalness occurred regularly in scientific literature from the life sciences, social sciences, and ethics, yet was most common in life science articles. Authors for instance refer to '*natural proteins'* in contrast to the recombinant

proteins produced by companies like Genentech (98) and to the '*natural system*' to refer to the CRISPR/Cas9 system used by bacteria to defend themselves against phages in contrast to CRISPR/Cas9 technology (99). Similarly, nature is used in contrast to the human-made in value-neutral ways, for instance when it is stated that *"it is now known that there are several mechanisms for DNA transfer and that these occur in nature on a large scale"* (p. 1035) (100). The terms 'unnatural' and 'artificial', in contrast, were only sporadically used in value-neutral ways, for instance when it was stated that genetic modification provides the "*ability to design new artificial genes"* (p. 619) (101).

2.4.2 Value-laden references to nature and (un)naturalness

Nature and (un)naturalness were also commonly used in value-laden ways in the scientific literature. Value-laden uses occurred regularly in scientific literature from the life sciences yet was most common in social science and ethics articles. In the scientific literature in general, many instances in which naturalness was used in value-laden ways referred to the relationship between naturalness and public acceptability. In a paper on GM crops, for instance, it was stated that "*whether food products are processed or appear in their natural form is an important factor in determining the acceptance of GM products"* (p. 130) (102). Similarly, a paper on the public acceptability of gene therapy states that *"the most common ethical concern was that genetic modification was interfering with nature (unnatural) and that it was 'playing God'"* (p. 27) (103). At other times, it was mentioned that some consider genetic modification unnatural and therefore wrong, for instance in the context of germline modification (104).

The tendency to 'naturalize' biotechnology that was identified in the grey literature could also be observed in the scientific literature. In these cases, the terms 'nature' and '(un)natural' are used to invoke positive or negative connotations. In the context of Mitochondrial Replacement Therapy (MRT), for instance, it was argued that while genetic modification would be a valid source of ethical concern, "*using the term genetic engineering to describe MRT would be inaccurate and misleading. MRT is a genetic recombination, which is actually no different from what occurs naturally in sexual reproduction when germ cells recombine different alleles both before and during fertilization*" (p. 386) (105). The tendency to 'naturalize' biotechnology was also mentioned as a strategy used by proponents of biotechnology, for instance in the context of cloning where it was mentioned that "*according to [scientists and intellectuals that oppose cloning], the proponents of cloning want to naturalize and normalize asexual replications by arguing that it is just like having natural twins"* (p. 22) (106).

The reverse tendency, to 'denaturalize' nature was also described in the scientific literature. A scientific article on Monsanto (a company that produces GM crops), for instance, quotes an advertisement banner produced by this company that read:

> *Some people think anything chemical is bad and anything natural is good. Yet nature is chemical. Plant life generates the oxygen we need through a chemical process called photosynthesis. When you breathe, your body absorbs that oxygen through a chemical reaction in your blood. Life is chemical. And with chemicals, companies like Monsanto are working to help improve the quality of life* (p. 434) (11).

This advertisement attempts to decouple associations between the 'natural' and the good and the 'unnatural' - the chemical - and the bad. 'Naturalizing' and 'denaturalizing' strategies could also be observed in the ethics literature yet were most common in life sciences articles and in social science articles that discussed communication strategies of life science companies.

2.4.3 Underlying values or concerns

As was observed in the grey literature, many value-laden references to nature and (un)naturalness did not imply naturalness was valuable or unnaturalness objectionable as such, but rather coupled naturalness to other underlying values or concerns. In the scientific literature, these references also coupled naturalness to the three values that were previously identified: safety and uncertainty, the integrity or intrinsic value of the modified entities, and the appropriate attitude, place, or role of humans in the world around us. In what follows, examples of these different uses are discussed in more detail. Each section is followed by a short summary and reflections on the identified similarities and differences between the life science, social science and ethics literature, which is highlighted in grey.

a) Safety and uncertainty

Many scientific articles drew a connection between naturalness and safety or between unnaturalness and risks and uncertainty. In some cases, this connection was associative and mentioned without a rationale regarding how unnaturalness and uncertainty are connected. In a study on consumer attitudes on GM foods, for instance, it was noted that "*genetic modification was believed to turn yoghurt into an unwholesome and unnatural product"* (p. 350) and that this association was connected to its undesirable consequences, particularly the perceived unknown long-term consequences on human health and the environment (107). A similar association was found in relation to cultured meat (108,109). Likewise, a study on gene editing in wildlife found a strong correlation between beliefs that gene editing in wildlife 'messes with nature' and beliefs about the risks of this approach (110).

Other articles provided more explicit rationales regarding how unnaturalness and uncertainty are connected. Some articles, for instance, mentioned that limited experiences with GMOs, insufficient understanding of the complexity of nature and the fact that GMOs may have "*genetic compositions that do not reflect evolutionary processes occurring under natural conditions"* (p. 234) (111) can increase the uncertainty about their (negative) effects. Consequently, it was argued in this article that "*if we respect evolution's restrictions on genetic alterations, the products of our interventions will be more predictable because we refrain from experimenting with the unknown*" (p. 236) (111). Relatedly, other authors point out that genetic modification "*challenges the natural or God-given order of things and thus bypass[es] certain (..) safety mechanisms that are inherent in nature*" (p. 998) (112), would upset "*intricate organismic and ecological balances*" (p. 295) (113) or would "*counteract natural selection (..) and cause unanticipated effects*" (p. 481) (114). In some of these references, nature is personified. In the so-called 'master engineer argument', natural selection is construed as a 'master engineer' that should be able to do its work without human interference. According to this argument, "*the evolutionary process is beyond humans' capacity to understand. Therefore, interfering with that process through applications of gene-editing technologies will likely result in suboptimal outcomes"* (p. 29) (115). In other instances, it is argued that nature will *"'hit back' at inappropriate intervention"* (p. 281), which has been used to argue against

GM foods (116). These references express the view that interfering in the natural order or balance could have unanticipated negative effects.

Like in the grey literature, the connection between unnaturalness and uncertainty was pointed out as particularly relevant for GMOs that cross species boundaries. Jane Calvert, for instance, mentions that "*putting genes together that were previously separate could lead to the creation of new organisms that have unpredictable emergent properties, making the risks of accidental release very difficult to assess in advance*" (p. 102) (117). For some, this was a reason to argue in favor of cisgenic rather than transgenic approaches (38,111,118). Some authors, for instance, argue that:

> *In the case of a cisgenic plant, the gene of interest, together with its promoter, has been present in the species or in a sexually compatible relative for centuries. Therefore cisgenesis does not alter the gene pool of the recipient species and provides no additional traits. No changes in fitness occur that would not happen through either traditional breeding or natural gene flow. Similarly, cisgenesis carries no risks — such as effects on nontarget organisms or soil ecosystems, toxicity or a possible allergy risk for GM food or feed — other than those that are also incurred by traditional breeding. This is the fundamental difference between cisgenesis and transgenesis. Consequently (..) [o]n the issue of safety, regulators could treat cisgenic plants the same as conventionally bred plants* (p. 750) (38).

In a few instances, in contrast, the tables were turned, and opposite associations were made between (un)naturalness and (un)safety. In some of these references, *un*naturalness (rather than naturalness) was related to safety. In one such reference it was for instance claimed that some argue that "*making synthetic organisms less natural will make them less risky, because they will be more easily separable from the natural world*" (p. 102) (117). It would for instance be an option to create synthetic organisms that are dependent on nutrients that cannot be found in nature, such that these organisms could not survive if they accidently escaped from the laboratory. In some other references, it was argued that biotechnologies should be seen as natural and therefore could be considered safe. The previously mentioned article on Monsanto, for instance, mentions that advocates of biotechnology in the U.S. House of Representatives argued that "*biotechnology is merely an extension of nature and, consequently, can be expected to be safe"* (p. 434) (11). Similarly, a few authors used references to nature to underline that crossing species barriers is safe. Paul Berg, for instance, argued that "*the concern of some that moving DNA among species would breach customary breeding barriers and have profound effects on natural evolutionary processes has substantially disappeared as the science revealed that such exchanges occur in nature*" (119).

As these reflections make clear, different perspectives on the relationship between (un)naturalness, safety and uncertainty exist. An article by Lotte Asveld, Patricia Osseweijer and John Posada (120) provided a potential explanation for this: they argue that different perspectives on nature and naturalness give rise to divergent perspectives on the management of risk and uncertainty. They identify different views on nature, which are visualized by a ball in different positions in Figure 1. In this figure, seeing nature as a resource is represented as a ball that is "*safely contained and can easily take a hit*" (p. 128) (120), whereas seeing nature as controllable is represented as a ball that is somewhat contained but its balance could also be disrupted if enough force is applied. If nature is seen as capricious, in turn, it is seen as uncontrollable; this is represented as a ball that could freely roll away. The last view, in which nature is seen as vulnerable, is represented as a ball in a precarious balance (120).

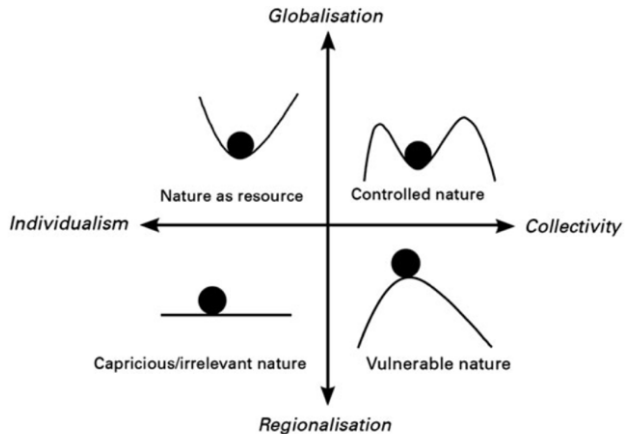


Figure 1: Worldviews (figure reproduced from Asveld, Osseweijer & Posada (2020) (120)*; no changes made; CC BY).*

These different views on nature, they argue, also affect the way in which the relationship between naturalness, risks and uncertainty are interpreted:

> *From the perspective that nature is essentially something vulnerable, approaching living organisms as entities that can be controlled and designed is a seriously flawed misconception about how we should deal with living organisms. In this perspective, living organisms are inherently unpredictable and should be treated as such. (..) From the perspective that nature is a resource that is essentially robust, industrial biotechnology is an excellent opportunity to find optimal solutions to pressing problems such as climate change and scarce resources* (p. 128-9) (120).

All in all, (un)naturalness is often seen as a proxy for (un)safety and (un)certainty, which may also be connected to different underlying views of nature as vulnerable, controllable or as a resource. References in which (un)naturalness was connected to (un)safety and (un)certainty occurred in scientific articles from all disciplines, but most frequently in social science articles. In terms of the context, it was brought up most frequently in relation to genetic modification in microbes, synthetic biology, and cultured meat. It was also brought up frequently in relation to GM crops and animals, and to a much lesser extent in relation to genetic modification in humans.

b) The integrity or intrinsic value of the modified entities

A second set of references to nature in the scientific literature expressed concerns that (applications) of genetic modification would insufficiently acknowledge or harm the integrity, intrinsic value, or dignity of

the modified entities. As was the case in the grey literature, these references were related to different levels of biological organization: the genome, the individual organism, the population or species, the ecosystem in which GMOs are released, or nature as a whole.

At the level of the genome, some authors mentioned the concern that genetic modification could harm a crop's, animal's or human's genetic integrity (121–123). Jacky Leach Scully, for instance, argues that "*for some people, any change in genetic makeup per se is wrong because there is something intrinsically valuable about an individual's genome as it is; heavyweight justification is needed before it can be right to interfere with it*" (p. 39) (122). At the same time, the identified articles that mentioned this concern were also critical of it. Scully, for instance, contends that: "*Few bioethicists today find this a compelling argument, however, especially since the genetic diversity that we know exists naturally among humans makes it hard to see how simply introducing a genetic difference is ethically wrong*" (p. 39) (122).

At the level of the individual organism, some authors argue that genetic modification is unnatural and wrong if it violates the integrity of an organism, fails to respect its intrinsic value or dignity, makes significant changes to its nature or violates its telos (122) (112,113,121,124–126). Most references of this kind were made with regards to genetic modification in animals. Lassen, for example, mentions that "*for many people there may be something inherently unethical about using biotechnology to make significant changes in the nature of an animal, whether it hurts the animal or not"* (p. 1002) (112). Henk Verhoog, in turn, argues that biotechnological developments in animals – ranging from artificial selection and insemination to genetic engineering and cloning – are increasingly more unnatural because the "*animal's own role in the process of reproduction is completely taken away from the animal and brought under human control"* (p. 295) (113). As a result, the animal's intrinsic value, its otherness, its characteristic 'nature' or way of being is not respected (113). Objectionable changes of this kind were often linked to the inability to 'live naturally' and 'perform natural behaviors', such as the ability to calve without human assistance for (double-muscled) cows or rooting behavior in pigs (125).

At the level of the population or species, references to (un)naturalness and nature related to applications that would cross natural species boundaries or that would affect the nature of a particular species. In the scientific literature on genetic modification in animals, some authors highlight the crossing of natural species boundaries as one of the main concerns regarding genetic modification (127). In the context of genetic modification in humans, these references were often related to concerns that genetic modification would alter 'human nature' in a problematic way (15,104). In response to these concerns, some authors argue that genetic modification technologies could be used to preserve rather than violate human nature (15). Similarly, some authors point out that it is contested whether human nature has intrinsic value and "*how much of a departure from human biological nature is necessary to bring about the loss of intrinsic value associated with remaining 'fundamentally human'*" (p. 673) (15). Moreover, some references mentioned that genetic modification could be considered to problematically affect the sanctity (127), integrity (113) or order of nature (128–130).

Finally, various references related to the integrity or intrinsic value of the modified entities also voiced concerns about instrumentalization. In the scientific literature, these concerns mostly concerned nature as a whole (108,117,131). It has for instance been argued that "*consumers who object to unnatural agricultural products may have distinct worldviews in which 'the instrumentalization of the nonhuman world is questioned to a larger extent' — that is, they may be more concerned than others about people manipulating the environment for their own use*" (p. 28) (108).

All in all, references that connected (un)naturalness to the integrity or intrinsic value of the modified entities were also common in the scientific literature. Such references occurred in scientific articles from all disciplines, but most frequently in ethics articles and very rarely in life science articles. These references occurred most in relation to animals and humans, sometimes in relation to plants and very rarely in relation to micro-organisms.

c) The appropriate attitude, place, or role of humans

Finally, references to nature and (un)naturalness in the scientific literature also expressed convictions or concerns with regards to the appropriate attitude, place, or role of humans in nature.

On the one hand, some of these references implied that humans should have a humble attitude towards nature and should not act in hubristic ways. Bjørn Myskja, for instance, mentions that:

> *Lay people's objections are directed at illegitimate intervention in nature, neglecting the restrictions of one's own power, captured in the Greek notion of hubris. (..) It is not the alteration of the species that is unacceptable, but rather the overestimation of control that is implicit in this particular technology. Such interventions are taken to display a lack of respect for nature as a form of existence that cannot and should not be completely controlled by humans* (p. 228) (111).

These concerns are often related to the stories of Frankenstein (a fictional scientist that created a monster) and Icarus (a character in Greek mythology who flew too close to the sun with wings constructed from feathers and wax) (129).

On the other hand, other references with regards to the appropriate attitude, place, or role of humans in nature implied that humans should interfere in nature using genetic modification. In these cases, nature is portrayed as something that can or should be improved by humans using genetic modification. Sheldon Krimsky describes, for instance, how the problem of vitamin A deficiency is "*seen as one of nature's failings, namely that its rice lacks beta carotene — something that can be easily fixed through biotechnology*" (p. 322) (132). Myskja, similarly, argues that "*reshaping nature according to our needs and desires is an expression of the essence of human nature. For humans, ''the artificial is natural''*" (p. 226) (111). According to Jane Calvert, this idea of improving nature underlies much of synthetic biology, as she illustrates by quoting the tag line of the website synthethicbiology.org: '*making life better, one part at a time'* (p. 100) (117). Some other references implied that it is 'natural' for humans to interfere in nature in this way. According to these authors, genetic modification is a natural extension of traditional breeding methods (107) or already existing medical interventions (133,134). Similarly, George Gaskell *et al.* mention that some people consider it "*natural for parents to want the best for their children"* (p. 1021) and to support germline modification for this reason (135).

Finally, some other references contend that humans should reveal nature's secrets (136) so these can be used for human benefit. This view is clearly linked to the previously discussed view of nature as a resource (120). Different references with regards to the appropriate attitude, place, or role of humans in nature also relate to the previously mentioned views of nature. For instance, if one views nature as vulnerable, it is especially important not to act in hubristic ways. And if one views nature as a resource,

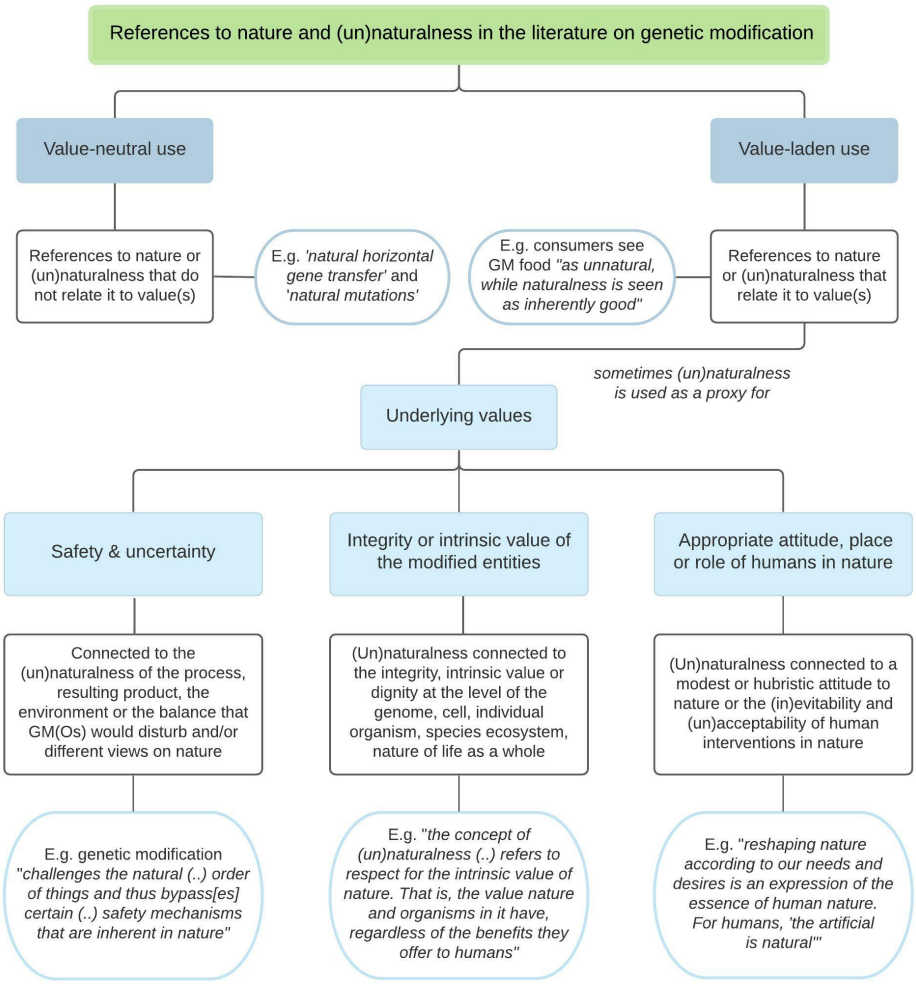
humans should use nature for their benefit. Henk Verhoog also reflects on this connection, distinguishing views of nature as "*benevolent and intrinsically good"* (warranting restraint in interventions in nature), as "*hostile and intrinsically bad"* (warranting interventions to tame nature or prevent bad consequences) or as "*neutral"* (with modern biotechnology as a neutral technique that can be used for good or evil) (p. 295) (113).

All in all, references to nature and (un)naturalness in the scientific literature also regularly expressed convictions or concerns with regards to the appropriate attitude, place, or role of humans in nature. This was most common in social science and ethics articles, and much less common in life science articles. References of this kind occurred in relation to applications in microbes, plants, animals, and humans alike.

2.5 Concluding reflections

In summary, references to nature and (un)naturalness in the literature on genetic modification were sometimes used in value-neutral, and sometimes in value-laden ways. The identified uses are summarized in Figure 2 below.

Figure 2: References to nature and (un)naturalness in the literature on genetic modification



Our analysis demonstrated that references to nature and (un)naturalness were used in different ways in different bodies of literature on genetic modification. While nature and (un)naturalness are more often used in value-neutral ways in laws and the life science literature on genetic modification, these terms are more often used in value-laden ways in the grey literature, social science literature and ethics literature.

Wherever the terms 'nature' and 'natural(ly)' are used in laws on genetic modification, they merely refer to the absence of human beings or human activity. Their use is value-neutral, as is also the case when 'natural' is used as an adjective in combination with 'person'. Occasionally, when the terms can be substituted with synonyms not merely referring to such absence (and without loss of meaning, by words like 'pristine', 'untouched', 'wholesome', 'traditional'), their use appears to be value laden. It is not implausible that these terms are more frequently used in a value-laden way in laws outside the realm of genetic modification.

In the grey literature and the scientific literature, nature and (un)naturalness are frequently used in value-laden ways. In these references, it frequently remains unclear what aspect or which consequence of genetic modification is considered unnatural and how, and for what reason this is considered problematic. Some value-laden references to nature and (un)naturalness bring up specific underlying concerns or values. These underlying concerns or values relate to (1) safety and uncertainty, (2) the integrity or intrinsic value of the modified entities or (3) the appropriate attitude or role of humans. The observed differences between positive law on the one hand and the grey literature and scientific literature on the other may be explained by the fact that – generally speaking – legislators attempt to be as neutral and factual as possible in the formulation of the law. Because laws need to be executable, the use of value-laden concepts could make a law too open to different interpretations. That is not to say that laws do not express values or moral choices; they do, of course, and a legislator can even choose to employ open norms and global concepts. In health laws for example, references to the 'professional standard' are numerous. Whenever health laws mention the professional standard, the legislator deliberately chose to rely upon the medical professional bodies to specify this. It is simply impractical (impossible even) for the legislator to determine upfront and in detail what exactly is meant by 'professional standard' in each and every circumstance. In this way, the legislator can willfully allow headroom for interpretation by others. But this is clearly not a choice the legislator – and subsequently the courts – made when using 'natural', 'unnatural', 'nature', 'naturalness' and 'unnaturalness' in the context of genetic modification.

As was discussed in the introduction, different applications of genetic modification have evoked discussions with different themes and dynamics. This could also be observed in the analyses presented here. Value-laden references to nature and (un)naturalness that linked to the integrity or intrinsic value of the modified entities for instance often concerned applications of genetic modification in animals and humans, sometimes in plants, and rarely in micro-organisms. This is in line with the general pattern observed in the literature that applications of genetic modifications in micro-organisms, for instance in industrial (white) biotechnology, are regarded more positively than applications of genetic modification in animals and, to a lesser extent, plants (40–42). This may, in turn, be explained by the fact that animals are commonly attributed a higher moral status or intrinsic value than plants and micro-organisms.

References that linked (un)naturalness to safety and uncertainty, and to the integrity or intrinsic value of the modified entities also more often concerned transgenesis than cisgenesis. The crossing of species boundaries was specifically mentioned as an intervention for which no 'natural reference' exists

to which a GMO can be compared, creating more uncertainty with regards to potential risks, and that could have a particularly large (negative) impact on an organism's integrity.

References to nature and (un)naturalness that expressed concerns about safety and uncertainty were most commonly related to animals, sometimes to plants, and less frequently to micro-organisms or humans. This may be considered surprising, given the fact that concerns about safety and risks feature frequently in discussions about genetic modification in humans (137,138). This finding could be explained by the fact that different underlying meanings of nature and (un)naturalness are used in this context, an issue that has not yet been analyzed and discussed in this chapter. As the introduction underlined, these terms are notoriously ambiguous and elusive, raising the question: what different meanings of nature and (un)naturalness can be identified and distinguished? This is investigated in more detail in the following chapters.

Chapter 3 – The meaning of nature: identifying overarching concepts

The previous chapter investigated the use of references to nature and (un)naturalness in laws, the grey literature, and the scientific literature on genetic modification. While it provided insights into the way in which references to nature and (un)naturalness feature in discussions on genetic modification, the *meaning* of the terms nature and (un)naturalness was not yet discussed in detail.

The aim of the upcoming chapters is therefore to create (more) clarity about this matter by exploring the meaning of nature and (un)naturalness in more detail. In this chapter, we start by identifying different *overarching* concepts of nature and (un)naturalness. Distinguishing between these concepts can stimulate and enrich discussions on genetic modification because it can avoid confusion between different concepts of nature and (un)naturalness. We take the philosophical literature on nature and (un)naturalness as a starting point, and use the concepts and ideas identified in this literature to reflect upon the analysis presented in the previous chapter in more detail.

3.1 Approach

Philosophers and ethicists have conceptually analyzed and debated the terms nature, naturalness, and unnaturalness for a very long time. In recent history, John Stuart Mill's essay on nature (7,139) in 1874 gave a new impetus to philosophical reflections on this topic. For this report, we conducted a narrative review[10] of conceptual analyses of nature and (un)naturalness. An initial list of relevant philosophy books and academic articles on nature and (un)naturalness, identified by the research team and the steering committee, was taken as a starting point. Subsequent screening of the reference lists of included books and articles – so-called cross-referencing – yielded many additional sources. Given the large amount of philosophical literature on this topic and since the way in which the terms nature and (un)naturalness are used has changed over time (140), we focused on contemporary books and articles on nature and (un)naturalness: books and articles that were published before Mill's essay were not included in our analysis. Moreover, since this report is written for a Dutch organization and situated in a Dutch and European context, we focused on analyses that may broadly be categorized under the header of contemporary Western philosophy. Only conceptual analyses, i.e. books or articles that distinguished various different meanings of nature and (un)naturalness were included and analyzed. In the process of analysis, different meanings of these terms were identified and the similarities and differences between these meanings were evaluated. The overview that was construed in this process was subsequently used to reflect upon the meaning of nature and (un)naturalness in the previously analyzed literature on genetic modification.

3.2 The meaning of nature and naturalness

An important point in an analysis about the meaning of the terms nature and naturalness is what 'meaning' itself is taken to mean. In the philosophy of language, writers on the theory of meaning distinguish two ways of indicating the meaning of a term (141), which are respectively referred to as its *extension* and its *intension*.

[10] A narrative review is a comprehensive yet non-systematic review of the literature on a particular topic (185).

The extension of a term is the set of objects in the world to which the term corresponds or to which it refers. The extension of the word 'cow', for instance, is all cows and cows only. The term nature, in turn, may refer to a particular set of animals, trees, plants, micro-organisms or landscapes. The *intension* of the word, in contrast, is the concept or idea that a term refers to. If one knows what characterizes a particular term – 'what it means' in the colloquial sense; what attributes can describe it – one knows its intension. A person that knows the intension of the word cow, for instance, knows that what characterizes cows is that they are domesticated animals, generally have four legs, have udders, etcetera. Intensions may also be abstractions that need not refer to anything that is real in the world[11].

Like the word cow, the term nature may both refer to concrete objects in the world and to more abstract concepts. It is "*as much a concept as a biophysical reality*" (p. 308) (17). In what follows, this is elaborated upon.

3.2.1 Nature as a biophysical reality

The meaning of the word 'nature' is less straightforward than that of the word 'cow' – to what specific objects in the world do we refer when we talk about nature? Would the tree in one's garden count as 'nature'? How about the plants in one's house? While it may be impossible to delineate the extension of nature[12], this short reflection underlines that 'nature' can refer to specific objects and observable features. In this case, nature refers to a biophysical reality (17,142): the nature of "*immediate experience and aesthetic appreciation*"[13] (p. 156) (21). It is invoked when we talk about nature referring to the "*ordinarily observable features of the world: the 'natural' as opposed to the urban or industrial environment (..), animals, domestic and wild, the physical body in space and raw materials*" (p. 156) (21). It is this nature that is at play when "*the Green movement speaks of nature*"; similarly, it is this nature that "*we have destroyed and polluted and are asked to conserve and preserve*" (p. 156) (21). It is also this nature that we see as a space for valuable experiences and activities, such as going hiking in the mountains, which bring us joy and may fill us with awe about the natural world (143). Questions around how we treat these 'natural' objects around us are one of the most pressing questions of our time. As the concerns about safety and uncertainty that were discussed in the previous chapter underline, these questions also play a role in the discussions on genetic modification. Similarly, references to nature in discussions about genetic modification frequently refer to (its effects on) nature as a biophysical reality, as is the case when it is stated that "*fears related to [the effects of] the escape of GMOs on public health have been accompanied by concerns about possible catastrophic effects on nature"* (p. 5) ever since the early years of DNA research (33).

[11] If I refer to 'the president of the Netherlands', for instance, I do not refer to any specific thing that exists in the world (while the Netherlands has a prime minister and a king, it does not have a president). Nonetheless, one can understand what this phrase means.

[12] As has for instance been pointed out by Gregory Kaebnick, 'nature' is not understood by learning rules on what belongs to its extension, but "by becoming familiar with the extension itself – by learning examples of the concept – and then, secondarily, on the basis of one's knowledge of the examples, gaining insight into the commonalities that knit the concept together" (p. 7) (24). He argues, based on Wittgenstein's account of concepts, that there is consequently a 'family resemblance' among the way in which people use the term. The next chapter, in which different conceptions of nature are discussed, also underlines this.

[13] Soper refers to this as the 'surface concept' of nature (21).

3.2.2 Concepts of nature

At the same time, references to nature and (un)naturalness not only refer to nature as a biophysical reality, but may also express a certain stance or conviction about this reality (5). These stances or convictions may be expressed in concepts (144). We make sense of the world around us through language, and through a worldview that is intricately connected to our culture, our time, and the words that are available to us. Rolston Holmes III argues that this makes concepts similar to maps, underlining that – like maps – concepts can represent particular parts of reality or represent them in a certain way. He writes:

> *There is always some sort of cognitive framework within which nature makes its appearance, but that does not mean that what appears is only the framework. Maps map the world; they selectively represent some of it, and 'nature' refers to this world-making activity out there* (p. 43) (145).

The results of this 'world making activity', the concepts postulated, are the subject of the analysis that follows. The map metaphor underlines that the natural world is something to be *discovered* (like the area that is represented on a map), but at the same time something that is *also* actively *constructed* (by the way in which it is represented) (140). When maps leave out particular parts of reality, we may get lost. When they only focus on representing the train rails, maps may be helpful for the train driver, but not to get a grasp of what other objects and infrastructure a certain area contains. And just like maps can leave out particular parts of reality or represent them in certain ways, concepts can too, and this very fact should make us critical about the way in which we systematize and articulate whatever it is we theorize or talk about. Only if it is substantiated what is (and is not) referred to when speaking about nature or the (un)natural, we can bring the way(s) in which nature is constructed more sharply into focus. By doing so, it becomes possible to critically assess what is seen as nature and (un)natural and what is not.

The urgency of such an evaluation is illustrated by the fact that a wide range of contentious issues have been defended with appeals to nature, including slavery, the man as the head of the household, and the condemnation of homosexuality (44). This underscores that what is seen as natural may itself be a cultural construct that also tends to anchor the interests of those in power (146). These insights serve as a warning that appeals to nature may "*be used to objectively present one's own prejudice*" (p. 110) (44). Therefore, such appeals should be critically examined to ensure that they do not have unjust implications, motivations or uses (21,24). At the same time, the relevance of this analysis is underlined by the reality 'out there'[14] whose existence raises questions about what we should and should not do to it.

In what follows, different concepts of nature that have been identified in the philosophical literature are discussed in general terms. It is shown that references to nature and (un)naturalness invoke different concepts of nature, and that separating these concepts provides insights regarding how to interpret the meaning of nature and (un)naturalness in the previously analyzed discussions on genetic modification.

[14] Without this reality 'out there', in the words of Svein Anders Noer Lie (186), "*fighting pollution, [or] defending a (..) forest from 'destruction' are just meaningless phrases produced by a social group that wants to defend a particular constructed idea about how that group wants nature to be*" (p. 4).

3.3 A conceptual analysis of nature and (un)naturalness

As the previous chapters have made clear, the terms nature and (un)naturalness are used in myriad ways. The way in which these terms are used has changed over time (140), varies across cultures (147), and may change in response to technological developments (148). As a result, any attempt to cluster the ways in which these terms are used will be incomplete, as well as time- and context-dependent. Despite this, however, our narrative review of contemporary conceptual analyses of nature and (un)naturalness also demonstrated significant overlap between different conceptualizations and categorizations. In what follows, we describe three overarching concepts of nature encountered in this literature, which may be described as respectively (1) nature as the 'non-human'; (2) 'entangled nature'; and (3) nature as the 'essential characteristics of a thing'.

In what follows, these overarching concepts are summarized shortly, and related to the analysis of the law, grey literature, and scientific literature on genetic modification. For each of the identified concepts, different interpretations have been postulated, which are discussed in more detail in the next chapter.

3.3.1 Nature as the non-human

The first overarching concept that arguments concerning nature, naturalness and unnaturalness may refer to is the concept of nature as the non-human: nature as "*the concept through which humanity thinks its difference and specificity*" (p. 155) (21). Dieter Birnbacher defines nature as that which "*would exist without humans and would exist in the way it does without humans*" (149) and John Stuart Mill as that "*what takes place without the agency, or without the voluntary and intentional agency of man"* (139). The 'natural' conceptualized this way thus refers to the living and non-living entities that are independent from human beings or human influence. It is often contrasted to the 'unnatural', the 'artificial' or the 'artifactual (4,139,150). This concept of 'nature' is also contrasted to 'culture', which correspondingly refers to the 'human-made' (143,151,152).

As the previous chapter made clear, this concept of nature features very frequently in laws, the grey literature, and the scientific literature on genetic modification. It is, for instance, this concept that is invoked when authors speak of '*natural mutation*s' (16) in contrast to mutations that happen due to genetic modification induced by humans. In these references, the terms nature and natural are regularly used to refer to organisms, genetic constructs or processes in the 'wild', i.e. that have not been constructed or modified by humans, for instance in a laboratory. Indeed, references to nature in the grey literature also often explicitly contrast nature to society (153), culture (153) or ourselves (i.e. humans) (87). Various different interpretations of this concept of nature as the non-human also feature in discussions about the role of humans in nature or the attitude humans should have towards nature, i.e. whether humans should for instance be 'dominators', 'stewards' or 'partners' of nature (5,78,92,154). The fact that this concept excludes humans from nature may explain the fact that the references to nature and (un)naturalness that expressed concerns about safety and uncertainty less frequently concerned humans. Even though safety concerns are prominent in discussions on genetic modification in humans, these would not be associated with (un)naturalness if humans are considered 'unnatural' to begin with.

When it comes to distinguishing the 'natural' from the 'unnatural', some positions view all human actions or entities influenced by humans as unnatural, whereas other positions look at (un)naturalness as a gradual or multidimensional property. These different positions are explored in the next chapter.

3.3.2 Entangled nature

The second overarching concept of nature refers to what may be called 'entangled nature'. According to this concept, humans are a part of, rather than separate from nature. Humans and nature are, in other words, entangled in one or various ways. Some authors for instance refer to nature as the "*totality of all there is"* (21): the entire physical world that is controlled by the laws of physics, chemistry, and evolutionary biology. It is this nature we refer to when we speak of 'natural laws' or of 'Mother Nature' (17). Mill referred to it as "*all the powers existing in either the outer or the inner world and everything which takes place by means of those powers*" (139). This idea has been tied to religion as much as to modern science. In a religious context, observations of order and principles in nature have been taken to imply that it must have been designed by a supernatural entity, i.e. God. In a scientific context, it is tied to what has been called the 'world machine'; the view of nature as a great machine that is driven by particular principles (140). It is this concept that is expressed when we talk about 'natural laws' or 'laws of nature', and this concept that is invoked when concerns about disrupting the 'natural order' are expressed.

This concept of nature is also expressed by authors like William Cronon, Donna Haraway and Val Plumwood, who have argued that we should abandon the dichotomy between the natural and the artificial, between nature and culture, between the non-human and the human altogether (155–157). According to these authors, nature and culture are not contradictions: culture shapes nature and nature influences culture. For this reason, Haraway and others speak of 'naturecultures' rather than referring to nature and culture as domains that can be separated (151,156). Positions that consider humans a 'participant' in nature profess a similar view (5,78,92,154).

This concept of nature also features in the grey literature and scientific literature on genetic modification. The debate participant that states that "*it is inevitable that humankind harms nature, humankind is a part of nature, after all"* (p. 62) (41), for instance, considers humans to be part of nature. This concept is also invoked when it is stated that 'naturalness' may refer to being "*in congruence with the laws of nature*" (p. 18) (5). Similarly, it features in references to nature and (un)naturalness that underline that genetic modification could disturb a certain balance in nature, and thereby cause unpredictable and undesirable effects. In these references, humans are not placed outside of nature, but the focus is rather on the natural order, and what consequences disturbances of this order can have.

3.3.3 Nature as the essential characteristic of a thing

The third overarching concept of nature is that of nature as the essential characteristics of a thing, i.e. "*that which makes it what it is and not something else, its ontological identity card*" (p. 7) (158). This concept of nature relates to the scientific study of taxonomy, which categorizes different organisms into different organic species that have characteristic features, properties and tendencies (158). It is the kind of concept of nature that is invoked in discussions about the crossing of species boundaries or when it is claimed that something is or is not in line with 'human nature' (21,150,158). Different conceptions of this

concept exist that each provide their own specific view on what they take nature to consist of. Some conceptions ground this concept of nature in a common biological essence, whereas others ground it in the way a particular type of being behaves (21). These conceptions are explored in more detail in the next chapter.

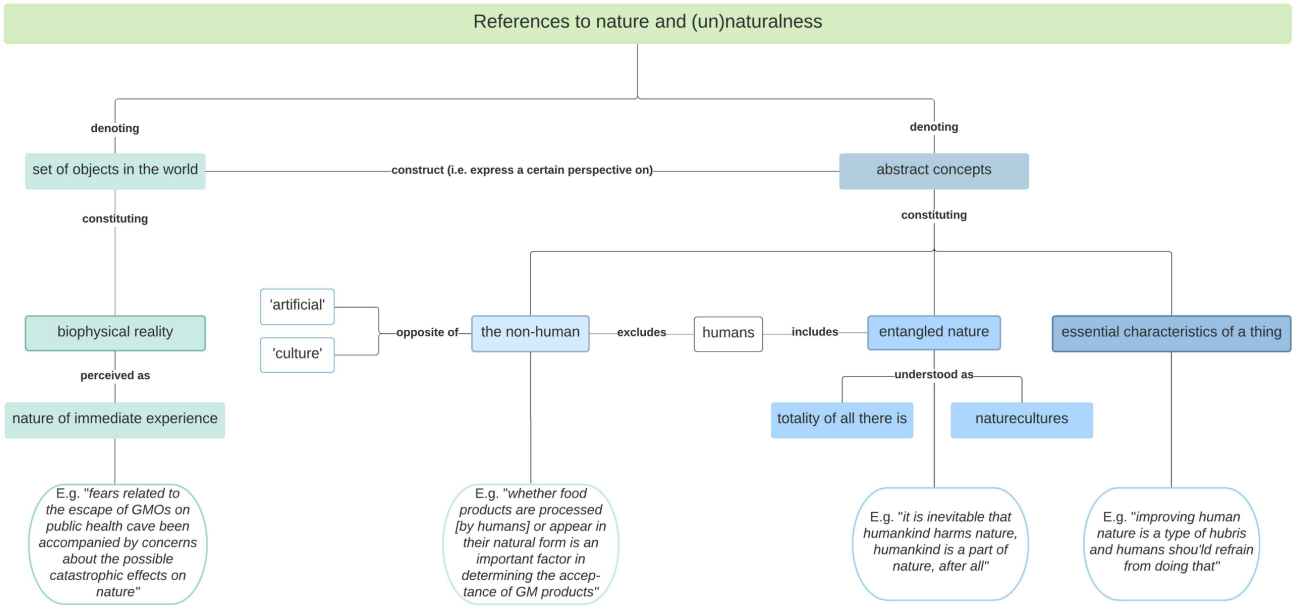
This concept also featured in the grey literature and scientific literature on genetic modification, albeit less frequently than the other concepts of nature. Where it was used, it either referred to 'human nature' or the nature of animals. With regards to the former, a report commissioned by the Rathenau Institute for instance mentioned that some bioconservative ethicists argue that "*improving human nature is a type of hubris and humans should refrain from doing that*" (p. 48) (159). Similarly, it is this concept of nature that was invoked when it is argued that "*reshaping nature according to our needs and desires is an expression of the essence of human nature. For humans, 'the artificial is natural'*" (p. 226) (111). It is natural to reshape (non-human) nature, according to this argument, because our tendency to reshape it according to our needs and desires is part of who we are; it is one of our essential characteristics.

With regards to the nature of animals, this concept for instance featured in references to nature and (un)naturalness in which it was argued that animals should be able to portray their natural (species-specific) behavior (83). Similarly, this concept was invoked in references that connected the naturalness or integrity of animals to their 'telos', i.e. their "inherent nature" (p. 120) (82).

3.4 Concluding reflections

This chapter has set a first step in the journey of exploring the meaning of nature and (un)naturalness. The identified overarching meanings are summarized in Figure 3 below.

Figure 3: Overarching meanings of nature and (un)naturalness



Our analysis has demonstrated that nature is both a biophysical reality and an abstract concept, and that it important to critically reflect on the relationship between the two. Just like maps can represent the

world in certain ways, leaving out particular parts or only showing particular perspectives (such as those that were relevant to the mapmaker), concepts of nature can also represent the biophysical reality they refer to in certain ways and leave out particular parts. The fact that a wide range of contentious issues, ranging from slavery to the condemnation of homosexuality, have been defended with appeals to nature underlines how important it is to identify how particular concepts construct nature.

In this initial analysis of the meanings of nature and (un)naturalness, three key overarching concepts of nature were identified: (1) nature as the non-human; (2) entangled nature; and (3) nature as essential characteristics. To understand the meaning of references to nature and (un)naturalness in the literature and discussions about genetic modification, these different concepts should be distinguished to avoid confusion about the terms we use and the meanings they convey. Looking back upon the examples of references to nature and (un)naturalness that were mentioned in the introduction, for instance, we can now deduce that different concepts of nature were used as if they were interchangeable. When it is argued that "*the creation of genetically modified plants is unnatural*" (p. 41) (18), this is based on a concept of nature as the non-human, whereas people that contend that "*all technological actions that make use of scientific knowledge of the physical environment are natural*" (p. 18) (5) base their argument on a concept of nature as 'entangled nature'. George Church, the synthetic biologist who argued that "*engineering is one of the main things that humans do well. (…) It's just what we do and it's natural"* because "*we're not doing something we're not designed (and microevolved) to do"* (p. 114) (20), seems to base his argument on yet another concept of nature: nature as essential characteristics. As engineering our environment – for instance through genetic modification – is one of humankind's essential characteristics, the argument goes, it is entirely natural.

As these examples illustrate, distinguishing these concepts may enable a more effective discussion. People that discuss the (un)naturalness of (applications of) genetic modification can base themselves on different concepts of nature, and thereby speak past each other. If the aim of a discussion is to attempt to engage with what one's discussion partner says, mixing up these different concepts results in confusion that can and should be avoided.

At the same time, this overview of overarching meanings of nature is just that: an overview of *overarching* meanings. For the different concepts that were identified, different specific formulations – so-called 'conceptions' that each provide their own specific view on what they take nature and naturalness to mean – have been postulated. These different conceptions are investigated in more detail in the next chapter.

Chapter 4 – Identifying different conceptions of nature and (un)naturalness

As will be clear by now, nature and (un)naturalness are notoriously elusive terms. Although their ambiguity may be reduced by distinguishing between the *overarching concepts* of nature that were identified in the previous chapter, these concepts are still quite imprecise. What do these concepts imply for what it means for something to be natural or unnatural?

In what follows, we explore this in more detail by identifying *specific conceptions* of the natural and unnatural that have been identified in the philosophical literature. These different conceptions all relate to the same concept (e.g. nature as the non-human), but each put forward a different view on what nature and (un)naturalness are taken to mean. In doing so, we pay particular attention to the way in which these different conceptions distinguish between the natural and the unnatural and relate these to the references to nature and (un)naturalness that were identified in Chapter 2.

4.1 Nature as the non-human: a further exploration

4.1.1 An all-or-nothing conception

In the broadest conception of nature as the non-human identified in the philosophical literature, anything that humans do is unnatural, as is any entity that is either human in origin or influenced by humans in the course of its history (4). As has been noted by various authors, this 'all-or-nothing' conception of nature as the non-human has far-reaching implications for our evaluation of nature on planet earth. Not only large cities or industrial areas are shaped and influenced by humans; wilderness areas, too, are actively managed by humans. From the Oostvaardersplassen in the Netherlands (160) to Yellowstone National Park in the USA (161) or Kruger National Park in South Africa (162), humans play an essential role in shaping wilderness areas worldwide. Although these areas may commonly be viewed as prime examples of non-human nature, they are actually deeply influenced by humans (p. 7) (155)[15]. Contrary to this, on an all-or-nothing conception of nature these parcs would not be considered nature, and 'nature management' would be a *contradiction in terminis* (142).

The world around us is also influenced by humans in other ways, such as through the effects of climate change on ecosystems, species and biodiversity across the world. In fact, living in the 'Anthropocene', the geological epoch determined by human impact[16] on geology and ecosystems, our influence may be so big that nothing is free of human interference. Some authors have indeed argued that as a result of this large-scale influence, our planet no longer possesses any nature. Environmental journalist Bill McKibben, for example, has argued:

> *We have changed the atmosphere and so we are changing the weather. By changing the weather, we make every spot on earth man-made and artificial. We have deprived nature of its*

[15] It has also been pointed out that an all-or-nothing conception of nature as the non-human has been used to justify oppression of particular groups of people, including but not limited to the prior inhabitants of wilderness areas (21,155).

[16] It should be noted that this impact is not created equally by all humans, but predominantly by rich Westerners (146).

> *independence, and that is fatal to its meaning. Nature's independence is its meaning; without it there is nothing but us* (p. 56; emphasis in original) (163).

If one adopts this all-or-nothing conception of nature as the non-human, then it would be impossible to delineate the natural from the unnatural, for there would be no nature left in the world. Moreover, from this perspective, genetic modification could not be said to have any particular effect on nature whatsoever, as each and any human act or intervention in the non-human world would be considered unnatural. If unnaturalness is interpreted in a value-laden way, this goes against the commonly accepted viewpoint that at least *some* human actions are morally neutral or good. As a report on genetic engineering by the 'President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research' phrased it:

> *In one sense all human activity that produces changes that otherwise would not have occurred interferes with nature. Medical activities as routine as the prescription of eyeglasses for myopia (..) are in this sense 'unnatural'* (p. 55; emphasis added) (164).

These activities, the report appears to suggest, can impossibly be considered morally objectionable, and the conception of nature that underlies it can thus not serve as a moral foundation for what we should and should not do. It is for this reason that Mill has argued that arguments that base themselves on this conception of nature should be considered irrational (139). On similar grounds, Cronon has contended that a focus on this conception prevents us from taking our negative effects on the environment seriously; to the extent we see nature as the non-human in this radical way, he contends, "*we give ourselves permission to evade responsibility for the lives we actually lead*" (p. 17) (155). Interestingly, and likely for these same reasons, this conception of nature as the non-human was not encountered in the references to nature and (un)naturalness in laws, the grey literature, and the scientific literature on genetic modification.

4.1.2 Gradual and multidimensional conceptions

Rather than viewing all human action as unnatural and nature as those entities that are *completely* free from human interference, other less radical philosophical conceptions of nature as the non-human distinguish between the natural and the unnatural on other grounds and in more nuanced ways. Rather than merely viewing all human action and entities influenced by humans as unnatural, these conceptions raise the question: "*natural with respect to what or in comparison to what?*" (p. 17) (24).

Some philosophers defending these conceptions have argued that 'nature' does not refer to those entities that are *completely* free from human interference, but rather, free from *particular types* of human interference. In this view, specific human interferences are deemed unnatural, as are the entities which are subject to them. Others see (un)naturalness as something that comes in degrees and that can be represented as a spectrum or continuum, with that what is clearly produced by humans (such as the laptop on which this report is typed) on one end of the spectrum, and that what is (most) free of human intervention (such as much of the universe beyond the earth) on the other end (24,150). In the grey literature on genetic modification, gradual conceptions of nature as the non-human also feature

frequently. It is, for instance, often stated or implied that things can be *more* or *less* natural. A report on organic agriculture, for instance, states:

> *A striking example of becoming increasingly unnatural (..) is the breeding of larger farm animals. Step by step (selection, artificial insemination, in vitro fertilization, embryo transplantation, genetic manipulation and cloning) the reproduction of the animal is 'expropriated'* (p. 23) (91).

A report commissioned by the European Parliament on governance challenges in 21st century bio-engineering also uses a gradual conception of naturalness; it features a figure that classifies organisms on a spectrum from 'altogether natural' to 'altogether synthetic' (p. 192) (165,166) depending on the way and 'level' at which humans have interfered with these organisms.

Finally, other philosophers see naturalness as a multidimensional concept, in which entities can be natural or unnatural on different dimensions (and may be considered natural on one dimension, yet unnatural on another). Birnbacher for instance contends that:

> *a bonsai can clearly be seen from its relation of size to be 'artificial'. Yet because, according to its composition, it is made up of the same lignin as a normal tree, it can without doubt be judged to be more 'natural' than an ornamental tree out of plastic, which according to form correlates more strongly with a natural tree* (p. 13) (150).

In the grey literature on genetic modification, the references that rested upon a gradual or multifactorial conception of nature as the non-human generally did not specify *what* makes something more or less (un)natural. In the philosophical literature, two overarching conceptions of naturalness were identified: 'history-based' conceptions of naturalness that consider something unnatural based on a particular type of human interference, and 'property-based' conceptions of naturalness that consider something unnatural based on its properties. These conceptions are explored in some more detail in what follows.

a) History-based naturalness

According to some conceptions in the philosophical literature, particular human actions can be considered unnatural, as can any entity that is affected by these actions in their history. Helena Siipi refers to this as 'history-based (un)naturalness' (3), whereas Birnbacher calls it 'genetic naturalness or artificiality' (150). These conceptions of naturalness – some of which are discussed in what follows – differ in terms of what interferences are considered to render something unnatural.

Some conceptions that conceive of naturalness as a continuous gradient consider entities more unnatural if humans "*have spent more time, effort, and/or more interfering types of actions*" to modify these entities (p. 81) (4). Clearly, this conception raises questions about how effort is determined and, particularly, on what grounds actions can be considered 'more interfering' (3). To provide insight into the meaning of naturalness, this conception would thus need to be complemented by an account that stipulates which types or kinds of human activities are more interfering. An example of such a conception can be found in a paper on (un)naturalness in which it is argued that one can determine the degree of

unnaturalness by distinguishing between human interventions that directly "*alter an entity's essence*" and interventions that indirectly cause an entity to change its essence itself in response to human action (p. 11) (126). It is, in this view, more natural to indirectly cause a non-virulent bacterium to develop into a virulent bacterium (by exposing it to the dead remains of virulent bacteria), than to directly insert human DNA into a bacterium through genetic engineering to create insulin-producing bacteria.

Another history-based conception understands naturalness as "*independence from certain types of human activities*" (p. 81) (4). In her discussion of examples in which these conceptions of naturalness were brought forward, Siipi mentions several activities that have been contended to make entities (more) unnatural, such as the use of technology. History-based (un)naturalness can also be related to *artifactuality* (4). According to this interpretation, an entity is unnatural if it *is an artifact,* and an action is unnatural if it *turns an entity into an artifact.* This conception, in other words, problematizes the fact that 'natural' processes come under human control. For this conception, a specific definition of artifactuality would be needed to distinguish the natural from the unnatural in a meaningful way. On a more general level, it is interesting to note that this conception of naturalness relates closely to the references to nature and (un)naturalness in the grey literature that expressed concerns that genetic modification could instrumentalize organisms and insufficiently acknowledge or harm their integrity or intrinsic value.

b) Property-based naturalness

Other conceptions of nature as the non-human in the philosophical literature instead focus on the properties of an entity, rather than on its history. Siipi refers to this kind of naturalness as 'property-based' naturalness (3), whereas Birnbacher calls it 'qualitative naturalness' (150). In contrast to history-based accounts, these conceptions of nature as the non-human do not consider entities unnatural because they were influenced by (particular forms of) human intervention in their history, but instead evaluate their properties. Siipi illustrates the general idea with an example:

> *A genetically modified sheep that produces human proteins in its milk, for example, is unnatural with respect to its (..) properties, because it has a property (the production of human protein) that is usually foreign to sheep* (p. 173) (3).

This conception of naturalness is also adopted by proponents of 'retouched' nature, environmental restoration and 'rewildling' (24). Proponents of these approaches propose to recreate the nature that has already been lost to create environments with the same properties, whereas opponents - adopting a history-based conception of naturalness - consider the idea of 'nature' that is 'retouched' by humans a contradiction in terms.

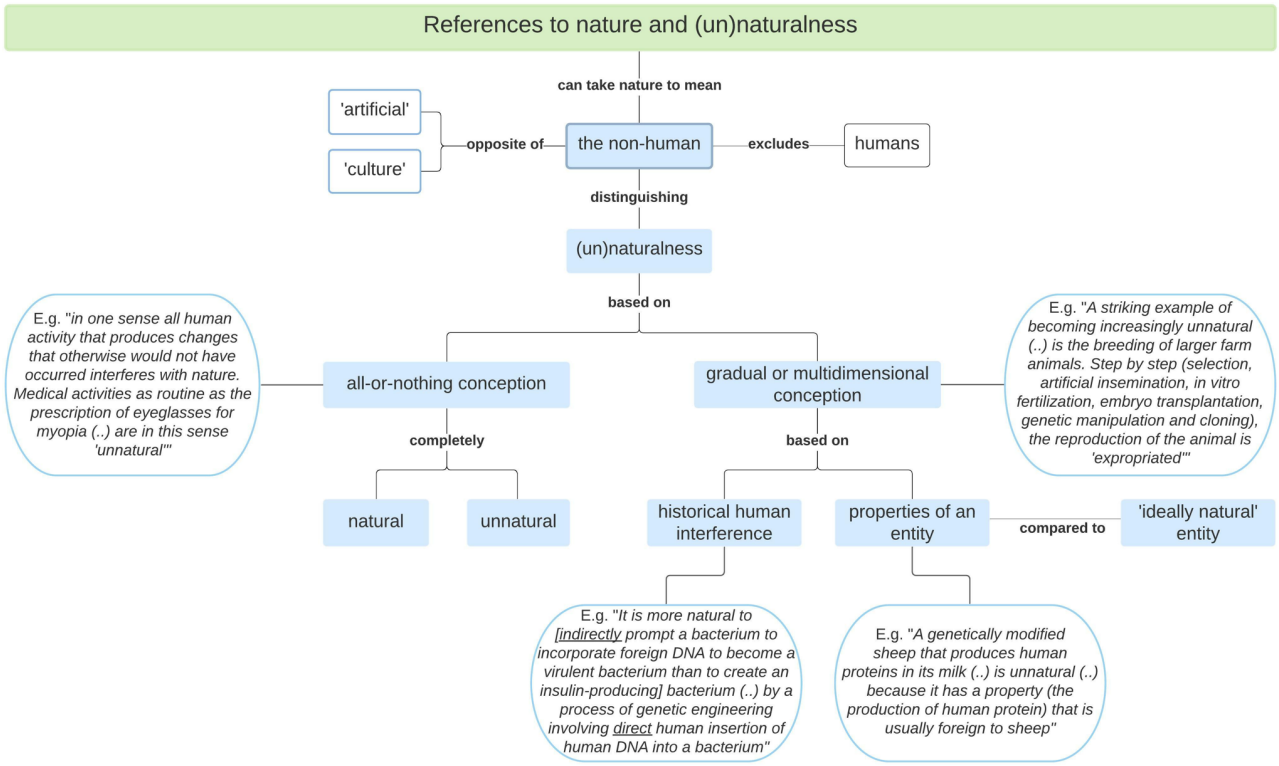
Property-based conceptions of naturalness focus on the *current* properties of an entity, always in comparison to the properties of some 'ideally natural' entity (3). If the properties of the entity are in line with the properties of this ideal entity, the entity is considered natural. If this entity is an *object* (e.g. an organism or a genome) it may for instance be compared with what Siipi calls 'historically natural' entities, i.e. entities that are independent of particular human activities. On this conception of naturalness, entities can be natural even though they have been influenced by particular human activities (such as the activities mentioned in the previous section, like the use of technology), as long as their *properties* resemble the

properties of entities that were not influenced by these activities. This is, essentially, the conception of naturalness of those that propagate a 'product view' in the GMO debate that was discussed in Chapter 2. In this view, naturalness is determined based on "*the way the genetic material is rearranged*" (p. 12, footnote) (79). In other words: "*the technique used to rearrange the DNA is irrelevant, as long as the rearrangement could have taken place in nature",* thus excluding many organisms modified by CRISPR from the GMO legislation (p. 12, footnote) (79).

Other property-based conceptions of nature, in contrast, compare the properties of an *action* with the properties of another "*genetically and biologically based action*" (p. 183) (3). Indeed, the 'process view' in the GMO debate is based on this conception of naturalness. In this view, it is not the way in which the genetic material is rearranged that counts, but the method used: "*all techniques that do not take place naturally fall within the scope of the GMO Directive. In nature, CRISPR-Cas9 does not cut genetic material in plants and therefore the CRISPR crops should be regulated as GMOs"* (p. 12, footnote) (79).

All in all, then, large differences can be identified between conceptions of nature as the non-human. Some conceptions view all actions or entities influenced by humans as unnatural, whereas others only view particular actions or entities as unnatural based on their history or their properties. Moreover, conceptions differ regarding whether they consider (un)naturalness as a dichotomy (natural versus unnatural) or a continuum. The identified conceptions are summarized in Figure 4 below.

Figure 4: Different conceptions of 'nature as the non-human'



4.2 Entangled nature: a further exploration

According to the concept of entangled nature, humans are seen as a part of rather than as separate from nature. In one of its broadest conceptions, this implies that every human action and every entity on earth can be considered natural. A report commissioned by the COGEM also identifies this conception, stating that:

> *According to some, all technological acts that make use of scientific knowledge of the physical environment are natural. In this meaning, 'naturalness' is taken to mean 'according to the laws of nature', and every human and non-human activity is natural. Neither xenotransplantation nor genetic modification goes against natural laws. In this view, naturalness is not a morally charged qualification, but an indication of an object area* (p. 18) (5).

John Stuart Mill expressed a similar view in stronger terms, arguing that this type of naturalness not only is not, but *cannot* be a morally charged qualification. He stated:

> *Taken to be the entire system of things, with the aggregates of all their properties, the doctrine that man ought to follow nature is unmeaning; since man has no power to do anything else than to follow nature; all his actions are done through, and in obedience to, some (..) or many of nature's physical or mental laws* (139).

Other appeals to entangled nature stress that while humans *are* in fact part of nature, they sometimes mistakenly do not consider themselves to be. In other words, these references are value-laden and relate to the appropriate place of humans in nature or the appropriate attitude of humans to nature. They express the views that while humans, being part of nature, are generally free to interact with the non-human environment, *particular* types of actions in or attitudes towards this environment are not acceptable. References to unnaturalness based on this conception of entangled nature are closely connected to the idea of 'playing God'. Such references voice the intuition that humans should not consider themselves capable of controlling the 'totally of all there is', for instance by means of biotechnology (44). Sometimes, references of these kind are tied to 'God' in its religious meaning. A report on biotechnology and philosophies of life, for instance, mentions that:

> *At the center of [the Hindu] ethic is respect for all living things (..). Some contend that genetic modification is not allowed in any shape or form, because God created the laws of nature. Whoever violates these laws must reckon with the sanctions of God* (p. 8) (97).

In many other instances, these references are not tied to 'God' in its religious meaning. Rather, they express that humans should not pretend to be omnipotent, and underline that messing with the laws of nature can have a large, inherent uncertainty. If humans interfere in this nature too lightly or in particular ways, so these arguments go, they can (and perhaps will) wreak great havoc (44). As Henk van den Belt observes:

> *The God of 'playing God' is not necessarily the God of the Bible, but rather 'deified nature' (..) Also to modern secular minds, there appear to be lines that may not be crossed and boundaries that may not be breached (..) Overstepping these boundaries may be construed as inviting unknown and unprecedented risks* (p. 265) (167).

This was also expressed by some value-laden references to nature and (un)naturalness in the grey literature. The previously quoted report on biotechnology and philosophies of life, for instance, also mentions that:

> *New Age representatives have an elaborate philosophical belief system: everything is energy and interconnected. The body is just appearance, a shell, and therefore individuals have different views on genetic modification. There is a universal source of love, which connects everything with each other and with nature. (..) [According to some New Age representatives,] genetic modification is seen as a "disruption of the whole": "If you change one characteristic, you change more than that."* (p. 53-4) (97).

Some of the references to nature and (un)naturalness based on this conception of nature may also be interpreted as warnings against hubris: if the natural order is violated, like was the case when Icarus engaged in the superhuman act of flying, the consequences may be severe – to which Icarus' fate testifies.

In the philosophical literature, finally, other scholars have argued that we should altogether abandon the dichotomy between the natural and the artificial, between nature and culture, and between the non-human and the human (155). Plumwood, for instance, has argued that this separation both denies "*the mind-like aspects of nature and the nature-like aspects of the human: for example, human immersion in and dependency on an ecological world*" (p. 116-7) (157). The point that authors such as Plumwood make is that nature and culture are not contradictions: culture shapes nature and nature influences culture. Such a view of nature is also common in many non-Western settings (157,168). Acknowledging this entanglement of nature and culture, Haraway and others speak of 'naturecultures' rather than referring to nature and culture as domains that can be separated (151,156). The plurality of the term 'naturecultures' implies that nature and culture are imagined and produced in various ways (169,170). Nature and culture are, in other words, "*inseparable, entangled and mutually constituted"* and encompass and "*include the multiple perspectives of disciplines and worldviews"* (p. 11) (147).

This also has ethical ramifications in relation to how we regard and live in the world (171). On the one hand, it "*resituates humans in ecological terms*" (p. 2) (172)[17] , i.e. it underlines that we "*should both understand ourselves to be, and actually live with a recognition that we are, a part of the broader more-than-human community of life on which we all depend*" (p. 108) (171). On the other hand, it "*resituates non-humans in ethical and cultural terms*" (p. 2) (172)[18], i.e. it underlines that we should acknowledge that "*non-humans are valuable in and of themselves, that they very often possess their own 'cultures', their own ways of relating and living that should be respected in as much as it is possible to do so*" and that they "*contribute vitally to our own ethical and cultural worlds*" (p. 108) (171)(172). This does not mean that it

[17] Quoted in (171).
[18] Quoted in (171).

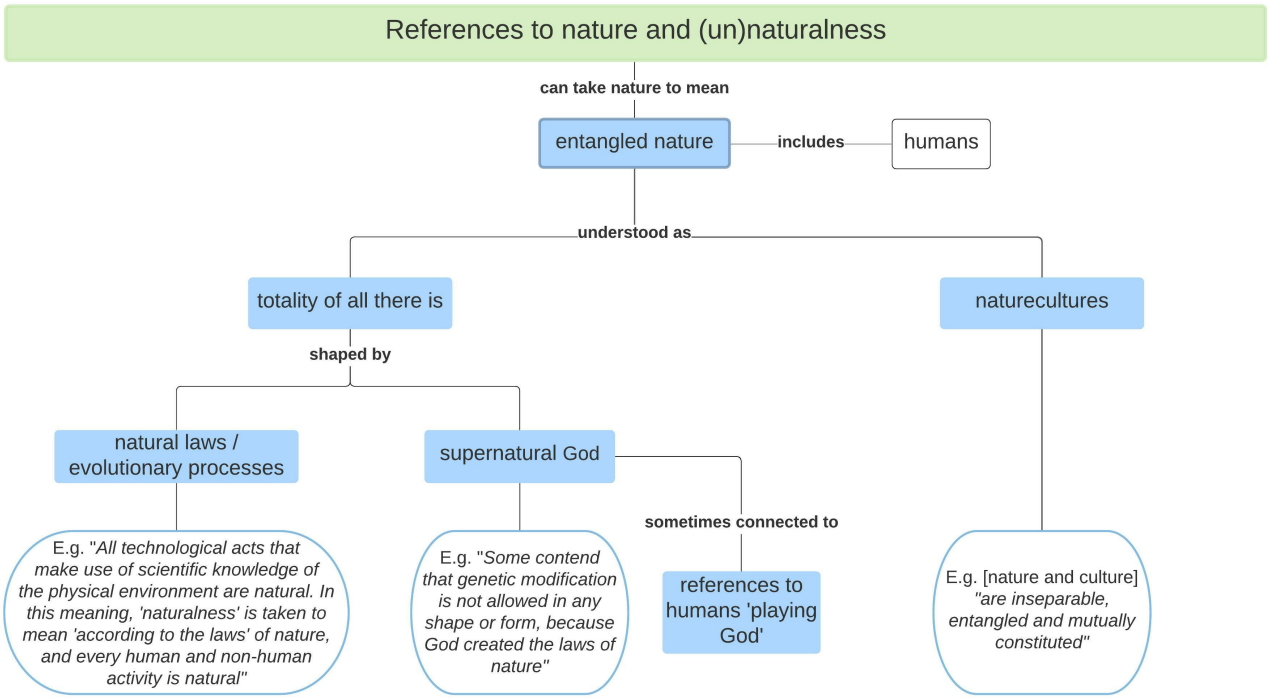
is necessarily wrong (or possible to avoid) to use non-humans, but it does invoke discussions about how this can be done in a way that non-humans are not only seen and valued to the extent that they are useful to humans (171). This view thus links closely to two underlying values and concerns that were identified in references to nature and (un)naturalness in the grey literature: the integrity or intrinsic value of non-human entities, and the appropriate attitude of humans towards or place of humans in nature.

A similar attitude, finally, is expressed in views that consider humans as participants of nature, which is also discussed in various reports in the grey literature on genetic modification. Biological, organic and biodynamic agricultural practices are often considered to be examples in which this view on nature is embodied. A report on biotechnology in plants, for instance, states that in this view:

> *Nature is the whole of interdependent and intertwined life forms. Man is an inseparable part of this nature. Therefore, he owes respect to the various forms of life, not only on the basis of the intrinsic value of other organisms, but also on the basis of the complexity of nature: the countless relationships between organisms have a surplus value that exceeds the usefulness to humans. The participant (..) cannot avoid intervening in nature for food production, but he tries to respond as much as possible to the inherent dynamics of natural processes. Biodynamic agriculture tries to give further substance to this (..)* (p. 30) (78).

In summary, conceptions of entangled nature all consider humans a part of nature. In some conceptions, nature is tied to God, whereas other conceptions consider nature to be shaped by natural laws and evolutionary processes. The identified conceptions are summarized in Figure 5 below.

Figure 5: Different conceptions of 'entangled nature'



4.3 Nature as the essential characteristics of a thing: a further exploration

Finally, nature may also refer to the 'essential characteristics of a thing'. As the previous chapter outlined, this concept of nature is for instance invoked when genetic modification creates organisms that cross species boundaries or when it is used to alter humans in ways that are considered 'enhancement' (21,150,158). According to this concept, those changes that affect or remove any of these essential characteristics could be seen as going against nature[19].

This concept was least commonly invoked in the grey literature on genetic modification. Sometimes, it was used to justify or normalize particular behavior, such as when it was suggested that "*anthropomorphism is part of our nature*" or that "*transhumanists do not consider it unnatural to change 'humankind'. Instead, they contend we have been doing that since time immemorial*" (p. 47) (159). At other times, it was used to condemn interventions that changed particular characteristics of a species that were deemed essential or fundamental in some way. Sometimes, this was also more implicit, as was the case in references that stressed that animals should be able to carry out their 'natural (species-specific) behavior' (83).

References in the grey literature that invoked this concept of nature generally did not specify which characteristics are taken to be the essential characteristics that should not be infringed upon. In the philosophical literature, however, different conceptions (each providing their own specific view on what they take this concept of nature to consist of) exist. As is discussed in what follows, some conceptions ground this concept of nature in a common (biological) essence, whereas others rather understand it along evolutionary lines (24).

4.3.1 Essentialist conceptions

Essentialist conceptions take the strongest view of what the nature of a species is: "*a metaphysical explanation of why things in that category belong to that category*" (p. 158) (24). According to these conceptions, all members that belong to a particular category – such as the human species – share this essence, whereas the members that belong to other categories lack it. It is this kind of nature Jürgen Habermas talks about when he raises questions about a 'species ethic': questions about what is needed to protect the essence of the species (16).

What precisely essentialist conceptions take to be the substrate of the essence of different species, differs per conception: some conceptions focus on biological aspects, and for instance take a species' genetic code as the basis for its nature. Francis Fukuyama, for instance, refers to human nature as "*the sum of the behavior and characteristics that are typical of human species, arising from genetics rather than environmental factors*" (p. 130) (173). Other conceptions also include other characteristics as essential to particular species, including characteristics in the sphere of culture and technology and those that relate to how a species behaves (150). Whereas some conceptions explicate which characteristics are essential to this kind of nature, other conceptions do not. Fukuyama, for instance, considers human nature to be a non-definable range of traits that he dubs 'Factor X' (173). According to him, in other words, human

[19] According to some, this is considered a bad thing. Some bioconservatives, for instance, argue that we should refrain from interfering with 'human nature'. On the other side of the spectrum, so-called 'transhumanists' believe doing so would be morally desirable, as doing so would allow us to overcome the limitations of our current existence (150).

nature cannot be reduced to the possession of some particular human quality but constitutes a range of indeterminate qualities that make us human and that provide the foundation for human dignity.

4.3.2 Evolutionary conceptions

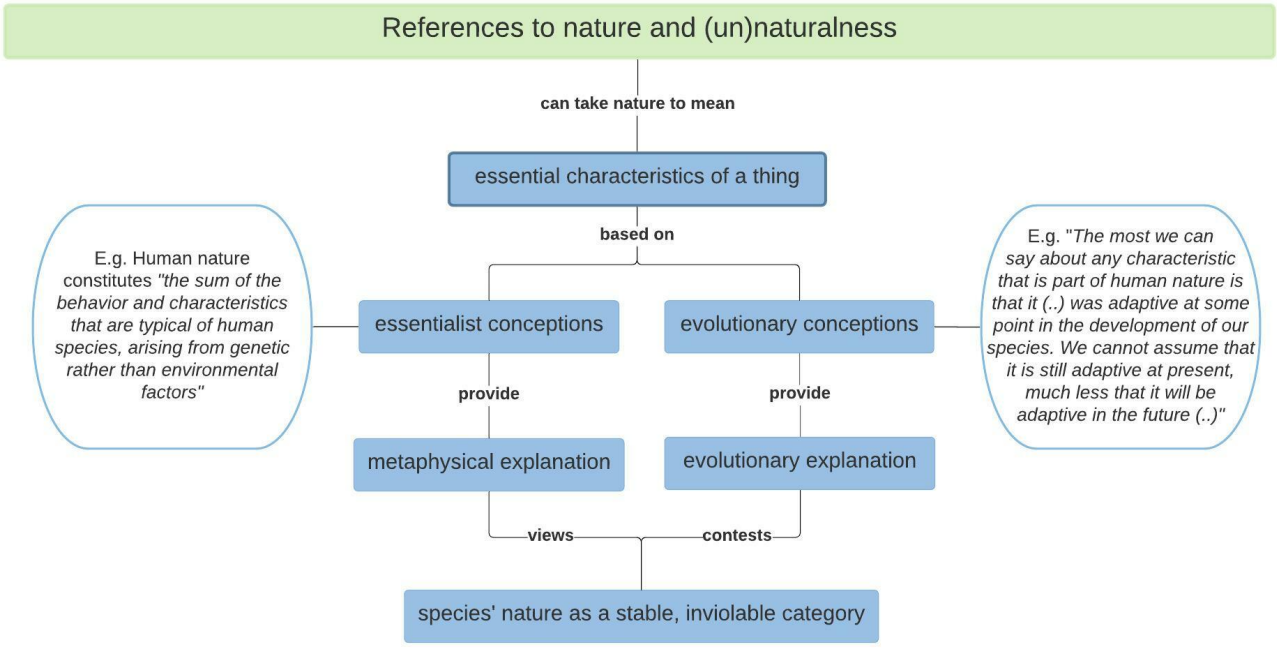
In biology, in contrast, species are understood along evolutionary lines (24). Compared to essentialist conceptions, evolutionary conceptions take a less stringent view of what a species' nature consist of. Rather than viewing a species' nature as an inviolable category that is stable over time and demarcates a particular ontological category, these conceptions distinguish species based on the evolutionary explanations that can be given for how a particular species appeared and persists (24). This conception can for instance be identified in an article by Allan Buchanan on human nature and enhancement, in which he states that if we think of humans in the way evolutionary biologists do:

> *the most we can say about any characteristic that is part of human nature is that it, or some characteristic to which it is tied in the processes of human biological development, was adaptive at some point in the development of our species. We cannot assume that it is still adaptive at present, much less that it will be adaptive in the future or that it is inextricably tied to something that is or will be adaptive* (p. 143-4) (174).

In this view, a species' nature is ever changing as part of evolution; while some traits are essential to an organism – for instance because they safeguard or increase their chance of survival and reproduction – at some point in time, that does not mean that will remain the case.

In sum, a concept of nature as the essential characteristics of a thing can be based on an essentialist or an evolutionary conception of nature. These conceptions are summarized in Figure 6 below.

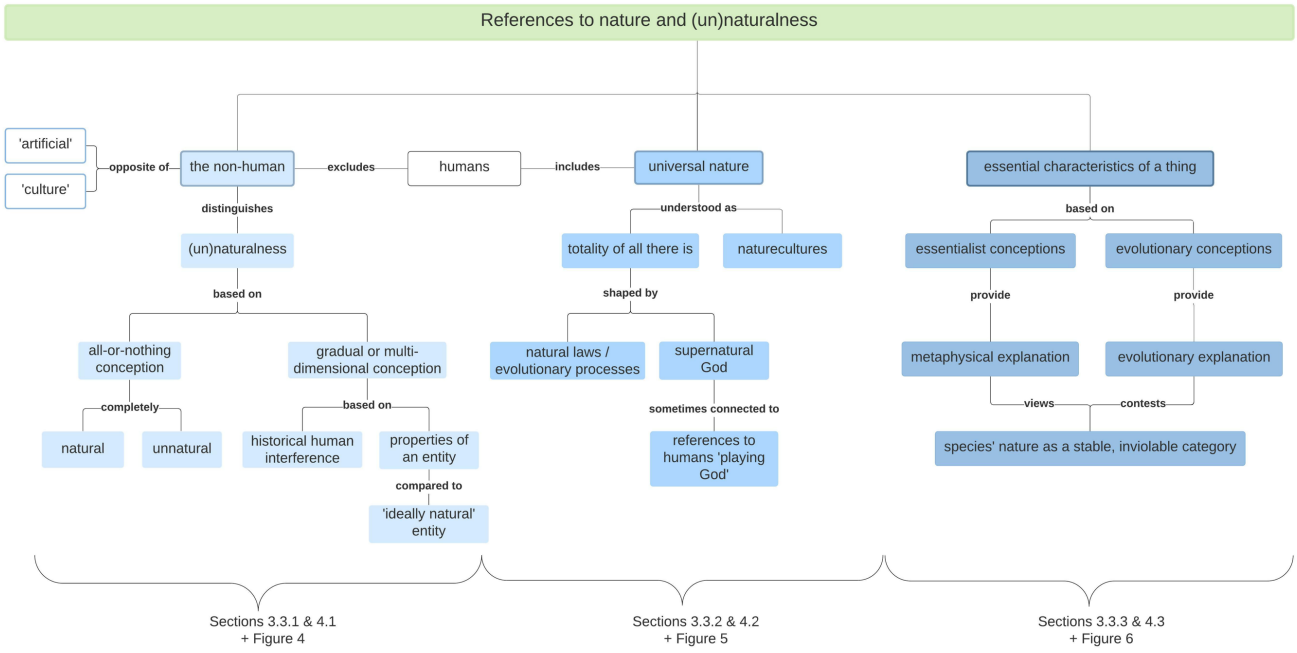
Figure 6: Different conceptions of 'nature as the essential characteristics of a thing'



4.4 Concluding reflections

This chapter has expanded upon the previous chapter and explored the previously identified concepts of (1) nature as the non-human; (2) entangled nature; and (3) nature as the essential characteristics of a thing in more detail. For each of these concepts, different conceptions were identified and similarities and differences between these conceptions were highlighted. An overview of these different concepts and their conceptions is given in Figure 7 below.

Figure 7: Different concepts and conceptions of nature



Reflecting on the analyses in Chapter 2, it was demonstrated that the different meanings identified in the philosophical literature also provided additional insights with regards to the meanings attributed to nature and (un)naturalness in laws, the grey literature, and the scientific literature on genetic modification.

Like was the case for the overarching concepts of nature, distinguishing between these conceptions may help to avoid confusion in discussions about genetic modification. At the same time, this more thorough review of conceptions of naturalness also illustrated that few conceptions of naturalness enable us to distinguish clearly between the natural and unnatural. It also showed that there was a discrepancy in the level of specificity in references to nature and (un)naturalness in the philosophical literature compared to those in laws, the grey literature, and the scientific literature on genetic modification, with the philosophical literature stipulating in more detail what aspects render something (un)natural or part of nature. In the next chapter, we explore a hypothesis that may explain this difference: references to nature and (un)naturalness may not only refer to particular meaning(s) of these terms but may also be a way to spell out certain feelings, emotions and intuitions.

Chapter 5 – Understanding and valuing intuitions related to (un)naturalness

As the previous chapters illustrated, a conceptual analysis can provide insights into different concepts of nature and naturalness that should be distinguished from each other to prevent confusion. Moreover, this analysis underlined that while the ambiguity of the terms nature and naturalness may be reduced, it is unlikely that it can fully be overcome. According to some, this is a reason to dismiss naturalness arguments as morally irrelevant altogether. Guido de Wert, for instance, contends:

> *The argument that 'x is wrong because it is unnatural' can only succeed if there is an interpretation of the term 'unnatural' which enables us both to distinguish clearly between natural and unnatural actions, and to understand what there is about the latter which is morally objectionable. It is doubtful whether there are any such interpretations which are convincing or even plausible* (p. 223) (175).

Arthur Caplan offers a similar critique of arguments based on human nature[20]. He argues:

> *To support their position the [authors that put forward such arguments] must state what human nature is. Despite a great deal of hand-waving about this they do not. (..) And they must advance an argument about why human nature (..) tells us anything about what is good or desirable in terms of the traits humans should possess. They cannot.* (p. 201) (176).

Despite such longstanding critiques, however, these arguments reappear time and again in discussions about emerging technologies and genetic modification.

In what follows we explore one of the factors that may contribute to this persistent use of references to nature and (un)naturalness: these references may also be a way to spell out certain feelings, emotions and intuitions (3,44,158). This may also explain the discrepancy in the level of specificity in references to nature and (un)naturalness in the philosophical versus the non-philosophical literature that was identified in the previous chapter. Whereas philosophical conceptual analyses are specifically focused on the meaning(s) of particular terms, these terms may be used more loosely to spell out certain feelings, emotions and intuitions in other types of literature and discussions.

This chapter investigates this in more detail. It is argued that references to nature and (un)naturalness can be seen as requests for more in-depth discussion exploring the background of feelings, emotions, and intuitions regarding how we should deal with our newfound ability to control what was previously out of our control through genetic modification.

[20] Caplan offers his critique in the context of discussions around enhancement, but it can also be considered relevant to other arguments which invoke this concept of nature.

5.1 Pre-reflective emotions and intuitions about nature and (un)naturalness

As was hypothesized in the previous chapter, references to nature and (un)naturalness can voice various feelings, emotions[21] and intuitions. When it is said something is unnatural, this can also be a way to express disgust and repugnance with the act or creature in question. When this is the case, references to (un)naturalness are considered instances of the so-called 'yuck factor' – an emotional reaction to a violation of a perceived moral order, that we may for instance feel when we see the picture of a mouse with a human ear growing on its back (3). Moreover, references to (un)naturalness can express a feeling of (un)familiarity. According to Frans Brom, arguments related to nature and naturalness emerge in discussions when a new part of reality comes under our control, becomes 'make-able' (p. xi) (44). In his view, these arguments express discomfort with this newfound ability to make and control what was previously given and outside of our control. Brom argues that references to nature and (un)naturalness voice moral intuitions about how this newfound ability should be put to use (142).

Lorraine Daston similarly argues that breaches of the perceived natural order can evoke strong emotive and intuitive responses in which feelings and intellectual judgement about these breaches are intertwined in an unusual way. These emotional and intuitive responses can be so strong that she calls them "*the passions of the unnatural*"[22] (p. 34) (158). Daston contends that these passions are evoked in particular when breaches of the perceived natural order are caused by humans.

Insightful and interesting as this is, inferences of the good from the 'natural' and the bad from the 'unnatural' have been heavily critiqued as they inadvertently derive ought-statements from is-statements. Daston is well aware of this, and her account may in this sense be seen as an explanation rather than a justification of the passions that disturbances of the natural orders evoke. This suggests that these emotions and intuitions cannot simply be taken at face value. So, the question rises, what is the relevance of underlying feelings, emotions, and intuitions in references to nature and (un)naturalness in discussions about genetic modification?

5.2 The relevance of emotions and intuitions in discussions about nature, (un)naturalness and genetic modification

The fact that references to nature and (un)naturalness can be a way to spell out certain feelings, emotions and intuitions has been viewed in different ways. According to some, it is a reason to take such references particularly seriously. Leon Kass, for instance, has argued that repugnance (which he felt in relation to the cloning of humans) "*is the emotional expression of deep wisdom, beyond reason*" (p. 687) (178). In this view, the negative emotions that are sometimes voiced through references to (un)naturalness can be seen as definitive evidence for the morally problematic character of the action or entity in question.

[21] Whether and if so, how, emotions can be differentiated from feelings is a hotly contested issue, that we unfortunately cannot discuss in depth in this report. Amongst a range of different views, some for instance contend that emotions are a class of feelings, whereas others deny that emotions are feelings (187,188). One aspect on which emotions are commonly – yet not by all – believed to differ from emotions, is that emotions are thought to involve cognitions. See e.g. (187) and (188) for more elaborate reflections on this topic.

[22] While Daston does not elaborate on the history of the notion of the 'passions' she mentioned, it may well be that she uses it the same way that David Hume did. Whereas the 'passions' are nowadays frequently understood to be "*feelings of infatuation or excitement*", Hume instead referred to "*a 'perception of the mind' (..) that is deeply and maybe ineradicably within oneself*" (p. 24) (24). He contrasted the passions to 'ideas', perceptions that arise through reason alone, and to immediate sense impressions (24,189).

Others, in stark contrast, have instead considered it to be yet another reason to ban these kinds of arguments from ethical and societal discussions altogether. Wouldn't taking emotions seriously result in a far-reaching type of subjectivism and relativism, in which people could simply state something 'does not feel right' and that would be the end of the story? (24).

While these two conclusions about the value of emotions in moral reasoning are very different, they also share an important feature: they consider feelings, emotions, and intuitions to be the *end* of an ethical inquiry – to, in fact, replace this inquiry altogether. Other authors, in contrast, rather see them as the *start* instead of the end of an ethical evaluation. To the extent that references to (un)naturalness are a way to voice pre-reflective disgust, fear or anger, these emotional responses may rightfully be approached with a degree of skepticism. After all, the fact that something is unfamiliar, or that one has never seen something before, does not mean it is immoral (3,179). Nonetheless, viewing emotions only this way does not do them justice. As Martha Nussbaum has argued, emotions can also be seen as intelligent responses to the perception of value. This does not mean that we should accept emotions uncritically, but rather that we should see them as parts – "*highly complex and messy parts*" (180) – of our moral reasoning.

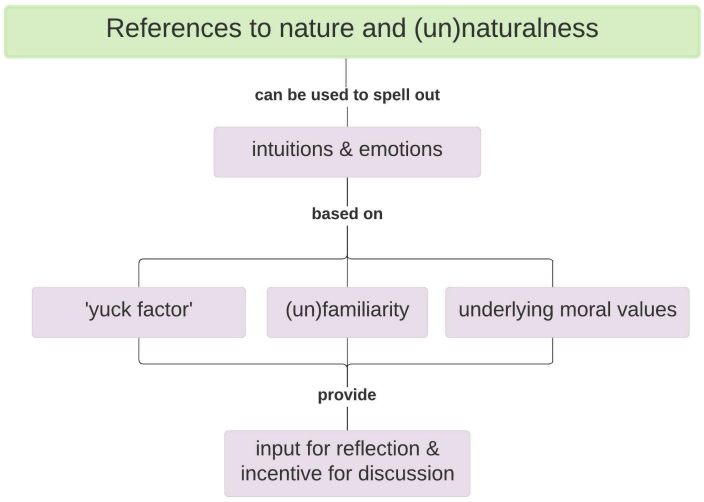
Indeed, the feelings and emotions elicited by breaches of the natural order as well as naturalness arguments more broadly may be viewed as a way to spell out underlying concerns or values. As the analysis of laws and the grey literature on genetic modification that was presented in Chapter 2 illustrated, some references to nature and (un)naturalness indeed explicitly linked (un)naturalness to particular underlying concerns or values with regards to safety and uncertainty, the integrity or intrinsic value of species, or the appropriate attitude or place of humans in nature. A report by the Nuffield Council on Bioethics, similarly, pointed out that references to nature and (un)naturalness in public and political debates about science, technology and medicine are frequently placeholders for other concerns or values (2). The reflections in this chapter, in turn, suggest that intuitions about such and other matters may (also) be present when people do not make them explicit.

Viewing references to (un)naturalness this way has important implications for how these concerns should be approached. While different concepts of nature and naturalness do not allow us to distinguish clearly between the natural and the unnatural and do not provide clear moral guidance, references to nature and (un)naturalness may still be seen as a relevant starting point for discussion. As Gail Davies argues, such statements or discussions need not necessarily "*lead to principled refusal of any new (..) biotechnology*" (p. 432) (181), but can instead lead to a discussion about how we should deal with our newfound ability to control what was previously given and outside of our control (44,142). Rather than merely seeing these arguments as invitations for semantic discussions about what it means for something to be (un)natural or countering them with examples disproving the connection between the natural and the good (or the unnatural and the bad), these arguments can also be seen as requests for more in-depth discussion exploring the background of one's feelings, emotions, and intuitions. In some cases, such discussions may lead the discussants to conclude that the voiced naturalness arguments were indeed based on pre-reflective intuitions that should – upon further consideration and critical reflection – be discredited. In other instances, however, such discussions may bring up relevant underlying moral questions and concerns that bring to light important matters about what it means to be human and what humans should and should not do.

5.3 Concluding reflections

As this short investigation has illustrated, references to nature and (un)naturalness can also be seen as a way to voice feelings, emotions, and intuitions with regards to genetic modification. This is visualized in Figure 8 below. On the one hand, these intuitions may rightfully be approached with a degree of skepticism – they may for instance voice pre-reflective disgust, fear or anger that are caused by mere unfamiliarity. On the other hand, however, these intuitions can also be expressions of the value or importance of underlying moral concerns. Viewing references to (un)naturalness this way has important consequences for how naturalness arguments should be approached. Rather than merely discrediting these arguments on semantic and logical grounds, they can also be explored and investigated in more detail by clarifying, questioning, and discussing potential underlying concerns and values.

Figure 8: Emotions and intuitions about nature and (un)naturalness



This raises an important question: how can the potential underlying concerns that may be at play when people refer to nature or (un)naturalness in the context of genetic modification be reflected upon and brought into discussion? This question will be answered in the next chapter, where we first summarize the final conclusions and implications of this report. Based on the obtained insights, we subsequently formulate a set of questions that may aid in clarifying, examining, and discussing these underlying concerns. We hope this set of questions will help to facilitate critical reflection on one's own stances as well as to provide pointers for a fruitful debate about these issues with others.

Chapter 6 – Final conclusions and implications

References to nature and (un)naturalness play a prominent role in discussions on genetic modification. While these notions are very familiar to us, they are at the same time elusive: it can be hard to grasp what is meant by them, and to understand why these terms pop up in debates about science and technology time and time again. This report aimed to unravel the conceptual and normative complexity of these terms by investigating the use and meaning of nature and (un)naturalness in the literature on genetic modification. In what follows, we discuss the conclusions of our analyses of these matters, reflect on their implications, and formulate recommendations for organizations such as the COGEM.

A first source of the ambiguity of nature and (un)naturalness could be that these terms are used in different ways. To investigate this, we first analyzed the use of nature and (un)naturalness in laws, the grey literature, and scientific literature on genetic modification (Chapter 2). This analysis showed that these terms are sometimes used in value-neutral, and sometimes in value-laden ways. When these terms were used in value-laden ways, they were related to goodness, badness, or to particular underlying concerns or values. Our analysis showed that references to nature and (un)naturalness often brought up underlying concerns or values with regards to (1) safety and uncertainty, (2) the integrity or intrinsic value of the modified entities or (3) the appropriate attitude or role of humans. This analysis also showed that the use of nature and (un)naturalness varied across different contexts. Nature and (un)naturalness were more often used in value-neutral ways in laws and the life science literature, whereas the grey literature, social science literature and ethics literature most often featured value-laden uses. Moreover, nature and (un)naturalness were used in different ways in relation to different applications of genetic modification. Value-laden references to nature and (un)naturalness that linked to the integrity or intrinsic value of the modified entities, for instance, most often concerned applications of genetic modifications in animals and humans, sometimes in plants, and rarely in micro-organisms. This is in line with the general pattern observed in the literature that applications of genetic modification in micro-organisms are regarded more positively than applications of genetic modifications in animals and, to a lesser extent, plants (40–42).

Overall, these findings underline and further specify the conclusion of a report on naturalness by the Nuffield Council on Bioethics which contended that references to nature and (un)naturalness often function as 'placeholders' to convey different values, beliefs, hopes and anxieties (2). To avoid talking past one another in discussions on genetic modification, it is important to be aware of this and to reflect on these underlying values when the terms nature and (un)naturalness are used. Given the identified differences in the use of these terms among different disciplines, it is especially important to be attentive to this in communication between professionals from different disciplines or contexts. Moreover, it is important to be attentive to nuance; different underlying values may be at play for different applications of genetic modification. Organizations such as the COGEM also have an important role to play in identifying whether, when, and which underlying values are at play in references to nature and (un)naturalness, and to contribute to further discussion on these matters. When the COGEM uses these terms in its reports and communication, it should reflect on whether and which values underlie them.

A second source of the ambiguity of nature and (un)naturalness could be that these terms are attributed different meanings. To investigate this, we analyzed the philosophical literature on nature and (un)naturalness to elucidate the different meanings of nature and (un)naturalness (Chapter 3 and 4). This

analysis demonstrated that the natural world is not merely something to be discovered, but also something that is at the same time actively constructed: concepts of nature can represent the reality they refer to in certain ways and selectively in- or exclude specific parts. In this analysis, three key overarching concepts of nature were identified: (1) nature as the non-human; (2) entangled nature; and (3) nature as the essential characteristics of a thing. To understand the meaning of references to nature and naturalness in the debate about genetic modification, these different concepts should be distinguished to avoid confusion and prevent people from talking past each other. This is also important for organizations such as the COGEM; where possible, the COGEM should distinguish between different concept(ion)s of nature and (un)naturalness in its communication and reports on genetic modification.

At the same time, distinguishing between these different meanings does not suddenly render these terms unambiguous. Our analysis also showed that while conceptual analyses of nature and (un)naturalness in the philosophical literature sometimes posit detailed conceptions of what nature and (un)naturalness are taken to mean, references to nature and (un)naturalness in laws, the grey literature, and the scientific literature on genetic modification were often much less specific in this regard. This may be explained by the fact that references to nature and (un)naturalness often voice feelings, emotions, and moral intuitions regarding how we should deal with our newfound ability to control what was previously out of our control through genetic modification (as was reflected upon in Chapter 5). In some cases, this may be based on the so-called 'yuck factor' – a feeling of disgust and repugnance to the violation of a perceived moral order – or a feeling of (un)familiarity. In other cases, our feelings, emotions, and intuitions can also be expressions of underlying moral concerns.

6.1 Reflecting on references to nature and (un)naturalness through a set of questions

All in all, our analyses have identified different sources of ambiguity that may explain why nature has been contended to be the most complex term in the English language (22) and why the terms nature and (un)naturalness are "*at once both very familiar and extremely elusive"* (p. 1) (21). The findings of these analyses have also led to different recommendations regarding how references to nature and (un)naturalness in the context of genetic modification may be approached to avoid confusion and miscommunication.

While these recommendations may help to reduce the ambiguity of nature and naturalness, it is nonetheless improbable that it can fully be overcome. As was mentioned in Chapter 5, some consider this a reason to propose banning related arguments from discussions on genetic modification altogether. In our view, such a strategy is not only highly unlikely to succeed – after all, despite vigorous pleas from opponents, these references continue to pop up time and again in the literature and discussions on genetic modification – but doing so would also constitute throwing out the baby with the bathwater. As the analyses in this report have underlined, nature and (un)naturalness can express relevant underlying values that should be identified, investigated, and brought into discussion rather than pushed to the side. Considerations with regards to safety and uncertainty, the moral status of the modified entities, and the attitude and role that humans should have in nature are essential in carving out how we should deal with our newfound ability to control what was previously out of our control through genetic modification.

In our view, in other words, references to nature and (un)naturalness in the context of genetic modification should be seen as starting points for further reflection and/or discussion of potential

underlying moral questions and concerns. The previous chapters have provided various insights that lead us to formulate a set of questions that can guide reflection and discussion when one encounters a reference to nature or (un)naturalness in literature or discussions on genetic modification (see Figure 9). These questions can be used to reflect upon one's own views on nature and (un)naturalness in the context of genetic modification, to reflect on views expressed in the literature on genetic modification, and to start a conversation with others about this when nature or (un)naturalness are brought up in discussions on genetic modification.

On the one hand, we formulated questions to investigate the intuitions, feelings, and underlying values with regards to nature and (un)naturalness more generally. To get a first impression of one's own or another's thoughts and emotions regarding nature and (un)naturalness, it can be helpful to start by reflecting on what words come to mind when one thinks of nature or (un)naturalness (see Question 1 in Figure 9). These associations can subsequently form the start of further reflections on one's convictions and emotions regarding nature and (un)naturalness in the context of genetic modification. Chapter 2 and 4 also illustrated the importance of reflecting on one's view on nature more generally, such as whether nature is seen as vulnerable, as controllable, as a resource for humans, as something good and pure, or as something evil that causes suffering (see Question 2 in Figure 9). As Chapter 3 and 4 illustrated, an important difference between different concepts of nature relates to whether they consider humans to be part of nature, so it is relevant to reflect on one's own and others' views on this matter (see Question 3 in Figure 9). This also brings up the question what kind of role or attitude humans should have in nature: should they, for instance, be dominators, stewards, or partners of nature (see Question 4 in Figure 9)? Depending on how one sees nature and the role of humans in nature, different kinds of interventions in nature may be considered (im)permissible and (un)necessary (see Question 5 in Figure 9). Finally, as Chapter 3 and 4 underlined, a third concept of nature relates to the essential characteristics of a thing. In that regard, it is relevant to reflect on views regarding whether organisms have a 'nature', a set of essential characteristics that defines them (see Question 6 in Figure 9).

On the other hand, we formulated questions to investigate the intuitions, feelings, and underlying values with regards to the (un)naturalness of a specific application of genetic modification in more depth. To do so, one can start by reflecting upon whether one considers (a specific application of) genetic modification natural or not, and why (see Question 7 in Figure 9). To uncover and discuss potential underlying values, it can be helpful to ask oneself or someone else: 'What intuitions or emotions does the idea of (this application of) genetic modification elicit from you? Why?' (see Question 8 in Figure 9). Once these intuitions and emotions have been identified and reflected upon, additional questions may help to identify potential underlying values or concerns. As Chapter 2 illustrated, references to nature and (un)naturalness often express underlying concerns or values with regards to (1) safety and uncertainty, (2) the integrity or intrinsic value of the modified entities or (3) the appropriate attitude or role of humans. These underlying values may be investigated in more detail by asking questions about these issues (see Questions 9, 10 and 11 in Figure 9).

Figure 9: a set of questions to provide starting points for further discussion in response to references to nature and (un)naturalness

General questions about nature and (un)naturalness

1. What comes to mind when you think of naturalness or unnaturalness? And what comes to mind when you think of nature?
2. How do you view nature?
    - Do you, for instance, see it as vulnerable, controllable, a resource for humans, as something good and pure, or something evil that causes suffering?
3. Do you consider humans to be part of nature? Why or why not?
4. What role should humans have in nature? Why?
    - Should humans, for instance, be dominators, stewards, or partners of nature? Why?
5. Do you consider particular interventions in nature impermissible?
    - If so, which ones and why?
    - If not, why not?
6. Do you think (particular) organisms have a 'nature', a set of essential characteristics that defines them? Do you, for instance, think there is something such as 'human nature'?
    - If so, what does it consist of? How does that affect your views on what kinds of interventions are (im)permissible?
    - If not, why not?

Questions with regards to the (un)naturalness of (specific applications) of genetic modification

7. Do you consider (a specific application of) genetic modification natural or unnatural? Why?
8. What intuitions or emotions does the idea of (this application of) genetic modification elicit from you? Why?
9. How do you view the risks or uncertainty of (this application of) genetic modification? Why?
    - If there are any risks you are particularly concerned about, which ones and why?
10. How do you view the impact of (a specific application) of genetic modification on the organisms that are genetically modified or the way they are treated if they are genetically modified? Why?
11. Do you consider (a specific application of) genetic modification in line with the attitude or role that humans should have towards/in nature? Why or why not?

While this report was specifically focused on genetic modification, its findings are also relevant for other contexts. References to nature and (un)naturalness are, after all, common in relation to many – or maybe even all – biotechnological developments. The relevance of this analysis in other contexts is for instance underlined by the current COVID-19 pandemic, where references to nature and (un)naturalness also feature frequently[23]. Of course, the literature on genetic modification as well as the literature on nature and (un)naturalness is vast, and much more could be said about what has been described in this report. Nonetheless, this report has provided various key insights and concrete suggestions regarding how to approach references to nature and (un)naturalness in discussions about genetic modification and beyond.

[23] See for instance (190–192).

Overall, we hope the report allows those with different views and opinions on genetic modification to investigate their own and others' stances on genetic modification, nature and (un)naturalness in more detail. After all – to paraphrase Christopher Preston – if there was ever a time when it was important to think hard about nature and its relationship to genetic modification, that time is now (p. 162) (1).

Acknowledgements

We would like to thank the steering committee consisting of Paul Struik (chair), Marjan Bovers, Clemens Driessen, Tessa Lange, Lonneke Poort, Marthe Smedinga, Cécile van der Vlugt-Bergmans and Arend Jan Waarlo for their helpful feedback on earlier versions of this report. Moreover, we would like to thank Frans Brom, Niels Geijsen, John van de Oost, Dirk Stemerding and Kees Zoeteman for checking and complementing the list of scientific articles that were included in that subanalysis. Similarly, we would like to thank Frank Meijboom for interesting previous discussions on nature and (un)naturalness, and Jan Vorstenbosch for generously sharing various paper copies of reports and PhD theses that were not digitally available and that turned out to be very relevant for this project. Last but not least, we would like to express our gratitude to Jannieke Simons. During her internship at the department of Medical Humanities (UMC Utrecht) she was not only a cheerful colleague, but also conducted helpful preliminary investigations regarding references to nature and (un)naturalness in the scientific literature. She also designed the first version of some of the concept maps that feature in this report.

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Appendix 1 – Analysis of the positive law

Dutch positive law is partly of national and partly of international origin. With regard to the latter, we have focused on binding United Nations treaties, binding treaties of the Council of Europe (CoE) as well as CoE recommendations, and European Union (EU) legislation (regulations, directives and decisions). Nationally, the focus was on legislation and regulation (up to ministerial decrees).

Legal sources were found by using wetten.nl, EUR Lex and coe.int. The first website provides access to positive law ranging from all treaties to which the Netherlands is a party to ministerial decrees. Relevant sources were found by using 'natuurlijkheid', (on)natuurlijk(e)', 'natuur', 'genetisch(e)', 'gemodificeerd(e)' and 'modificatie' as key words. The website is in Dutch. EUR Lex was used to find EU regulations, directives and decisions. Since EUR Lex is accessible for all EU languages, the same Dutch key words were used.

Coe.int is the CoE portal, which was used to find relevant Recommendations. Since this website is not accessible in Dutch, 'naturalness', '(un)natural(ly)', 'nature', 'genetic(al)', 'genetical(ly)', 'modified' and 'modification' were used as key words. All CoE treaties to which the Netherlands is a party, can be found used by wetten.nl. Since there were no relevant CoE treaties, coe.int was used to see whether the key words appeared in (non-binding) Recommendations of the CoE's Committee of Ministers.

Relevant legal sources were identified by using 'genetisch(e)', 'gemodificeerd(e)' and 'modificatie' ('genetic(al)', 'genetical(ly)', 'modified' and 'modification') for each databank. The identified relevant legal sources were subsequently scanned by using 'natuurlijkheid', ('(on)natuurlijk(e)' and 'natuur' ('naturalness', '(un)natural(ly)' and 'nature'). Although these latter are used abundantly in non-relevant legal sources, their use is relatively rare in relevant ones.

On April 1st 2021, 'natuurlijkheid' ('naturalness') did not appear in relevant national legislation and regulation nor was it found in relevant treaties. It did, however, appear 47 times in relevant EU legislation and 95 times in relevant Council of Europe documents, only two of which were Recommendations. '(On)natuurlijk(e)' ('(un)natural(ly)') on the other hand, did appear 33 times in relevant national legislation and regulation, only once in relevant treaty law, 2.123 times in relevant Council of Europe documents and 2.061 times in relevant EU legislation. Finally, 'natuur' ('nature') was found 6 times in relevant national laws, 3.591 times in relevant Council of Europe documents and 449 times in relevant EU legislation. It did not appear in relevant treaties.

In addition, we also analyzed rulings by Dutch national courts, the Court of Justice of the European Union and the European Court of Human Rights, using the same key words. The rulings were found by using rechtspraak.nl, Curia and HUDOC. It should be remembered that not all rulings of Dutch courts of law are published on rechtspraak.nl. Only those rulings that meet the requirements of the Besluit selectiecriteria uitsprakendatabank rechtspraak.nl 2012 are published in this way. We found 5 relevant rulings by Dutch courts of law and 9 by the Court of Justice of the European Union.

Appendix 2 – Analysis of the grey literature

For the analysis of the grey literature, an initial list of relevant organizations was identified by the research team and the steering committee, which included the following organizations:

Dutch organizations
Centrum voor Bio-ethiek en Gezondheidsrecht
Commissie Genetische Modificatie (COGEM; Commission on Genetic Modification)
Commissie van Advies Ethiek en Biotechnologie bij Dieren
Denktank Respectvolle Landbouw
Nederlandse Organisatie voor Technologisch Aspecten onderzoek (NOTA)
Nederlandse Vereniging voor Bioethiek (NVBe)
Raad voor Dieraangelegenheden (RDA)
Rathenau Instituut
Wetenschappelijke Raad voor Regeringsadvies (WRR)

International organizations
ETC group
Friends of the Earth
GeneWatch
GM Watch
Greenpeace
Nuffield Council on Bioethics
World Health Organization

Subsequently, all (online) reports of these organizations were screened to identify reports on genetic modification. Where relevant, reports that predominantly focused on biotechnology, synthetic biology, cloning, and organic farming were also included for analysis.

Next to this, the database of the National Library of the Netherlands ('Koninklijke bibliotheek') was searched to identify additional relevant reports using the search terms 'genetic modification', 'genetic manipulation', 'genome editing', 'cloning' and 'synthetic biology' (in Dutch and English). Moreover, screening of the reference lists of included articles – so-called 'snowballing – also yielded several relevant reports. We focused on reports that were published in Dutch[24] and English. The included reports were published between 1976 and 2021.

Subsequently, the references to nature and (un)naturalness were analyzed and contrasted in more detail. In doing so, we identified whether these terms were used in value neutral or value-laden ways, and clustered references that were similar in terms of the context in which these references were brought up. This clustering was an iterative process in which the clusters or categories of different uses were re-evaluated and adjusted various times.

[24] In this report, all quotations from Dutch reports were translated to English by the authors.

Appendix 3 – Analysis of the scientific literature

Given the large amount of scientific literature that exists on genetic modification, the analysis of the scientific literature inevitably had to be limited to a sample of the scientific literature. This literature was selected based on input from the research team, the steering committee, and several experts on the scientific literature on genetic modification (Frans Brom, Niels Geijsen, John van de Oost, Dirk Stemerding and Kees Zoeteman).

As anchor points, we used a list of key moments that were expected to have stimulated the discussion on genetic modification, namely (in chronological order): Asilomar, Genentech, GM crops, gene therapy, Dolly sheep, Herman bull, Mitochondrial Replacement Therapy (MRT), synthetic biology (e.g. the production of artemisinin and vanillin, cultured meat (e.g. the Impossible burger), germline modification, gene drives, epigenome editing, and the European Court's ruling on modern mutagenesis techniques.

The following criteria were used as inclusion criteria: the articles had to (1) concern one of the stipulated key moments; (2) contain the term(s) nature, (un)natural and/or (un)naturalness; and (3) be written in Dutch or English. Both review articles about the key moments and original primary research articles in which the key moments were described were included. Where relevant, cross-referencing was used to include additional relevant references by screening the reference lists of included articles. Inclusion of articles was ended when saturation was reached, i.e. when screening additional articles no longer yielded novel uses of nature and (un)naturalness.

The identified references to nature and (un)naturalness were analyzed and contrasted in more detail. In doing so, we identified whether these terms were used in value neutral or value-laden ways, and clustered references that were similar in terms of the context in which these references were brought up. This clustering was an iterative process in which the clusters or categories of different uses were re-evaluated and adjusted several times. In doing so, differences and similarities between references to nature and (un)naturalness in life science, social science and ethics articles were also identified.